From:	Marks, Gilbert (OS/ASPR/BARDA) (CTR) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=449EDC5BC9594EB287C4C4B9123551C9-MARKS, GILB <Gilbert.Marks@hhs.gov>
To:	Disbrow, Gary (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0fd5845defda4dc0bb45f8fac629cf09-Disbrow, Ga <Gary.Disbrow@hhs.gov>; Lambert, Linda (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ce6824b6a92a4a4e893ea7b54e17eb3c-Lambert, Li <Linda.Lambert@hhs.gov>; Bright, Rick (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=53034752f35a4317aa74f46348442d39-Bright, Ric <Rick.Bright@hhs.gov>
CC:	Walker, Robert (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7a02e128c60f4a7195532a1545af9556-Walker, Rob <Robert.Walker@hhs.gov>
Subject:	FW: Published today in one of my journals
Date:	2020/04/09 20:34:45
Priority:	Normal
Type:	Note

fysa

From: Buchman, Tim (OS/ASPR/BARDA) (CTR) <Tim.Buchman@hhs.gov>
Sent: Thursday, April 9, 2020 3:52 PM
To: Risi, George (OS/ASPR/BARDA) <George.Risi@hhs.gov>; Erlandson, Karl (OS/ASPR/BARDA) <Karl.Erlandson@hhs.gov>; Walker, Robert (OS/ASPR/BARDA) <Robert.Walker@hhs.gov>; Marks, Gilbert (OS/ASPR/BARDA) (CTR) <Gilbert.Marks@hhs.gov>
Cc: Sciarretta, Kimberly (OS/ASPR/BARDA) <Kimberly.Sciarretta@hhs.gov>; Pennini, Meghan (OS/ASPR/BARDA) <Meghan.LoftusPennini@hhs.gov>; Wax, Marie (OS/ASPR/BARDA) (CTR) <Marie.Wax@hhs.gov>; Woodbury, Robyn (OS/ASPR/BARDA) (CTR) <Robyn.Woodbury@hhs.gov>; Simpson, Steven (OS/ASPR/BARDA) (CTR) <Steven.Simpson@hhs.gov>
Subject: RE: Published today in one of my journals

As promised…

https://journals.lww.com/ccejournal/Fulltext/2020/04000/Fact_Versus_Science_Fiction__Fighting_Coronavirus.15.aspx

Timothy G. Buchman, PhD, MD
Senior Advisor
IPA to the DRIVe (Division of Research, Innovation and Ventures)
Biomedical Advanced Research and Development Authority (BARDA)
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200 C St SW
Washington, DC 20024
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"Note: This email is intended to provide information and is not to be taken as a directive. If the recipient(s) believe(s) the information provided herein may be construed as a directive, the recipient(s) should disregard that portion of the email."

From: Risi, George (OS/ASPR/BARDA) <George.Risi@hhs.gov>
Sent: Wednesday, April 8, 2020 10:58 AM
To: Buchman, Tim (OS/ASPR/BARDA) (CTR) <Tim.Buchman@hhs.gov>; Erlandson, Karl (OS/ASPR/BARDA) <Karl.Erlandson@hhs.gov>; Walker, Robert (OS/ASPR/BARDA) <Robert.Walker@hhs.gov>; Marks, Gilbert (OS/ASPR/BARDA) (CTR) <Gilbert.Marks@hhs.gov>
Cc: Sciarretta, Kimberly (OS/ASPR/BARDA) <Kimberly.Sciarretta@hhs.gov>; Pennini, Meghan (OS/ASPR/BARDA) <Meghan.LoftusPennini@hhs.gov>; Wax, Marie (OS/ASPR/BARDA) (CTR) <Marie.Wax@hhs.gov>; Woodbury, Robyn (OS/ASPR/BARDA) (CTR) <Robyn.Woodbury@hhs.gov>; Simpson, Steven (OS/ASPR/BARDA) (CTR) <Steven.Simpson@hhs.gov>
Subject: RE: Published today in one of my journals

Well done. Thanks. the HCQ letter should be interesting.

From: Buchman, Tim (OS/ASPR/BARDA) (CTR) <Tim.Buchman@hhs.gov>
Sent: Wednesday, April 8, 2020 10:49 AM
To: Erlandson, Karl (OS/ASPR/BARDA) <Karl.Erlandson@hhs.gov>; Risi, George (OS/ASPR/BARDA) <George.Risi@hhs.gov>; Walker, Robert (OS/ASPR/BARDA) <Robert.Walker@hhs.gov>; Marks, Gilbert (OS/ASPR/BARDA) (CTR) <Gilbert.Marks@hhs.gov>
Cc: Sciarretta, Kimberly (OS/ASPR/BARDA) <Kimberly.Sciarretta@hhs.gov>; Pennini, Meghan (OS/ASPR/BARDA) <Meghan.LoftusPennini@hhs.gov>; Wax, Marie (OS/ASPR/BARDA) (CTR) <Marie.Wax@hhs.gov>; Woodbury, Robyn (OS/ASPR/BARDA) (CTR) <Robyn.Woodbury@hhs.gov>; Simpson, Steven (OS/ASPR/BARDA) (CTR) <Steven.Simpson@hhs.gov>
Subject: Published today in one of my journals

<< File: Misinformation_During_the_Coronavirus_Disease_2019.8.pdf >>

Attached is the first of the misinformation pieces that will be coming out in one of the journals I edit.
There is a fairly scathing letter to the editor about HCQ that will come out tomorrow.
There is also a piece already out a few items about neuro complications of severe viral contagions.
More are in the pipieline.

www.ccejournal.org

TGB

Timothy G. Buchman, PhD, MD
Senior Advisor
IPA to the DRIVe (Division of Research, Innovation and Ventures)
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Office of Assistant Secretary for Preparedness and Response (ASPR)
U.S. Department of Health and Human Services (HHS)
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200 C St SW
Washington, DC 20024
Cell: (b)(6)
Email: Tim.Buchman@hhs.gov

"Note: This email is intended to provide information and is not to be taken as a directive. If the recipient(s) believe(s) the information provided herein may be construed as a directive, the recipient(s) should disregard that portion of the email."

Sender:	Marks, Gilbert (OS/ASPR/BARDA) (CTR) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=449EDC5BC9594EB287C4C4B9123551C9-MARKS, GILB <Gilbert.Marks@hhs.gov>
Recipient:	Disbrow, Gary (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0fd5845defda4dc0bb45f8fac629cf09-Disbrow, Ga <Gary.Disbrow@hhs.gov>; Lambert, Linda (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ce6824b6a92a4a4e893ea7b54e17eb3c-Lambert, Li <Linda.Lambert@hhs.gov>; Bright, Rick (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=53034752f35a4317aa74f46348442d39-Bright, Ric <Rick.Bright@hhs.gov>; Walker, Robert (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7a02e128c60f4a7195532a1545af9556-Walker, Rob <Robert.Walker@hhs.gov>
Sent Date:	2020/04/09 20:34:44
Delivered Date:	2020/04/09 20:34:45

From:	Houchens, Christopher (OS/ASPR/BARDA) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7AC94A574BD04528B7C91BBD61893975-HOUCHENS, C <Christopher.Houchens@hhs.gov>
To:	Bright, Rick (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=53034752f35a4317aa74f46348442d39-Bright, Ric <Rick.Bright@hhs.gov>
CC:	Ventura, Christy (OS/ASPR/BARDA) (CTR) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=9bb949caca464329823ca3cf77654a06-Ventura, Ch <Christy.Ventura@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0851e89240324306b78740a4a60745e2-Johnson, Ro <Robert.Johnson@hhs.gov>; Blatner, Gretta (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=623cb123c2324236b1db6fb9153e0bbf-Blatner, Gr <Gretta.Blatner@hhs.gov>; Oshansky, Christine (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d7bd764440b44b06af644cdcd22e42d6-Oshansky, C <Christine.Oshansky@hhs.gov>; Boucher, David (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=41293945651d475fa0413062a819aac5-Boucher, Da <David.Boucher@hhs.gov>
Subject:	RE: TPs
Date:	2020/03/25 22:53:06
Priority:	Normal
Type:	Note

Rick – One more update…

Yesterday Regeneron opened 11 new clinical sites and dosed 35 new patients with an antibody-based therapy in a single day. To date, 31 total sites have been opened and 120 total patients have been dosed. Five new sites are expected to open today.

From: Houchens, Christopher (OS/ASPR/BARDA)
Sent: Wednesday, March 25, 2020 10:02 PM
To: Bright, Rick (OS/ASPR/BARDA) <Rick.Bright@hhs.gov>; Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>
Cc: Ventura, Christy (OS/ASPR/BARDA) (CTR) <Christy.Ventura@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) <Robert.Johnson@hhs.gov>; Oshansky, Christine (OS/ASPR/BARDA) <Christine.Oshansky@hhs.gov>; Boucher, David (OS/ASPR/BARDA) <David.Boucher@hhs.gov>
Subject: RE: TPs

Adding Gretta here.

From: Houchens, Christopher (OS/ASPR/BARDA)
Sent: Wednesday, March 25, 2020 9:31 PM
To: Bright, Rick (OS/ASPR/BARDA) <Rick.Bright@hhs.gov>
Cc: Ventura, Christy (OS/ASPR/BARDA) (CTR) <Christy.Ventura@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) <Robert.Johnson@hhs.gov>; Oshansky, Christine (OS/ASPR/BARDA)

<Christine.Oshansky@hhs.gov>; Boucher, David (OS/ASPR/BARDA) <David.Boucher@hhs.gov>
Subject: RE: TPs

Rick – One edit to my clarifying response to the very last issue. Chris

Is the blood collecting today the same as yesterday? This is different. Today's was about convalescent serum, this is about obtaining COVID-19 patient samples that may be used for isolating antibody producing cells from infected patients and other efforts critical to MCM development

---

From: Houchens, Christopher (OS/ASPR/BARDA)
Sent: Wednesday, March 25, 2020 9:28 PM
To: Bright, Rick (OS/ASPR/BARDA) <Rick.Bright@hhs.gov>
Cc: Ventura, Christy (OS/ASPR/BARDA) (CTR) <Christy.Ventura@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) <Robert.Johnson@hhs.gov>; Oshansky, Christine (OS/ASPR/BARDA) <Christine.Oshansky@hhs.gov>; Boucher, David (OS/ASPR/BARDA) <David.Boucher@hhs.gov>
Subject: RE: TPs

Rick,

Thanks Chris. These are great but eerily similar to todays. There was not a lot that was reported today from those that reported (only three reported). I have emphasized to the TF that criticality of reporting out daily but I can only report what is provided to me. I will emphasize this again tomorrow at my daily MCM TF leadership meeting and it would be very helpful if you are able to do the same if you can attend.

Except the moderna number has gone down. Something switched with numbers. This shows the challenge that we have had getting the data from WGs (which give one number) and agencies (which give another). This is why I am hoping that a more streamlined, top-down reporting approach that I described earlier to you will improve the process.

What's status of the NIH RCt for chloroquine? Hydroxychloroquine? The NIAID HCQ/CQ study is being run by ACTG. They met earlier this week to discuss the protocol. Hilary said today that there is nothing that can be reported at this time.

Status of Genentech Il-6 study? The IL-6R Ab study has not yet started.

Status of remdesivir manufacturing? I will ask Mike A. I do not know.

Is the blood collecting today the same as yesterday? This is different. Today's was about convalescent serum, this is about obtaining COVID-19 patient samples that may be used for isolating antibody producing cells from infected patients and other efforts critical to MCM development

---

From: Bright, Rick (OS/ASPR/BARDA) <Rick.Bright@hhs.gov>
Sent: Wednesday, March 25, 2020 8:59 PM

To: Houchens, Christopher (OS/ASPR/BARDA) <Christopher.Houchens@hhs.gov>
Cc: Ventura, Christy (OS/ASPR/BARDA) (CTR) <Christy.Ventura@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) <Robert.Johnson@hhs.gov>; Oshansky, Christine (OS/ASPR/BARDA) <Christine.Oshansky@hhs.gov>; Boucher, David (OS/ASPR/BARDA) <David.Boucher@hhs.gov>
Subject: Re: TPs

Thanks Chris. These are great but eerily similar to todays. Except the moderna number has gone down. Something switched with numbers.

What's status of the NIH RCt for chloroquine? Hydroxychloroquine?

Status of Genentech Il-6 study?

Status of remdesivir manufacturing?

Is the blood collecting today the same as yesterday?

Sent from my iPhone

On Mar 25, 2020, at 8:25 PM, Houchens, Christopher (OS/ASPR/BARDA) <Christopher.Houchens@hhs.gov>wrote:

Rick – Please see attached and below. Trying a new format here. TPs are below and on page 1. More details of all other activities are on following pages. Chris

Agencies reporting: BARDA, NIAID, DoD
Agencies not reporting: FDA, CDC, DHS, USDA

- NIAID multi-center, multi-country, multi-arm adaptive RCT with remdesivir
- 28 sites (24 US, 4 global)
- 113/440 enrolled (101 US, 12 global)

- Moderna mRNA-1273 vaccine: 19/45 healthy volunteers vaccinated as of 03/25/2020
- 15 subjects in cohort 1 (25mcg) completed
- 4 sentinel subjects in cohort 2 (100mcg) vaccinated
- 4 sentinel subjects in cohort 3 (250mcg) will be vaccinated following completion of cohort 2

- Blood samples are being collected from infected patients in Washington, DC and Hawaii. These blood samples are being provided to scientists and may contain antibody producing cells that can be used to make new therapies. (Note: This study is being supported by NIAID VRC)

Christopher Houchens, PhD
Director (Acting) Division of CBRN Countermeasures
Biomedical Advanced Research and Development Authority (BARDA)

Office of Assistant Secretary for Preparedness and Response (ASPR)
Department of Health and Human Services (DHHS)
Office: 202-205-3633
BB: (b)(6)
Christopher.houchens@hhs.gov

<MCM Task Force Update_03262020_v3.docx>

Sender:	Houchens, Christopher (OS/ASPR/BARDA) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7AC94A574BD04528B7C91BBD61893975-HOUCHENS, C <Christopher.Houchens@hhs.gov>
Recipient:	Bright, Rick (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=53034752f35a4317aa74f46348442d39-Bright, Ric <Rick.Bright@hhs.gov>; Ventura, Christy (OS/ASPR/BARDA) (CTR) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=9bb949caca464329823ca3cf77654a06-Ventura, Ch <Christy.Ventura@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0851e89240324306b78740a4a60745e2-Johnson, Ro <Robert.Johnson@hhs.gov>; Blatner, Gretta (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=623cb123c2324236b1db6fb9153e0bbf-Blatner, Gr <Gretta.Blatner@hhs.gov>; Oshansky, Christine (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d7bd764440b44b06af644cdcd22e42d6-Oshansky, C <Christine.Oshansky@hhs.gov>; Boucher, David (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=41293945651d475fa0413062a819aac5-Boucher, Da <David.Boucher@hhs.gov>
Sent Date:	2020/03/25 22:53:05
Delivered Date:	2020/03/25 22:53:06

From:	Merkeley, Tyler (OS/ASPR/BARDA) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=USERF1F9626F <Tyler.Merkeley@hhs.gov>
To:	Bright, Rick (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=53034752f35a4317aa74f46348442d39-Bright, Ric <Rick.Bright@hhs.gov>
Subject:	Re: Clinical Trial - BARDA lead for chloroquine/hydroxychloroquine
Date:	2020/03/24 21:36:52
Priority:	Normal
Type:	Note

Sounds good. Let me know what time
I have a small team that is now meeting each morning at 8am

Get Outlook for iOS
From: Bright, Rick (OS/ASPR/BARDA) <Rick.Bright@hhs.gov>
Sent: Tuesday, March 24, 2020 9:05:13 PM
To: Merkeley, Tyler (OS/ASPR/BARDA) <Tyler.Merkeley@hhs.gov>
Subject: Re: Clinical Trial - BARDA lead for chloroquine/hydroxychloroquine

Sorry it took me long. Been slammed and just seeing emails in many areas. And falling asleep already. Today was insane.

Tomorrow we need to talk about RISTORE. I've put a lot of thought into it. Have a call with global good for lost cost dipstick. Readable by smartphone. Beamed to HC provider. Confidence to go back outside.

Thank you Tyler. Rick

Sent from my iPhone

On Mar 24, 2020, at 8:52 PM, Merkeley, Tyler (OS/ASPR/BARDA) <Tyler.Merkeley@hhs.gov>wrote:

Roger
That's why i asked
Thanks Tyler

Get Outlook for iOS
From: Bright, Rick (OS/ASPR/BARDA) <Rick.Bright@hhs.gov>
Sent: Tuesday, March 24, 2020 8:48:47 PM
To: Merkeley, Tyler (OS/ASPR/BARDA) <Tyler.Merkeley@hhs.gov>
Cc: Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) <Robert.Johnson@hhs.gov>
Subject: Re: Clinical Trial - BARDA lead for chloroquine/hydroxychloroquine

No press on this just yet. Lots of moving parts on it today that need to settle out tomorrow. Fantastic that the team is now performing miracles. But please hold the media for a bit. This one is a little tricky. Thank you all for understanding.

I definitely want to all to get credit and visibility for miracles. And we will. Just a little pause on media for a minute though.

Thank you all. Rick.

On Mar 24, 2020, at 8:43 PM, Merkeley, Tyler (OS/ASPR/BARDA) <Tyler.Merkeley@hhs.gov>wrote:

Rick

Need an answer from you please on the below. Team is Deferring to you
We made an award to PPD today for the Expanded Access
Protocol for chloroquine/hydroxychloroquine that BARDA is running.

Are we going to want a comms package and web announcement around this effort. Before I start the process I just want to confirm since this is a unique situation. I am assuming yes but would like to confirm

Thanks

Tyler

Get Outlook for iOS
From: Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>
Sent: Tuesday, March 24, 2020 8:07 PM
To: Merkeley, Tyler (OS/ASPR/BARDA)
Cc: Johnson, Robert (OS/ASPR/BARDA)
Subject: Re: Clinical Trial - BARDA lead for chloroquine/hydroxychloroquine

Tyler
Please ask Rick. I am not certain how much press we want beyond the WH and HHS press releases that will go out

Sent from my iPhone

On Mar 24, 2020, at 8:03 PM, Merkeley, Tyler (OS/ASPR/BARDA) <Tyler.Merkeley@hhs.gov>wrote:

Just want to put this at top of your box again. Know your busy.
I just saw award to PPD. Should I start comms process or are we going to pass on this?

Get Outlook for iOS
From: Merkeley, Tyler (OS/ASPR/BARDA) <Tyler.Merkeley@hhs.gov>
Sent: Tuesday, March 24, 2020 3:17 PM
To: Disbrow, Gary (OS/ASPR/BARDA) (Gary.Disbrow@hhs.gov); Johnson, Robert (OS/ASPR/BARDA)
Cc: Bright, Rick (OS/ASPR/BARDA) (Rick.Bright@hhs.gov); Blatner, Gretta (OS/ASPR/BARDA)
Subject: Clinical Trial - BARDA lead for chloroquine/hydroxychloroquine

Gary and Robert

I learned today we are leading the Expanded Access Protocol for chloroquine/hydroxychloroquine that BARDA is running.
Are we going to want a comms package and web announcement around this effort. Before I start the process I just want to confirm since this is a unique situation. I am assuming yes

Thanks

Tyler

TYLER G. MERKELEY
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MedicalCounterMeasures.gov
DRIVe.HHS.gov

Sender: Merkeley, Tyler (OS/ASPR/BARDA) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=USERF1F9626F <Tyler.Merkeley@hhs.gov>

Recipient:	Bright, Rick (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=53034752f35a4317aa74f46348442d39-Bright, Ric <Rick.Bright@hhs.gov>
Sent Date:	2020/03/24 21:36:51
Delivered Date:	2020/03/24 21:36:52

From:	Faison, Tremel (OS/ASPR/BARDA) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=2BBAB0BCEB1342FBBEDBBCC94DEEB80F-FAISON, TRE <Tremel.Faison@hhs.gov>
To:	Lambert, Linda (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ce6824b6a92a4a4e893ea7b54e17eb3c-Lambert, Li <Linda.Lambert@hhs.gov>; Blatner, Gretta (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=623cb123c2324236b1db6fb9153e0bbf-Blatner, Gr <Gretta.Blatner@hhs.gov>; Walker, Robert (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7a02e128c60f4a7195532a1545af9556-Walker, Rob <Robert.Walker@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0851e89240324306b78740a4a60745e2-Johnson, Ro <Robert.Johnson@hhs.gov>; Oshansky, Christine (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d7bd764440b44b06af644cdcd22e42d6-Oshansky, C <Christine.Oshansky@hhs.gov>; Houchens, Christopher (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7ac94a574bd04528b7c91bbd61893975-Houchens, C <Christopher.Houchens@hhs.gov>
CC:	Disbrow, Gary (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0fd5845defda4dc0bb45f8fac629cf09-Disbrow, Ga <Gary.Disbrow@hhs.gov>; Bright, Rick (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=53034752f35a4317aa74f46348442d39-Bright, Ric <Rick.Bright@hhs.gov>
Subject:	RE: FOR REVIEW: Policy Options for Release of SNS-Held Chloroquine and Hydroxychloroquine
Date:	2020/04/08 15:23:47
Priority:	Normal
Type:	Note

I have no additional comments.

Tremel

From: Lambert, Linda (OS/ASPR/BARDA) <Linda.Lambert@hhs.gov>
Sent: Wednesday, April 8, 2020 3:21 PM
To: Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>; Walker, Robert (OS/ASPR/BARDA) <Robert.Walker@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) <Robert.Johnson@hhs.gov>; Faison, Tremel (OS/ASPR/BARDA) <Tremel.Faison@hhs.gov>; Oshansky, Christine (OS/ASPR/BARDA) <Christine.Oshansky@hhs.gov>; Houchens, Christopher (OS/ASPR/BARDA) <Christopher.Houchens@hhs.gov>
Cc: Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Bright, Rick (OS/ASPR/BARDA) <Rick.Bright@hhs.gov>
Subject: RE: FOR REVIEW: Policy Options for Release of SNS-Held Chloroquine and Hydroxychloroquine

Gretta,
I reviewed the options paper and do not have any edits.
Linda

Linda C. Lambert, PhD
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Biomedical Advanced Research and Development Authority (BARDA)
Assistant Secretary for Preparedness and Response (ASPR)
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From: Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>
Sent: Wednesday, April 8, 2020 12:06 PM
To: Walker, Robert (OS/ASPR/BARDA) <Robert.Walker@hhs.gov>; Lambert, Linda (OS/ASPR/BARDA) <Linda.Lambert@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) <Robert.Johnson@hhs.gov>; Faison, Tremel (OS/ASPR/BARDA) <Tremel.Faison@hhs.gov>; Oshansky, Christine (OS/ASPR/BARDA) <Christine.Oshansky@hhs.gov>; Houchens, Christopher (OS/ASPR/BARDA) <Christopher.Houchens@hhs.gov>
Cc: Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Bright, Rick (OS/ASPR/BARDA) <Rick.Bright@hhs.gov>
Subject: FW: FOR REVIEW: Policy Options for Release of SNS-Held Chloroquine and Hydroxychloroquine

Hi All,

Ensuring you all have seen this policy document for review from the DLG team. Comments are due back to them by 5PM today. Happy to collate comments if you send to me before 4.

Thanks
g

From: Bright, Rick (OS/ASPR/BARDA) <Rick.Bright@hhs.gov>
Sent: Wednesday, April 8, 2020 11:38 AM
To: Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>
Subject: Fwd: FOR REVIEW: Policy Options for Release of SNS-Held Chloroquine and Hydroxychloroquine

Are you collating this info from across BARDA or who is? Has it been shared with clinical and regulatory teams for review?

Sent from my iPhone

Begin forwarded message:

From: "DLGDESK (HHS/ASPR/OPP)" <DLGDESK@hhs.gov>
Date: April 8, 2020 at 11:07:25 AM EDT
To: "DLGDESK (HHS/ASPR/OPP)" <DLGDESK@hhs.gov>, "Stannard, Paula (HHS/IOS)" <Paula.Stannard@hhs.gov>, "Kadlec, Robert (OS/ASPR/IO)" <Robert.Kadlec@hhs.gov>, "Grigsby, Garrett (HHS/OS/OGA)" <Garrett.Grigsby@hhs.gov>, "Kerr, Lawrence (HHS/OS/OGA)" <Lawrence.Kerr@hhs.gov>, "Chang, William (HHS/OGC)" <William.Chang@hhs.gov>, "Sherman, Susan (HHS/OGC)" <Susan.Sherman@HHS.GOV>, "Ray Gorrie, Jennifer (HHS/OGC)" <Jennifer.Ray-Gorrie@hhs.gov>, "Strom, John (HHS/OGC)" <John.Strom@hhs.gov>, "Patel, Anita (CDC/DDID/NCIRD/OD)" <bop1@cdc.gov>, "Ethier, Kathleen (CDC/DDID/NCHHSTP/DASH)" <kbe0@cdc.gov>, "sh1@fda.hhs.gov" <sh1@fda.hhs.gov>, "Hinton, Denise (FDA/OC)" <Denise.Hinton@fda.hhs.gov>, "Mair, Michael (FDA/OC)" <Michael.Mair@fda.hhs.gov>, "Courtney, Brooke (FDA/OC)" <Brooke.Courtney@fda.hhs.gov>, "Collins, Francis (NIH/OD) [E]" <collinsf@od.nih.gov>, "Fauci, Anthony (NIH/NIAID) [E]" <afauci@niaid.nih.gov>, "Marston, Hilary (NIH/NIAID) [E]" <hilary.marston@nih.gov>, "Shuy, Bryan (OS/ASPR/IO)" <Bryan.Shuy@hhs.gov>, "Yeskey, Kevin (OS/ASPR/IO)" <Kevin.Yeskey@hhs.gov>, "Bright, Rick (OS/ASPR/BARDA)" <Rick.Bright@hhs.gov>, "Disbrow, Gary (OS/ASPR/BARDA)" <Gary.Disbrow@hhs.gov>, "Lambert, Linda (OS/ASPR/BARDA)" <Linda.Lambert@hhs.gov>, "Adams, Steven A. (ASPR/SNS)" <saa1@cdc.gov>, "Gorman, Susan (ASPR/SNS)" <spg4@cdc.gov>
Cc: "Phillips, Sally (OS/ASPR/SPPR)" <Sally.Phillips@hhs.gov>, "DeBord, Kristin (OS/ASPR/SPPR)" <Kristin.DeBord@hhs.gov>, "Dodgen, Daniel (OS/ASPR/SPPR)" <Daniel.Dodgen@HHS.GOV>, "Austin, Meredith (OS/ASPR/IO)" <Meredith.Austin@hhs.gov>, "Sheehy, Janice (FDA/ORA)" <Janice.Sheehy@fda.hhs.gov>, "Shirley, Mayo (FDA/OC)" <Mayo.Shirley@fda.hhs.gov>
Subject: RE: FOR REVIEW: Policy Options for Release of SNS-Held Chloroquine and Hydroxychloroquine

Good morning Disaster Leadership Group Members,

This is a friendly reminder to please provide your edits/comments to the "Release of SNS-Held Chloroquine and Hydroxychloroquine" policy options paper to DLGDESK@hhs.gov by **5:00 PM today**. I've reattached the policy options paper along with the International MCM Sharing Policy Framework for your convenience. Thank you to those who have already responded.

Respectfully,

Dan

Daniel Dodgen, Ph.D.
Senior Advisor

Office of the Assistant Secretary for Preparedness and Response (ASPR)
Office of Strategy, Policy, Planning and Requirements (SPPR)

HEALTH AND HUMAN SERVICES (DHHS) | O'Neill House Office Building | 200 C Street SW | Washington, DC 20515
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From: DLGDESK (HHS/ASPR/OPP) <DLGDESK@hhs.gov>
Sent: Tuesday, April 7, 2020 11:48 AM
To: Stannard, Paula (HHS/IOS) <Paula.Stannard@hhs.gov>; Kadlec, Robert (OS/ASPR/IO) <Robert.Kadlec@hhs.gov>; Grigsby, Garrett (HHS/OS/OGA) <Garrett.Grigsby@hhs.gov>; Kerr, Lawrence (HHS/OS/OGA) <Lawrence.Kerr@hhs.gov>; Chang, William (HHS/OGC) <William.Chang@hhs.gov>; Sherman, Susan (HHS/OGC) <Susan.Sherman@HHS.GOV>; Ray Gorrie, Jennifer (HHS/OGC) <Jennifer.Ray-Gorrie@hhs.gov>; Strom, John (HHS/OGC) <John.Strom@hhs.gov>; Patel, Anita (CDC/DDID/NCIRD/OD) <bop1@cdc.gov>; Ethier, Kathleen (CDC/DDID/NCHHSTP/DASH) <kbe0@cdc.gov>; sh1@fda.hhs.gov; Hinton, Denise (FDA/OC) <Denise.Hinton@fda.hhs.gov>; Mair, Michael (FDA/OC) <Michael.Mair@fda.hhs.gov>; Courtney, Brooke (FDA/OC) <Brooke.Courtney@fda.hhs.gov>; Collins, Francis (NIH/OD) [E] <collinsf@od.nih.gov>; Fauci, Anthony (NIH/NIAID) [E] <afauci@niaid.nih.gov>; Marston, Hilary (NIH/NIAID) [E] <hilary.marston@nih.gov>; Shuy, Bryan (OS/ASPR/IO) <Bryan.Shuy@hhs.gov>; Yeskey, Kevin (OS/ASPR/IO) <Kevin.Yeskey@hhs.gov>; Bright, Rick (OS/ASPR/BARDA) <Rick.Bright@hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Lambert, Linda (OS/ASPR/BARDA) <Linda.Lambert@hhs.gov>; Adams, Steven A. (ASPR/SNS) <saa1@cdc.gov>; Gorman, Susan (ASPR/SNS) <spg4@cdc.gov>
Cc: Phillips, Sally (OS/ASPR/SPPR) <Sally.Phillips@hhs.gov>; DeBord, Kristin (OS/ASPR/SPPR) <Kristin.DeBord@hhs.gov>; Dodgen, Daniel (OS/ASPR/SPPR) <Daniel.Dodgen@HHS.GOV>; (b)(6) ; Sheehy, Janice (FDA/ORA) <Janice.Sheehy@fda.hhs.gov>; Blatner@hhs.gov; Shirley, Mayo (FDA/OC) <Mayo.Shirley@fda.hhs.gov>; DLGDESK (HHS/ASPR/OPP) <DLGDESK@hhs.gov>
Subject: FOR REVIEW: Policy Options for Release of SNS-Held Chloroquine and Hydroxychloroquine

Dear Disaster Leadership Group Members and Colleagues:

Thank you for your participation in COVID-19 Disaster Leadership Group (DLG) Meetings. We are soliciting feedback to inform a policy recommendation regarding whether or not ASPR should support the release of chloroquine and hydroxychloroquine for clinical trials outside the United States. These two drugs are covered by the Emergency Use Authorizations requested by BARDA and approved by the FDA.

1. **FOR REVIEW**: Please find the attached "**Release of SNS-Held Chloroquine and Hydroxychloroquine**" policy options paper for your review.

Suspense Date: Please offer any edits to the "Release of SNS-Held Chloroquine and Hydroxychloroquine" policy options paper to DLGDESK@HHS.gov **by 5:00 PM on Wednesday April 8, 2020**.

<<File: Release of SNS-Held Chloroquine and Hydroxychloroquine.docx >>

2. **FOR INFORMATION**: Please find the attached "**International MCM Sharing Policy Framework**" document, which is an existing policy framework for any requests to use HHS-held MCMs internationally.

<<File: International MCM Sharing Policy Framework FINAL January 2014.pdf >>

We ask that DLG meeting participants ensure leadership within their respective HHS Staff and Operating Divisions are briefed on these materials, and that you do not forward this material beyond the distribution of this message. Please address any questions related to this request to the DLGDESK Resource Mailbox at DLGDESK@hhs.gov.

Respectfully,

Dan

Daniel Dodgen, Ph.D.
Senior Advisor
Office of the Assistant Secretary for Preparedness and Response (ASPR)
Office of Strategy, Policy, Planning and Requirements (SPPR)

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Sender:	Faison, Tremel (OS/ASPR/BARDA) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=2BBAB0BCEB1342FBBEDBBCC94DEEB80F-FAISON, TRE <Tremel.Faison@hhs.gov>
Recipient:	Lambert, Linda (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ce6824b6a92a4a4e893ea7b54e17eb3c-Lambert, Li <Linda.Lambert@hhs.gov>; Blatner, Gretta (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=623cb123c2324236b1db6fb9153e0bbf-Blatner, Gr <Gretta.Blatner@hhs.gov>; Walker, Robert (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7a02e128c60f4a7195532a1545af9556-Walker, Rob <Robert.Walker@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0851e89240324306b78740a4a60745e2-Johnson, Ro <Robert.Johnson@hhs.gov>; Oshansky, Christine (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d7bd764440b44b06af644cdcd22e42d6-Oshansky, C <Christine.Oshansky@hhs.gov>; Houchens, Christopher (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7ac94a574bd04528b7c91bbd61893975-Houchens, C <Christopher.Houchens@hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0fd5845defda4dc0bb45f8fac629cf09-Disbrow, Ga <Gary.Disbrow@hhs.gov>; Bright, Rick (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group

	(FYDIBOHF23SPDLT)/cn=Recipients/cn=53034752f35a4317aa74f46348442d39-Bright, Ric <Rick.Bright@hhs.gov>
Sent Date:	2020/04/08 15:23:45
Delivered Date:	2020/04/08 15:23:47

From:	Blatner, Gretta (OS/ASPR/BARDA) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=623CB123C2324236B1DB6FB9153E0BBF-BLATNER, GR <Gretta.Blatner@hhs.gov>
To:	Bright, Rick (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=53034752f35a4317aa74f46348442d39-Bright, Ric <Rick.Bright@hhs.gov>
Subject:	FW: A pilot study of hydroxychloroquine in treatment of patients with common coronavirus disease-19 (COVID-19)
Date:	2020/03/25 14:58:24
Priority:	Normal
Type:	Note

Google translation of the paper you wanted.

From: Livinski, Alicia (NIH/OD/ORS) [E] <livinska@od.nih.gov>
Sent: Wednesday, March 25, 2020 1:37 PM
To: Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>
Subject: RE: A pilot study of hydroxychloroquine in treatment of patients with common coronavirus disease-19 (COVID-19)

It's a Google Translate English version so use with some caution. The original Chinese PDF is attached in case you can find a Chinese speaker to confirm the translation accuracy.
R/Alicia

From: Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>
Sent: Wednesday, March 25, 2020 1:31 PM
To: Livinski, Alicia (NIH/OD/ORS) [E] <livinska@od.nih.gov>
Subject: A pilot study of hydroxychloroquine in treatment of patients with common coronavirus disease-19 (COVID-19)

Are we able to get this article in English? They translated the synopsis

Thanks
g

https://protect2.fireeye.com/url?k=3a7f05f3-662a0c23-3a7f34cc-0cc47a6a52de-0473b6fd41d84d17&u=http://www.zjujournals.com/med/EN/10.3785/j.issn.1008-9292.2020.03.03#1

A pilot study of hydroxychloroquine in treatment of patients with common coronavirus disease-19 (COVID-19)

Objective: To evaluate the efficacy and safety of hydroxychloroquine (HCQ) in the treatment of patients with common coronavirus disease-19 (COVID-19). **Methods:** We prospectively enrolled 30 treatment-na?ve patients with confirmed COVID-19 after informed consent at Shanghai Public Health Clinical Center. The patients were randomized 1:1 to HCQ group and the control group. Patients in HCQ group were given HCQ 400 mg per day for 5 days plus conventional treatments, while those in the control group were given conventional treatment only. The primary endpoint was negative conversion rate of COVID-19 nucleic acid in respiratory pharyngeal swab on days 7 after randomization. This study has been approved by the ethics committee of Shanghai public health clinical center and registered online (NCT04261517). **Results:** One patient in HCQ group developed to severe during the treatment. On day 7, COVID-19 nucleic acid of throat swabs was negative in 13 (86.7%) cases in the HCQ group and 14 (93.3%) cases in the control group (P>0.05). The median duration from hospitalization to virus nucleic acid negative conservation was 4 (1-9) days in HCQ group, which is comparable to that in the control group[2 (1-4) days, (U=83.5, P>0.05)]. The median time for body temperature normalization in HCQ group was 1 (0-2) after hospitalization, which was also comparable to that in the control group 1 (0-3). Radiological progression was shown on CT images in 5 cases (33.3%) of the HCQ group and 7 cases (46.7%) of the control group, and all patients showed improvement in follow-up examination. Four cases (26.7%) of the HCQ group and 3 cases (20%) of the control group had transient diarrhea and abnormal liver function (P>0.05). **Conclusions:** The prognosis of common COVID-19 patients is good. Larger sample size study are needed to investigate the effects of HCQ in the treatment of COVID-19. Subsequent research should determine better endpoint and fully consider the feasibility of experiments such as sample size.

Sent from my iPhone

Sender: Blatner, Gretta (OS/ASPR/BARDA) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=623CB123C2324236B1DB6FB9153E0BBF-BLATNER, GR <Gretta.Blatner@hhs.gov>

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Sent Date:	2020/03/25 14:58:22
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浙江大学学报(医学版)
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Journal of Zhejiang University (Medical Science), 2020, 49 (1): 0-0 doi: 10.3785 / j.issn.1008-9292.2020.03.03

original

Preliminary study of hydroxychloroquine sulfate in treating common coronavirus disease (COVID-19) patients in 2019

Chen Jun , , Liudan Ping , Liu Li , Liu Ping , Xu Qing years , Xia Lu , Ling Yun , Huang Dan , Song Shuli , Zhang Dandan , money Zhiping , Li Tao , Shen silver Zhong , Lu Hongzhou , (0000-0002-3850-4875) (mailto:qtchenjun@163.com) (0000-0002-8308-5534) (mailto:luhongzhou@fudan.edu.cn)

A pilot study of hydroxychloroquine in treatment of patients with common coronavirus disease-19 (COVID-19)

On Jun CHEN , , LIU Danping , LIU of Li , LIU the Ping , XU Qingnian , XIA Lu , LING Yun , HUANG Dan , the SONG Shuli , ZHANG Dandan, , QIAN Zhiping , LI Tao , SHEN Yinzhong , the LU of Hongzhou , (0000-0002-3850-4875) (mailto:qtchenjun@163.com) (0000-0002-8308-5534) (mailto:luhongzhou@fudan.edu.cn)

Abstract

Objective: To evaluate the efficacy and safety of hydroxychloroquine (HCQ) in the treatment of patients with common coronavirus disease-19 (COVID-19). **Methods:** We prospectively enrolled 30 treatment-na? Ve patients with confirmed COVID-19 after informed consent at Shanghai Public Health Clinical Center. The patients were randomized 1: 1 to HCQ group and the control group. Patients in HCQ group were given HCQ 400 mg per day for 5 days plus conventional treatments, while those in the control group were given conventional

treatment only. The primary endpoint was negative conversion rate of COVID-19 nucleic acid in respiratory pharyngeal swab on days 7 after randomization. This study has been approved by the ethics committee of Shanghai public health clinical center and registered online (NCT04261517).**Results:** One patient in HCQ group developed to severe during the treatment. On day 7, COVID-19 nucleic acid of throat swabs was negative in 13 (86.7%) cases in the HCQ group and 14 (93.3%) cases in the control group ($P > 0.05$). The median duration from hospitalization to virus nucleic acid negative conservation was 4 (1-9) days in HCQ group, which is comparable to that in the control group [2 (1-4) days, ($U = 83.5$, $P > 0.05$)]. The median time for body temperature normalization in HCQ group was 1 (0-2) after hospitalization, which was also comparable to that in the control group 1 (0-3). Radiological progression was shown on CT images in 5 cases (33.3%) of the HCQ group and 7 cases (46.7%) of the control group, and all patients showed improvement in follow-up examination. Four cases (26.7%) of the HCQ group and 3 cases (20%) of the control group had transient diarrhea and abnormal liver function ($P > 0.05$). **Conclusions:** The prognosis of common COVID-19 patients is good. Larger sample size study are needed to investigate the effects of HCQ in the treatment of COVID-19. Subsequent research should determine better endpoint and fully consider the feasibility of experiments such as sample size.

Keywords: Severe acute respiratory syndrome coronavirus 2 ; Corona virus disease-19 ; Novel coronavirus pneumonia ; Hydroxychloroquine ; Treatment outcome ; Safety

Article citation format

Chen Jun, Liu Danping, Liu Li, Liu Ping, Xu Qingnian, Xia Lu, Ling Yun, Huang Dan, Song Shuli, Zhang Dandan, Qian Zhiping, Li Tao, Shen Yinzhong, Lu Hongzhou. Preliminary study of hydroxychloroquine sulfate in treating common coronavirus disease (COVID-19) patients in 2019. *Zhejiang University (Medical Sciences)* [J], 2020, 49 (1): 0-0 doi: 10.3785 / j.issn.1008-9292.2020.03.03

CHEN Jun, LIU Danning, LIU Li, LI Ping, XU Qingxian, XIA Lu, LING Yun, HUANG Dan, SONG Shuli, ZHANG Dandan, QIAN Zhiping, Li Tao, SHEN Yinzhong, LU Hongzhou. A pilot study of hydroxychloroquine in treatment of patients with common coronavirus disease-19 (COVID-19). *Journal of Zhejiang University (Medical Sciences)*[J], 2020, 49 (1): 0-0 doi: 10.3785 / j.issn.1008-9292.2020.03.03

In December 2019, several cases of pneumonia of unknown cause have appeared in Wuhan City, Hubei Province, and spread rapidly [1]. On January 31, 2020, the WHO classified the epidemic as a public health emergency of international concern [2]. The results of gene sequence analysis showed that the pathogen of this epidemic was beta coronavirus, which was highly homologous with severe acute respiratory syndrome (SARS) virus. The International Virus Classification Commission named it coronavirus of severe acute respiratory syndrome. The virus 2 (severe acute respiratory syndrome coronavirus 2, SARS-CoV-2), WHO officially named the disease caused by its infection as 2019 corona virus disease (COVID-19) [3]. SARS-CoV-2 is highly infectious, and no specific anti-coronal virus or vaccine has been available [4].

Chloroquine is a widely used drug against malaria and autoimmune diseases, and has a broad spectrum of antiviral effects. Chloroquine exerts a direct antiviral effect by changing the pH value of endosomes and inhibiting the pH-dependent viral replication step. Inhibiting Dengue virus, Zika virus and HIV, etc. have a role in viral replication [5-6]. In 2005, Vincent et al. [7] found that chloroquine could effectively block SARS-CoV infection in cell lines. The National Health and Health Commission "Diagnosis and Treatment of New Coronavirus Pneumonia (Trial Version 6)" (hereinafter referred to as "Diagnosis and Treatment") recommends chloroquine phosphate for antiviral treatment of COVID-19 patients [8]. Hydroxychloroquine sulfate is a 4-aminoquinoline derivative antimalarial drug, which has an added hydroxyl group on the basis of chloroquine, which has comparable efficacy and low toxicity. As a traditional "old medicine", hydroxychloroquine sulfate has higher safety, so it is one of the drugs with potential curative effect on COVID-19. This study is a single-center, prospective, randomized, and open-label study designed to provide a data base for exploring the next step in the effectiveness and safety of chlorochloroquine sulfate for COVID-19.

1.1. Objects

Thirty confirmed COVID-19 patients who were hospitalized in Shanghai Public Health Clinical Center from February 6 to 25, 2020 were collected. Inclusion criteria: Age ≥18 years, COVID-19 was diagnosed according to the "diagnosis and treatment plan" and informed consent was signed. Exclusion criteria: ① Patients who are allergic to chloroquine and hydroxychloroquine; ② Pregnant women; ③ Patients with serious diseases such as heart, lung, kidney, brain, blood and other organs with insufficiency; Patients; ⑤ Patients with severe neurological or psychiatric disorders; ⑥ Researchers who believe that they cannot complete the study as required or are not suitable to participate in the research.

1.2. Grouping and treatment

The subjects were randomly assigned to the experimental group and the control group at a ratio of 1: 1. The test group received conventional treatment plus oral chlorochloroquine sulfate 400 mg once daily for 5 days. The control group received only conventional treatment, including bed rest, oxygen inhalation, and symptomatic supportive treatment. Viral drugs such as alpha interferon nebulization, oral lopinavir / ritonavir (clepivir), etc., and antibacterial drugs if necessary. All subjects were screened on the day of admission, completed randomization and started treatment (including antiviral therapy). There were no significant differences in general demographic data, clinical manifestations, laboratory findings, and chest CT findings between the two groups at the time of enrollment (Table 1). All patients received alpha interferon nebulization, while 12 (80.0%) of the experimental group received abidol; 10 of the control group (66.7%) received abidol, and 2 (13.3%) Received lopinavir / ritonavir treatment.

Table 1 Comparison of demographic data and clinical characteristics between the two groups

Tab 1 Demographic data and clinical characteristics of the two groups [$\bar{x} \pm s$ or M (Q_1 , Q_3) or n (%)]

Group	n	Male *	average age	Mean course of	heat	Basic diseases *

Group	*n*	Male [*n* (%)]	Average age	Average course of disease (d)	Chronic hypertension [*n* (%)]	Diabetes [*n* (%)]	Chronic obstructive pulmonary disease [*n* (%)]
test group	15	9 (60.0)	50.5 ± 3.8	6.6 ± 3.9	9 (60.0)	5 (33.3)	1 (6.7)
Control group	15	12 (80.0)	46.7 ± 3.6	5.9 ± 4.1	13 (86.7)	3 (20.0)	1 (6.7)
t / *U* value	—	—	0.72	0.45	—	—	—
P value	—	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05

Group	*n*	White blood cell count (× 10^9 / L)	Lymphocyte count (× 10^9 / L)	ALT (U / L)	eGFR (mL · min^{-1} · $1.73m^{-2}$)	Lactic acid (mmol / L)	$CD4^+$ cell count (cells / μL)	CT lesions of the chest (two lungs / one lung) *
test group	15	5.2 (3.9 ~ 6.7)	1.11 ± 0.43	18 (15 ~ 23)	117 ± 29	1.4 ± 0.4	415 (275 ~ 589)	12/3
Control group	15	4.9 (4.5 ~ 7.4)	1.18 ± 0.55	24 (14 ~ 47)	120 ± 29	1.4 ± 0.5	395 (272 ~ 710)	14/1
t / *U* value	—	101	0.39	87	0.30	0.19	110	—
P value	—	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05

"—" No relevant data. * Fisher test. ALT: alanine aminotransferase; eGFR: estimation of glomerular filtration rate.

New windowopen (20200108/Table1.html) | Download CSV (20200108/Table1.csv.zip)

1.3. Collection and follow-up of clinical data

When enrolled, subjects were collected for medical history, physical examination, epidemiological characteristics and laboratory examination. The clinical classification of the subjects was performed according to the "diagnosis and treatment plan". On the 0th, 3rd, 5th, and 7th days of enrollment, the vital signs, clinical symptoms, laboratory test results, and adverse events of the subjects were recorded. The follow-up observation period of the study was 2 weeks.

1.4. Study endpoint

The primary study endpoint was virological clearance of a throat swab, sputum, or lower respiratory tract secretion on day 7 or death of the patient within 2 weeks; the secondary study endpoint was a serious adverse drug event or a change in the subject's condition within 2 weeks Heavy and critical. For respiratory specimens, the detection of SARS-CoV-2 nucleic acid is based on the last test result and time. If the virus nucleic acid is negative for two consecutive tests, the time of the negative nucleic acid test is the time of the first test.

1.5. Statistical Methods

Statistical analysis was performed using STATA 13.0 software. Means ± standard deviation ($\bar{}$± S) described, does not meet the normal distribution of measurement data with a median (quartiles down) [M ($Q_{.1}$, $Q_{.3}$)] described in Example count data and the percentage of the number [n- (%)] is described. Comparisons between measurement data groups were performed using t test (normal distribution) or rank sum test (non-normal distribution). Comparisons between count data groups were performed using χ^2 test or Fisher test. P <0.05 was considered statistically significant.

2. Results

2.1. Comparison of curative effect between experimental group and control group

During the course of treatment, one patient in the test group developed severe and the test drug was discontinued on the fourth day. In the intention-to-treat analysis, on the seventh day after enrollment, 13 patients (86.7%) in the test group and 14 patients (93.3%) in the control group were negative for pharynx swab virus nucleic acid (P > 0.05). During the 2-week visit period, all subjects' throat nucleic acid swab virus nucleic acid test turned negative. The test group's throat swab virus nucleic acid negative time was 4 (1-9) days after admission. The control group For the second (1 ~ 4) days, the difference was not statistically significant (U = 83.5, P > 0.05). The body temperature returned to normal on the first day (0 ~ 2) after admission, and the body temperature returned to normal on the first (0 ~ 3) day after admission. In terms of imaging performance, 5 cases in the test group

(38.3%) and 7 cases (http://www.zjujournals.com) (46.7%) showed progress in the review after 3 days of enrollment. All patients showed improvement of the lesions in the subsequent review. By the end of the follow-up period, all subjects had survived.

2.2. Comparison of adverse reactions between the experimental group and the control group

No obvious new symptoms occurred in the control group, but three adverse events occurred, including one case (20%) with transient aspartate aminotransferase elevation and anemia, and one case with elevated serum creatinine; the test There were 4 adverse events in the group, including 2 cases of diarrhea, 1 case of weakness and development of severe disease, and 1 case of transient aspartate aminotransferase elevation. The occurrence of adverse events in the subjects in the experimental group was considered to be independent of medication. All adverse reactions disappeared after drug withdrawal or symptomatic treatment, and patients who developed into severe disease also improved after being given high-flow nasal catheter oxygen therapy and other treatments. There was no significant difference in the incidence of adverse events between the two groups ($P > 0.05$).

3 Discussion

"Diagnosis and treatment plan" recommends chloroquine phosphate as one of the COVID-19 antiviral treatment plans. As of February 25, 2020, there have been as many as 21 studies on the use of chloroquine to treat COVID-19 in the China Clinical Trial Registry (http://www.chictr.org.cn/). Most studies have used phosphoric acid. Chloroquine (500 mg twice daily for 10 d) or hydroxychloroquine sulfate (400 mg once daily for 10 to 14 d) [9] .

80% of patients with COVID-19 are mild or common. All patients in this document are of the common type, and the results show that the standard dose of hydroxychloroquine sulfate (400 mg, once per day) treatment has not shown clinical effects in improving patient symptoms and accelerating virological suppression. It is worth noting that the vast majority of patients in the data in this article returned to normal after 1 (0 to 3) days after enrollment, and virus nucleic

acids should not be detected in 2 (1 to 4) days of throat swabs. The analysis results of cases from January 20 to February 6, 2020 were significantly different. The cases from January 20th to February 6th, 2020 did not return to normal temperature until 4 days after enrollment, and the median time for pharyngeal swab virus nucleic acid to turn negative was approximately 7 days after admission [10] . This may suggest that the severity of COVID-19 may decrease over time due to epidemiological changes, temperature, humidity, and possible changes in viral virulence. In the case where the treatment effect of this control group is already relatively good, finding a more effective drug for ordinary COVID-19 patients will encounter the "ceiling effect". Based on the results of this trial, if you need to conclude that the efficacy of hydroxychloroquine sulfate is better or worse than that of the control group, at least 784 subjects are required. If the factors such as subject dropout and rejection are considered, the number of cases must reach nearly 900 cases. This is a huge challenge for current clinical research. Therefore, finding a more suitable population or endpoint to evaluate the effect of hydroxychloroquine sulfate (and indeed all other drugs) treatment may be more clinically feasible, such as assessing whether it can reduce mortality in critically ill or critically ill patients. rate. In addition, if the subject's condition does gradually decrease over time, it reminds us of the importance of conducting randomized controlled clinical studies. If a one-arm study is conducted and historical data is used as a control, false positive results may be obtained (ie, certain drugs are found to be effective) [11] .

In summary, this study suggests that the current general treatment of patients with general COVID-19 is better, and studies that use viral negative rate and severe rate as the main endpoints are difficult to judge the effect of treatment options. Carrying out subsequent research needs to determine more suitable population and endpoint indicators, and fully consider the feasibility of experiments such as sample size.

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From: Marston, Hilary (NIH/NIAID) [E] <hilary.marston@nih.gov>

To: Bright, Rick (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=53034752f35a4317aa74f46348442d39-Bright, Ric <Rick.Bright@hhs.gov>

Subject: Re: URGENT Questions on planned study

Date: 2020/03/26 09:56:10

Priority: Normal

Type: Note

What is the timing for that pilot rollout? Trying to get our study done before. Also if you know geographic areas, we can try to avoid.

From: Rick Bright <Rick.Bright@hhs.gov>
Date: Wednesday, March 25, 2020 at 6:00 PM
To: "Amin, Stacy (FDA/OC)" <Stacy.Amin@fda.hhs.gov>, "Walker, Robert (OS/ASPR/BARDA)" <Robert.Walker@hhs.gov>, "Faison, Tremel (OS/ASPR/BARDA)" <Tremel.Faison@hhs.gov>, "Farley, John (FDA/CDER)" <john.farley@fda.hhs.gov>, Linda Lambert <Linda.Lambert@hhs.gov>, "Oshansky, Christine (OS/ASPR/BARDA)" <Christine.Oshansky@hhs.gov>, "Disbrow, Gary (OS/ASPR/BARDA)" <Gary.Disbrow@hhs.gov>, Hilary Marston <hilary.marston@nih.gov>, Henry Lane <clane@niaid.nih.gov>, "Patel, Anita (CDC/DDID/NCIRD/OD)" <bop1@CDC.GOV>, "Uyeki, Timothy M. (CDC/DDID/NCIRD/ID)" <tmu0@CDC.GOV>, Matthew USARMY Hepburn <matthew.j.hepburn.civ@mail.mil>, "Birnkrant, Debra B (FDA/CDER)" <Debra.Birnkrant@fda.hhs.gov>, John Beigel <jbeigel@niaid.nih.gov>, Libby Higgs <ehiggs@niaid.nih.gov>, "Sherman, Susan (HHS/OGC)" <Susan.Sherman@HHS.GOV>, "Harper, Victor (OS/ASPR/ORM)" <Victor.Harper@hhs.gov>, "Adams, Steven A. (ASPR/SNS)" <saa1@CDC.GOV>, "Woodcock, Janet (FDA/CDER)" <Janet.Woodcock@fda.hhs.gov>, Robert Johnson <Robert.Johnson@hhs.gov>, "Hamel, Joseph (OS/ASPR/IO)" <Joseph.Hamel@hhs.gov>
Subject: Re: URGENT Questions on planned study

Apologies for the resend, I accidentally omitted Joe Hamel. He has a critical role. Thanks. Rick

FOUO, Confidential, Pre-Decisional

Dear All,

I am following up on our HHS task of implementing a "nationwide access plan" for chloroquine and/or hydroxychloroquine. This project has been discussed in multiple settings with multiple members of the larger group. As we proceed towards implementation, it is critical to keep the full agency visibility on the project to ensure each plays a role in execution. I have included HHS, ASPR/IO, ASPR SNS, NIH/NIAID, CDC,

ASPR/BARDA, FDA/OGC, FDA/OC, FDA/CDER, HHS/OGC. The distribution above can be reduced to the single agency representative once all roles are finalized.

We learned today from our FDA colleagues that plans are progressing quickly to move forward with an EUA (not an IND). The FDA will write the EUA(s). The following specific items will need to be fully understood and appropriate actions taken by our agency teams as indicated. Please update any errors or incorrect assumptions.

- First, question (focus on hydroxychloroquine only or also include chloroquine)?
- Chloroquine (Bayer donation)
- The current plan is to make chloroquine available under an Emergency Use Authorization.
- The indicated population remains to be determined. The MCM Task Force **clinical trial working group** will provide input into that decision.
- As has historically been the HHS approach for EUAs, **CDC will lead** for implementation of the EUA effort and distribution of product in collaboration with SNS.
- This will be an initial small-scale roll-out/pilot as discussed on the interagency call on March 23rd, in a limited number of locations.
- All questions about drug supply and other product specific concerns are directed to Joe Hamel in the ASPR Immediate Office.
- All product will be received, stored and distributed by the ASPR/SNS.

- Hydroxychloroquine (Sandoz/Novartis donation)
- FDA is actively considering making hydroxychloroquine available under an EUA.
- To better inform this decision, information is needed by FDA about drug supply to ensure that appropriate doses are set aside for clinical trials.
- As above, should the final decision of the HHS be to proceed with an EUA, the interagency team will look to CDC to lead the EUA implementation in collaboration with SNS.
- All questions about drug supply and other product specific concerns are directed to Joe Hamel in the ASPR Immediate Office.

All product will be received, stored and distributed by the ASPR/SNS.

ORACLE: We need to understand the full scope and nature of the Oracle donation and have a POC at Oracle to coordinate this portion of the plan. Who has been the HHS POC for Oracle to date?

Donations: Are all donations complete? Oracle? Bayer? Sandoz/Novartis?

- Dr. Bob Walker in BARDA is coordinating the group.

Thank you all for your critical and urgent contributions to these collaborative efforts.

Rick

From: "Bright, Rick (OS/ASPR/BARDA)" <Rick.Bright@hhs.gov>
Date: Monday, March 23, 2020 at 9:09 PM
To: "Amin, Stacy (FDA/OC)" <Stacy.Amin@fda.hhs.gov>
Cc: Janet Woodcock <Janet.Woodcock@fda.hhs.gov>, Robert Johnson <Robert.Johnson@hhs.gov>, Robert Walker <Robert.Walker@hhs.gov>, Tremel Faison <Tremel.Faison@hhs.gov>, "Farley, John (FDA/CDER)" <John.Farley@fda.hhs.gov>, Linda Lambert <Linda.Lambert@hhs.gov>, Christine Oshansky <Christine.Oshansky@hhs.gov>, Gary Disbrow <Gary.Disbrow@hhs.gov>, Hilary Marston <hilary.marston@nih.gov>, Cliff Lane <clane@niaid.nih.gov>, Anita Patel <bop1@cdc.gov>, Timothy Uyeki <tmu0@cdc.gov>, "Hepburn, Matthew J CIV USARMY DOD JPEO CBRND (USA)" (b)(6), Debra Birnkrant <Debra.Birnkrant@fda.hhs.gov>, John Beigel <jbeigel@niaid.nih.gov>, Elizabeth Higgs <ehiggs@niaid.nih.gov>, "Sherman, Susan (HHS/OGC)" <Susan.Sherman@HHS.GOV>
Subject: URGENT Questions on planned study

Hi Stacy,

I hope that you are doing well, given the extremely busy pace that everyone is working. I hope that you are able to assist us with an urgent matter.

HHS has been tasked to conduct what we understand to be a nationwide emergency access IND for Chloroquine or hydroxychloroquine. The HHS COVID19 clinical and regulatory teams urgently need to talk with you to understand the information that you have about this study and a potential combination with an experimental database system from Oracle.

The details available enable us to proceed are very sketchy and the directive is to move quickly. We understand that you might have helpful information from various conversations you have had with Oracle, the drug supplier and other entities planning the trial. In order to coordinate this USG/HHS-lead study, it will be very helpful if you can update us on any background information, either by email or a conference call.

Dr. Bob Walker is copied with the HHS team above. He can assist in coordinating a call at your earliest convenience.

Thank you for taking the time to assist in clarifying this task and a path forward.

Rick
Rick A. Bright, PhD
Director, BARDA
Deputy Assistant Secretary for Preparedness and Response
Office of the Assistant Secretary for Preparedness and Response
US Department of Health and Human Services

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Sent Date:	2020/03/26 09:55:59
Delivered Date:	2020/03/26 09:56:10

From:	Hamel, Joseph (OS/ASPR/IO) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=96D2C1602DFA45E5A5E21452A098B96D-HAMEL, JOSE <Joseph.Hamel@hhs.gov>
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Subject:	Chloroquine - latest as of 3:00 EDT
Date:	2020/03/19 14:59:54
Priority:	Normal
Type:	Note

Latest figures enclosed

iPhone friendly version:

NATCO:
What do you have on hand?
INVENTORY STATUS AT NATCO, KOTHUR
Natco has recently dispatched the following to the USA:
250 mg: 3788 bottles of 50's count on 12/18/2019
500 mg: 15612 bottles of 25's count on 03/11/2020 which has been received by Rising Pharma and is ready to be dispatched to customers.

How much can you make and how long does it take?
Natco expects to ship the following product in the next couple weeks:
(b)(4) additional batches which is approximately (b)(4) bottles of (b)(count by end March 2020
(b)(4) additional batches which is approximately (b)(4) bottles of (b)(count between 23rd-26th March 2020
After the current manufacturing campaign, (b)(4 of Ipca API remains in Natco's inventory and this represents:
Three batches of (b)(4) tablets of (b)(4) strength OR
Three batches of (b)(4) tablets of (b)(4) strength

How can we expedite this?

To meet the unprecedented additional demand, Natco requests the prioritization of review and approval of the PAS - sANDA# 090612 Chloroquine Phosphate Tablets USP, (b)(4) and sANDA# 091621 Chloroquine Phosphate Tablets USP, (b)(4) Assuming that this PAS is approved, Natco will be in a better position to address the need of this pandemic demand since we will be able to immediately supply, additional 3 batches of (b)(4) and 3 batches of (b)(4) which have been manufactured in our Vizag facility using Natco API and this data is part of the PAS package pending with the FDA.

These batches would represent close to:

(b)(4) Approximately 15300 bottles of (b)(count

(b)(4): Approximately 13340 bottles of (b)(count

Zydus:

What do you have on hand?

Zydus currently has sufficient inventory on hand to support our current market share of ~36% (equating to approximately 12.5mn tabs monthly). Below is the inventory snapshot as of today.

HYDROXYCHLOROQUINE TAB 200MG (100 CT)- 92,376 bottles on hand, 32,688 in transit from India manufacturing sites

HYDROXYCHLOROQUINE TAB 200MG (500 CT)- 18,300 bottles on hand, 8,844 in transit from India manufacturing sites

Please also note that Zydus has implemented an allocation on our inventory to ensure no speculative purchasing can occur and our customers / patients are protected.

How much can you make?

Currently Zydus can manufacture a total of (b)(4) pills monthly. We are working on initiatives to improve this by 25% and if successful additional product will be available by mid-April.

How long does it take?

Product is manufactured constantly during the month and the plant is running at capacity on this product. As mentioned above, we're looking to improve output by 25%.

How can it be expedited?

Zydus is doing everything it can to expedite the manufacture and shipping of Hydroxychloroquine. We will be shipping all new batches of HCQ via expedited AIR freight instead of via Ocean carriers.

Cardinal Health:

Brand – 33,244 bottles of 100 pills each.

We sell approximately 400 bottles/week normally. Demand has picked up slightly this week.

(b)(4) – of those bottles will reach 12 mo expiry on (b)(4)

Authorized Generic – Approx 250,000 bottles of 100 pills each, (but larger orders have come in this week)

No additional information

Amneal Pharmaceuticals:
How much do they have?
60,000 bottles of 100 hydroxychloroquine sulfate 200MG on hand

How much can they make and how fast can they make it?
(b)(4) bottles ready to ship from India on Tuesday to the US
End of next week they will have (b)(4) bottles of (b)(tablets
By the 27th of March they will have another (b)(4) bottles of (b)(Tablets
First week of April, they will have (b)(4) bottles
In May, they will have (b)(4) bottles ready by May 15th and another (b)(4) bottles by May 31st
Translation – about (b)(4) bottles of (b)(tablets available by end of May

What can we do to expedite?
(b)(5)

Appco Pharma:
How much do they have?
The product in the in-process is about 8 million tablets.

How much can they make?
API on hand can produce about (b)(4) million tablets.

How long does it take?
Additional API expected to be delivered in next month end which may be equivalent to (b)(million tablets. There may be some constraints (we just got some information from our API supplier) in procurement of API if the manufacturing country puts any restrictions in export of the API. We procure API from (b)(4) We request the US government to facilitate the release of material for US use. Our marketing partner, DRL, is holding about (b)(million on hand as on date in different pack configurations and they depleting very faster as there is lot of demand.

How can it be expedited?
We see some constraints from operational perspective because the following reasons:
(b)(4)

We are also in the process of qualification of alternate API from (b)(4)

(b)(4)

Sandoz

What do you have on hand?

ROUGHLY 56 MILLION TABLETS

How much can you make?

WITH ACTIVE INGREDIENT ON HAND WE COULD PRODUCE ROUGHLY (b) MILLION MORE TABLETS

How long does it take?

ROUGHLY (b) MONTHS (b) M/MONTH)

How can it be expedited?

(b)(4)

Teva

How much do they have?

36,000 bottles of 100 count 200mg tablets in US now

9,000 bottles of 500 count 200 mg tablets in US now

How fast can they make it?

(b)(4) bottles of (b) count expected end of March - It is made in (b)(4 with API from (b)(4)

(b)(4) bottles expected end of April (assuming export of API from India not blocked...which is becoming an issue and could be an increased issue following any significant public announcement).

How can we Expedite?

(b)(4)

Strategic Innovation and Emerging Technology Manager
Assistant Secretary for Preparedness and Response
Office: 202-969-3852
Cell: (b)(6)

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Sent Date:	2020/03/19 14:59:53
Delivered Date:	2020/03/19 14:59:54

From:	(b)(6) @gmail.com>
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Subject:	INDIA: ISSUED NATIONAL GUIDELINES HYDROXYCHLOROQUINE
Date:	2020/03/23 08:38:57
Priority:	Normal
Type:	Note

India just issued national guidelines for COVID-19 prophylaxis for high risk individuals including health care workers."guidelines"...

Sender:	(b)(6) @gmail.com>
Recipient:	Bright, Rick (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=53034752f35a4317aa74f46348442d39-Bright, Ric <Rick.Bright@hhs.gov>
Sent Date:	2020/03/23 08:38:21
Delivered Date:	2020/03/23 08:38:57

From:	Weir, Charles (OS/ASPR/IO) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=USER24F49DA6 <Charles.Weir@hhs.gov>
To:	SOC ASPR SLT /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=462b691cb8a743c6870dbb5626596c94-SOC ASPR SL <SOC-ASPR-SLT@hhs.gov>; OS Secretarys Operations Center /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=32b1f28d808b43b6903c00083291303e-Secretarys <hhs.soc@hhs.gov>; OS - ASPR - PDAS - EMMO - Readiness - HPP /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f60f5b3f68f241d3b60300245eaaf8b3-OS-ASPR-PDA <OS-ASPR-PDAS-EMMO-Readiness-HPP@hhs.gov>; Field Operations and Response Division /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c982b5811dce4a9ca3e4c454ece0d74a-ASPR.DFOR <ASPR.DFOR@hhs.gov>; Appler, Jessica (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=427afeb137394e3087b770779847904c-Appler, Jes <Jessica.Appler@hhs.gov>; Nevel, Amy (HHS/ASPE) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=user2448dd24 <Amy.Nevel@HHS.GOV>
Subject:	FW: COVID-19 - Science Update - Special Report hydroxychloroquine/chloroquine
Date:	2020/04/06 08:40:09
Priority:	Normal
Type:	Note

From: EOC Report (CDC) <eocreport@cdc.gov>
Sent: Friday, April 3, 2020 10:24 AM
To: CDC 2019 NCOV Response IMS Mailboxes <2019NCOVResponseIMSMailboxes@cdc.gov>; CDC 2019 NCOV Response Distro List <2019NCOVResponseWideDistro@cdc.gov>
Cc: EOC Report (CDC) <eocreport@cdc.gov>; CDC IMS Response Coordinator -2 <eocresp2@cdc.gov>
Subject: COVID-19 - Science Update - Special Report hydroxychloroquine/chloroquine

On behalf of the Office of the Chief Scientist, I am pleased to share our first "COVID-19 Science Update – Special Edition".

This is the first "special edition" where we will offer a deep dive into a subject relevant to the Response. In this report we focus on the emerging data about treatment of COVID-19 with hydroxychloroquine.

As more data on the subject emerge, we will append the most relevant findings (adjudicated in consultation with SMEs) to keep you up to date.

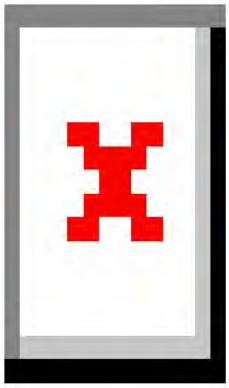
We welcome your feedback. Please send any comments/suggests to CDC IMS 2019 NCOV Response Chief of Science eocevent385@cdc.gov .

On behalf of the entire team,

-john

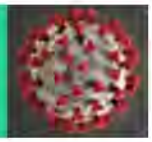
PS: **Want to make someone's day?** Send a thank you to the hard-working folks who put this together: Buchacz, Kate (CDC/DDID/NCHHSTP/DHPSE) acu7@cdc.gov ; Fishman, Julie (CDC/DDPHSS/OS/OLS) jbf4@cdc.gov ; Hassan, Rashida (CDC/DDID/NCHHSTP/DHPSE) ykm6@cdc.gov ; Kirkcaldy, Bob (CDC/OID/NCHHSTP) hgl8@cdc.gov ; Rushmore, Julie (CDC/DDID/NCHHSTP/DHPSE) pgx4@cdc.gov ; Town, Katherine (CDC/DDID/NCHHSTP/DSTDP) odb8@cdc.gov ; Brian A. King (CDC/DDNID/NCCDPHP/OSH) (iyn3@cdc.gov)

John T. Brooks, MD
Chief Medical Officer, CDC COVID-19 Response
Email: zud4@cdc.gov
Apologies for errors in my messages that may be due to my need to dictate because I am a horrible typist.



Sender:	Weir, Charles (OS/ASPR/IO) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=USER24F49DA6 <Charles.Weir@hhs.gov>
Recipient:	SOC ASPR SLT /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=462b691cb8a743c6870dbb5626596c94-SOC ASPR SL <SOC-ASPR-SLT@hhs.gov>; OS Secretarys Operations Center /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=32b1f28d808b43b6903c00083291303e-Secretarys <hhs.soc@hhs.gov>; OS - ASPR - PDAS - EMMO - Readiness - HPP /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f60f5b3f68f241d3b60300245eaaf8b3-OS-ASPR-PDA <OS-ASPR-PDAS-EMMO-Readiness-HPP@hhs.gov>; Field Operations and Response Division /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c982b5811dce4a9ca3e4c454ece0d74a-ASPR.DFOR <ASPR.DFOR@hhs.gov>; Appler, Jessica (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=427afeb137394e3087b770779847904c-Appler, Jes <Jessica.Appler@hhs.gov>; Nevel, Amy (HHS/ASPE) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=user2448dd24 <Amy.Nevel@HHS.GOV>
Sent Date:	2020/04/06 08:40:04
Delivered Date:	2020/04/06 08:40:09
Message Flags:	Unread

COVID-19 Science Update



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SPECIAL TOPIC: Hydroxychloroquine/Chloroquine and COVID-19

EXECUTIVE SUMMARY

U.S. and international efforts are underway to study the utility of hydroxychloroquine and chloroquine to prevent and treat COVID-19. Human data about these drugs' safety and effectiveness are limited at present to four small clinical studies of hydroxychloroquine as treatment. Two of the studies, one of which is pending peer review, demonstrated a possible benefit but both studies have methodologic limitations that in one case are substantial. The third study, which was randomized but limited in sample size, found no benefit. The fourth study, a small clinical case series, observed no clinical improvement and limited viral clearance among hydroxychloroquine-treated COVID-19 patients. Large randomized trials are needed to determine the efficacy and safety of these drugs for COVID-19.

BACKGROUND

Chloroquine (CQ) and hydroxychloroquine (HCQ) are used to treat malaria; HCQ is also used to treat rheumatoid arthritis and systemic lupus erythematosus. Both drugs have side effects and can cause a fatal heart rhythm disturbance (QT prolongation leading to torsades de pointes), especially when combined with other drugs that also prolong the cardiac QT interval (e.g., azithromycin).

Multiple clinical trials are planned, or ongoing, to investigate the potential efficacy and safety of CQ and HCQ as treatment for COVID-19. On March 29, 2020, the FDA issued an Emergency Use Authorization (EUA) for CQ and HCQ as treatment for COVID-19 in hospitalized adolescents and adults for whom a clinical trial is not available or participation is not feasible. Additionally, New York plans to distribute these drugs to severely ill patients through hospital networks, and some physicians have been prescribing HCQ for off-label treatment and prophylaxis. To date, CDC is aware of one death related to self-administration of non-pharmaceutical CQ.

In this issue, we summarize the existing human clinical data on HCQ to treat COVID-19. To date, no study has assessed CQ to treat persons with COVID-19 or the use of either CQ or HCQ to prevent infection with SARS-CoV-2, the virus that causes the illness COVID-19.

PEER-REVIEWED

Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. Gautret *et al.* IJAA 2020 (Mar 20, 2020)

Key findings:

- 70% of patients treated with HCQ (n=20) exhibited viral clearance of SARS-CoV-2 RNA in nasopharyngeal swabs within six days compared with 12.5% of control patients (n=16, p=0.001) (Figure).
- Six patients treated with HCQ also received azithromycin to prevent bacterial super-infection; all demonstrated virologic clearance within six days.

Methods: Non-randomized open-label trial from France that compared hospitalized patients treated with HCQ 200 mg three times daily (600 mg) for 10 days (n=20, of whom 6 also received azithromycin) with a hospitalized convenience sample (n=16). *Limitations:* Small sample size, control group included patients who declined HCQ treatment or were treated at other hospitals without a standard management protocol across sites; of 26 patients initially enrolled in the HCQ arm, 6 were excluded in the analysis due to death (n=1), ICU admission (n=3), and voluntary withdrawal (n=2); unclear whether the two arms were enrolled at the same points in their disease course; no data on clinical outcome or toxicity presented. These limitations are further discussed by Kim *et al.* and Dahly, Gates, and Morris.

Implications: The findings reported from this small, non-randomized trial found a possible benefit of HCQ for COVID-19 treatment, but the study has substantial limitations and must be interpreted with substantial caution.

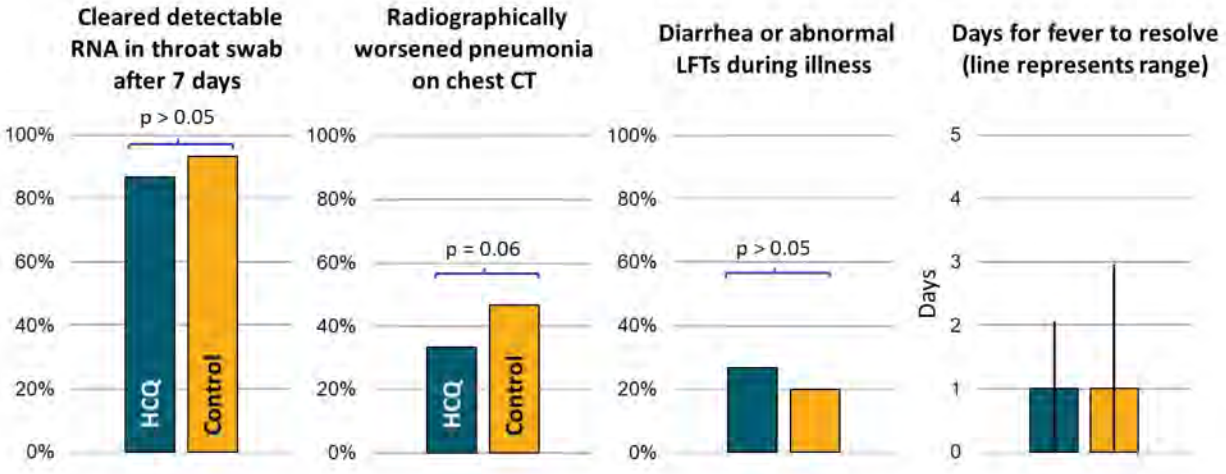
A pilot study of hydroxychloroquine in treatment of patients with common coronavirus disease-19 (COVID-19). Chen J *et al.* J Zhejiang Univ [Chinese][abstract in English] (Mar, 2020)

Key findings:

- Patients treated with HCQ (n=15) compared with control patients (n=15) demonstrated no significant difference in viral clearance by throat swab after 7 days (87% vs. 93%, p > 0.05).
- No differences were observed in median duration of hospitalization, time to defervescence, or adverse events (i.e., transient diarrhea or abnormal liver function tests).

Methods: Randomized open-label trial of HCQ 400 mg daily for five days plus conventional therapy vs. conventional therapy (control arm) among 30 treatment-naïve hospitalized patients with COVID-19 in Shanghai. Response assessed using throat swabs tested for SARS-CoV-2 RNA. *Limitations:* Small sample size; conventional therapy undefined.

Implications: The findings reported from this small randomized trial found that HCQ was not effective for COVID-19 treatment.



Note: adapted from Chen J *et al.* CT = computed tomography. HCQ = hydroxychloroquine. LFTs = liver function tests

No evidence of rapid antiviral clearance or clinical benefits with the combination of hydroxychloroquine and azithromycin in patients with severe COVID-19 infection. Molina *et al.* Médicine et Maladies Infectieuses (Mar 30, 2020)

Key findings:

- Among 11 patients treated with HCQ and azithromycin, 1 died, 2 were transferred to the ICU, and 1 was discontinued from the study due to dangerous cardiac QT prolongation.
- Among 10 surviving patients, 8 had detectable virus at least five days after starting treatment.

Methods: Clinical case series of 11 hospitalized patients with severe COVID-19, many with medical comorbidities: obesity (n=2), solid cancer (n=3), hematological cancer (n=2), HIV (n=1). All were administered HCQ (600 mg/day for 10 days) and azithromycin (500 mg on day 1 and 250 mg daily during days 2–5). Ten had fever and received supplemental O_2. *Limitations*: Small sample size; not randomized; no comparison group; no blinding; no description of baseline illness severity; limited data on clinical outcomes.

Implications: In this small, clinical case series of 11 patients treated with HCQ and azithromycin, a substantial fraction experienced severe outcomes from COVID-19; few of the surviving patients cleared the virus after five days of treatment.

PREPRINTS (NOT PEER-REVIEWED)

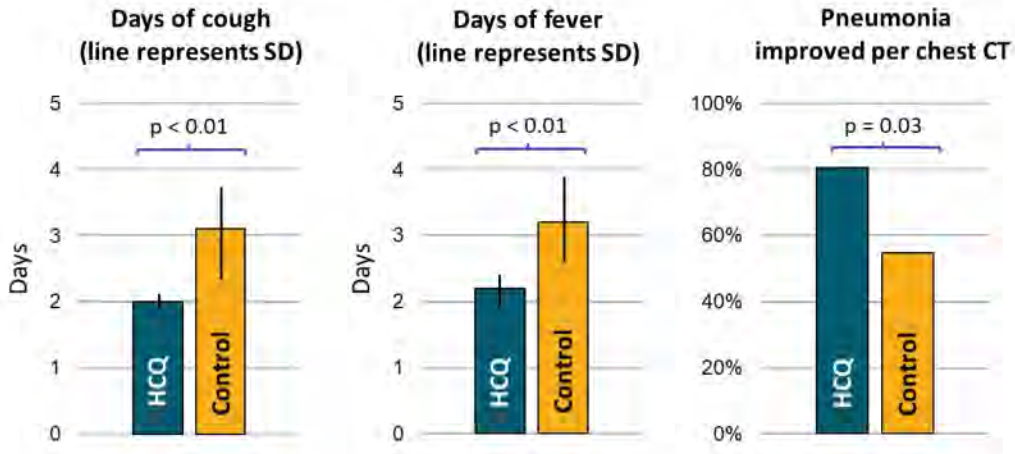
Efficacy of hydroxychloroquine in patients with COVID-19: results of a randomized clinical trial. Chen Z *et al.* medRxiv (Mar 30, 2020).

Key findings:

- Patients treated with HCQ (n=31) compared with control patients (n=31) experienced a shorter duration of fever (2.2 vs. 3.2 days, $p < 0.01$) and cough (2.0 vs. 3.1 days, $p < 0.01$), and demonstrated greater radiographic improvement in pneumonia by chest CT (81% vs. 55%%, $p = 0.03$)(Figure).
- No persons treated with HCQ progressed to severe illness (severe illness not defined) whereas 13% of control patients progressed. Among HCQ-treated patients, 6% experienced an adverse event (rash and headache) compared with none of the control patients.

Methods: Randomized trial of HCQ (200 mg twice daily for 5 days) plus standard therapy (supplemental O_2, antiviral agents, antibacterial agents, and immunoglobulin ± steroids) vs. standard therapy alone (control arm) among adults hospitalized with mild (SaO_2 >93%) COVID-19-associated pneumonia in Wuhan. Multiple reasonable exclusion criteria applied. *Limitations*: Small sample size; no viral burden data included; no description of randomization/enrollment; baseline severity of radiographic changes not described; inclusion of electrocardiogram (ECG) data would increase quality of the safety evidence.

Implications: The findings reported from this small unblinded randomized trial found that HCQ use was associated with improved clinical status. Data regarding SARS-CoV-2 burden were not reported.



Note: adapted from Chen Z *et al*. CT = computer tomography. HCQ = hydroxychloroquine. SD = standard deviation.

From:	Mike Merola <mike_merola@wswdc.com>
To:	Bright, Rick (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=53034752f35a4317aa74f46348442d39-Bright, Ric <Rick.Bright@hhs.gov>
Subject:	Pharma Company Assist with COVID-19 Response
Date:	2020/04/01 13:44:46
Importance:	High
Priority:	Urgent
Type:	Note

Director Bright – I hope this finds you well. Thank you for everything that you and your colleagues are doing to fight the pandemic.

I am reaching out to you today on behalf of Prashant Kohli of Rising Pharmaceuticals, located in East Brunswick, NJ and with distribution facilities in Somerset, NJ, to request a telephone meeting to update you on the company's capacities to assist in the effort to respond to the coronavirus disease 2019 (COVID-19) pandemic.

Rising Pharmaceuticals is a global pharmaceutical company and industry leader in marketing and distributing innovative pharmaceutical products including hydroxychloroquine and chloroquine. As you know, late last week the FDA announced Emergency Use Authorization for these two existing drugs, hydroxychloroquine sulfate and chloroquine phosphate, as health officials work to combat the rapid spread of COVID-19.

Should the FDA and other public health authorities determine that these products have broader use in response to COVID-19 as a result of clinical trials presently underway, Rising Pharmaceuticals wants to ensure that federal, state and public health authorities know that they have an existing available secure manufacturing pipeline that could be ramped up significantly to provide millions of courses of these treatments.

Rising has already committed to donating 1 million doses of these therapies in support of the immediate response to COVID-19 and consistent with the FDA Emergency Use Authority. Rising seeks your assistance to coordinate that donation as well as to better understand what the potential need may be so they may scale their operations in a timely and effective manner to meet that demand along with other suppliers.

Also of note, on March 27th, Rising announced its collaborative agreement with the Division of Infectious Disease and International Medicine at the University of Minnesota, Department of Infectious Disease which is conducting one of the key clinical trials exploring hydroxychloroquine as preventive treatment for COVID-19. More information on the partnership can be found here: https://protect2.fireeye.com/url?k=7a042456-26512d45-7a041569-0cc47adb5650-cfd0c7428c2118b1&u=https://risingpharma.com/category/press-releases/

We would appreciate scheduling a telephone call at your earliest convenience to introduce you to Rising and how they can assist with the national response to COVID-19 pandemic. We look forward to finding a mutually convenient time to talk.

Best regards, Mike Merola

Michael Merola
WSW
Managing Partner
409 7th St, NW, Suite 450
Washington, DC 20004
O: 202.589.0800
F: 202.589.1288
Winning Strategies. Proven Results.
Please check out our new website! https://protect2.fireeye.com/url?k=809e3383-dccb3a90-809e02bc-0cc47adb5650-11eb9b839729faa1&u=http://www.wswdc.com/

Sender:	Mike Merola <mike_merola@wswdc.com>
Recipient:	Bright, Rick (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=53034752f35a4317aa74f46348442d39-Bright, Ric <Rick.Bright@hhs.gov>
Sent Date:	2020/04/01 13:40:44
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RISING TO THE CHALLENGE:
CHLOROQUINE & HYDROXYCHLOROQUINE AS PART OF THE ARSENAL TO FIGHT COVID-19

Rising® PHARMACEUTICALS

April 2020

Confidential

WHO WE ARE

Deep roots in New Jersey:

- Headquartered in East Brunswick with a Distribution Center in Somerset – 112 employees
- Current ownership reconstituted the company in 2019

Secure and reliable supply chain for both medications

Existing federal contractor: Defense Logistics Agency and Department of Veterans Affairs

DONATING

Rising Pharmaceuticals is donating 1 million doses of Hydroxychloroquine Sulfate, USP Tablets between March and April to areas of greatest need through participating distributors and government agencies.

RISING PHARMACEUTICALS NEAR-TERM SUPPLY CAPACITY FOR BOTH DRUGS

- **Hydroxychloroquine:**
  - Capacity to supply ten-day 2 pill regimen by August 2020; treatment for 12 million patients
- **Chloroquine:**
  - Capacity to supply ten-day 2 pill regimen by August 2020; treatment for 6 million patients

CHLOROQUINE & HYDROXYCHLOROQUINE CURRENT MANUFACTURING CAPACITY OVERVIEW I

- **Chloroquine**
  - Natco Pharma, www.natcopharma.co.in headquartered in Hyderabad, India, a Special Economic Zone for export units, is our manufacture partner for Chloroquine US FDA ANDA #091621 and #090612
  - Supplies can NOT be diverted to domestic supply in India; EXPORT only
  - Natco has FDA approved finished dose and Active Pharmaceutical Ingredient (API) manufacturing facilities
    - Vertically integrated with own chloroquine API Drug Master File (DMF)
    - Also manufactures generic Tamiflu for a distributor who sells to the U.S. Government
  - Current Production Capacity:
    - Tablets: Ramping to ~50M tablets per month, totaling ~180M tablets by the end of August
    - Bottles: Ramping to ~2M bottles per month, totaling ~6M bottles by the end of August

CHLOROQUINE & HYDROXYCHLOROQUINE CURRENT MANUFACTURING CAPACITY OVERVIEW II

- **Hydroxychloroquine**
  - Laurus Labs, www.lauruslabs.com headquartered in Hyderabad, India, a Special Economic Zone for export units, is our manufacturing partner for Hydroxychloroquine Tablets US FDA ANDA #201959 (200MG)
    - Supplies can NOT be diverted to domestic supply in India; EXPORT only
    - Also vertically integrated with own Hydroxychloroquine API Drug Master File (DMF)
    - Tablets: Ramping to ~30M tablets per month, totaling ~250M tablets by the end of August
    - Bottles: Ramping to ~300K bottles per month, totaling ~2.5M bottles by the end of August
- Long Term Production Capacity based upon existing plant infrastructure is 800M-1B tablets monthly or 10-12B tablets annually
  - Capacity can be further expanded with additional infrastructure investment

ROBUST SUPPLY CHAIN NETWORK

Manufacturing	Distribution	Wholesalers	Retailers
Partners	Rising	Channel	Customer
India	**Rising's Warehouse** ▪ 125k sq. ft. warehouse and distribution center ▪ Distribution of Rising label generic products ▪ Capacity to expand	**McKesson** ▪ Ship Rising products to one location - McKesson's National Redistribution Center in Olive Branch, MS ▪ Ship Acetris products to McKesson's 30 forward Distribution Centers ("DCs")	**Walmart** ▪ Ship directly to 5 Walmart US distribution centers ▪ McKesson functions as secondary distributor
USA			
Canada	**3PL Provider A** ▪ 500k sq. ft. warehouse and distribution center ▪ Utilized for surge capacity and distribution of Rising label generic products	**Cardinal Health** ▪ Ship Rising products to one location – Cardinal's National Logistics Center in Groveport, OH ▪ Ship Acetris products to Cardinal's 23 forward DCs	**CVS** ▪ Ship directly to 11 CVS US distribution centers ▪ Cardinal functions as secondary distributor
France			
Ireland	**3PL Provider B** ▪ 250k sq. ft. warehouse and distribution center ▪ Distribution of Acetris label generic products to government customers	**AmerisourceBergen** ▪ Ship Rising products to one location - ABC's National Distribution Center in Lockbourne, OH ▪ Ship Acetris products to ABC's 25 forward DCs	**Walgreens** ▪ No direct shipments to Walgreens ▪ Products ship to Walgreens via ABC's network of DCs
China			

PARTNERSHIPS AND COLLABORATION

- Actively supporting research to help build better clinical guidelines
- Collaborative agreement with the University of Minnesota, Department of Infectious Disease on a clinical trial exploring hydroxychloroquine as preventive treatment for coronavirus disease 2019 (COVID-19).
- University of Minnesota study is underway on the efficacy for treatment of COVID-19 patients
- Pending collaborative agreement with Memorial Sloan Kettering for COVID-19 clinical trial

UNDERSTANDING AND RESPONDING TO GOVERNMENT NEED AND DEMAND: HHS, BARDA, SNS, FDA, DOD, FEMA

- Facilitating our donation to areas of greatest need consistent with health authorities guidance
- Planning for near-term demand to make necessary manufacturing and supply chain decisions
- Understanding FDA Emergency Use Authorization
- Other?

THANK YOU & CONTACT INFORMATION

- Prashant Kohli

  Rising Pharmaceuticals

  pkohli@rising.com

  609-649-9272

- Mike Merola

  Winning Strategies

  Mike_Merola@wswdc.com

  202-669-2960

Insistence on Prevention and Treatment

--Hubei's Combat against COVID-19 Outbreak

Mr. LIU Dongru

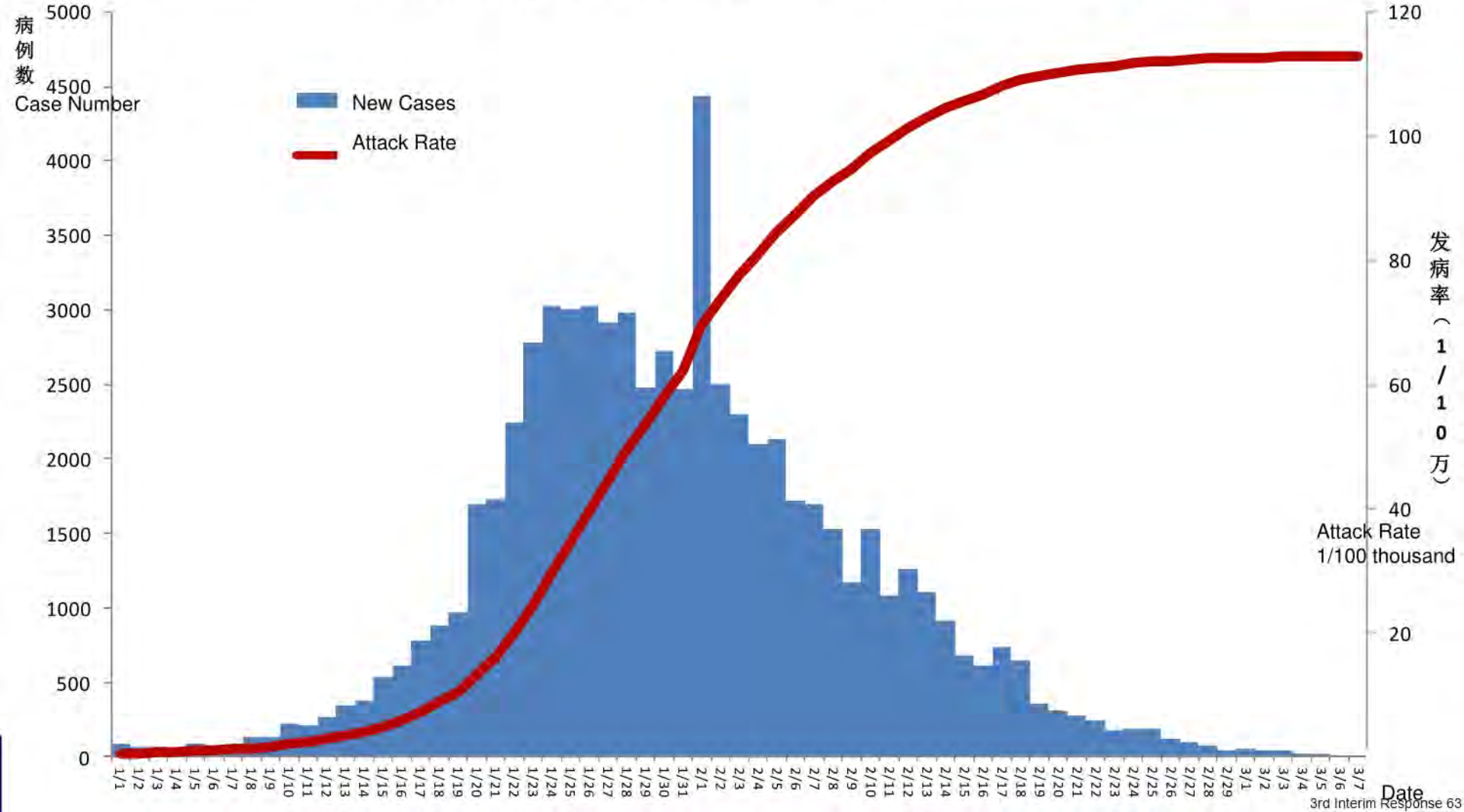
Health Commission of Hubei Province

March 12, 2020

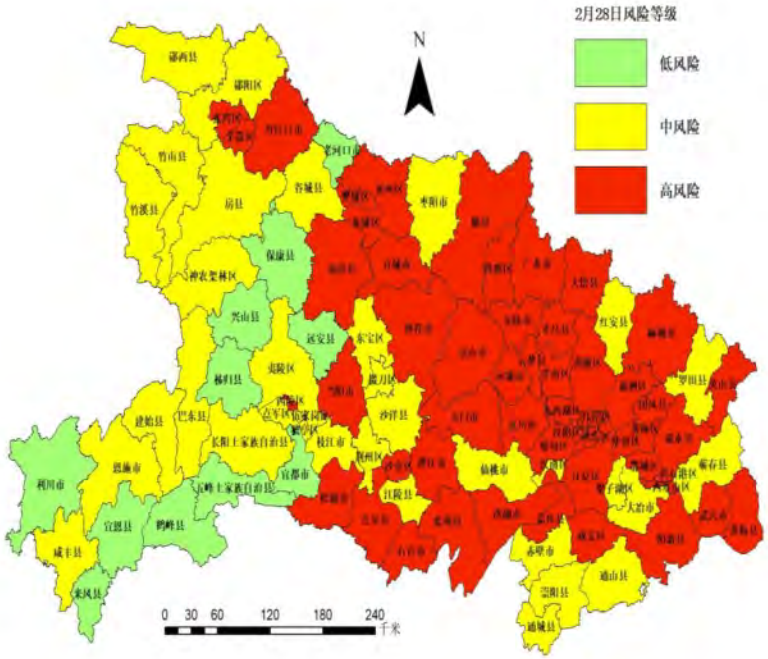
Major Measures

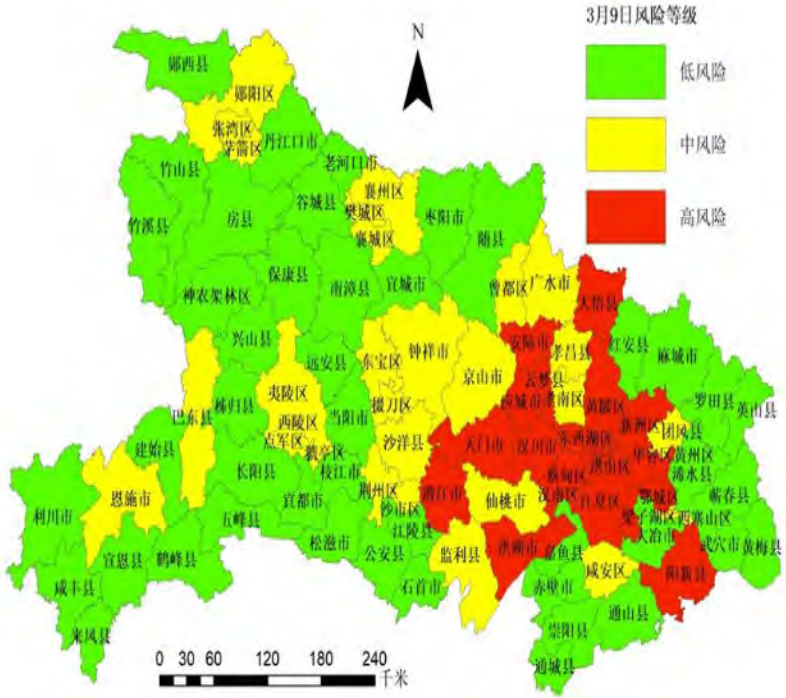
- To fully prevent and contain the epidemic and follow the principle of “four earlys”
- To fully treat and cure patients and follow the principles of “four concentrations”
- To fully construct the closed cycles of information and work
- To fully build epidemic-free communities and residential compounds

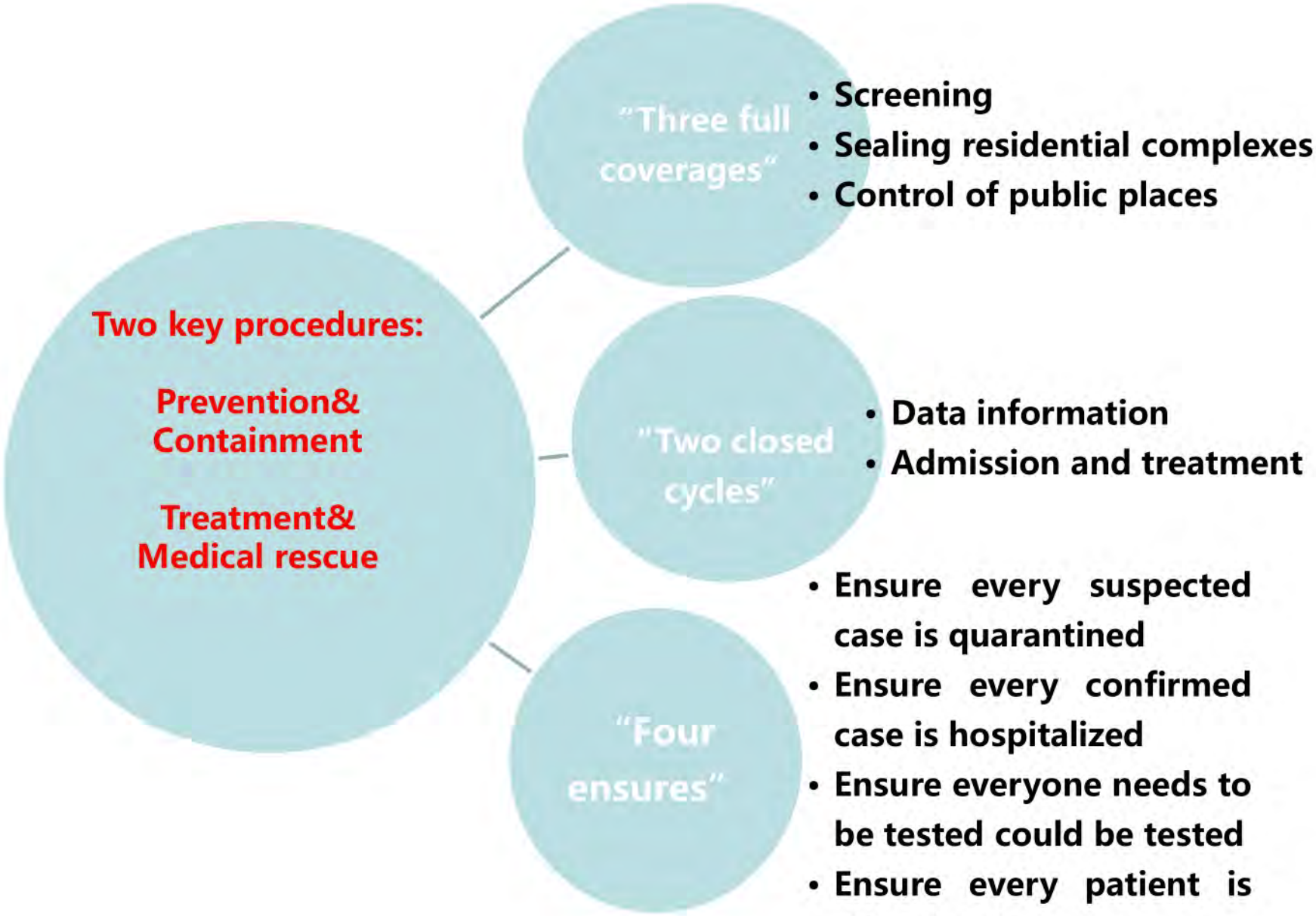
- The epidemic situation in Hubei province continues to improve.
- As of March 11, daily reported confirmed cases in Wuhan are under 20 for 5 straight days, and 0 reported cases in other cities for 7 straight days. The day of March 11 reported 8 confirmed cases.



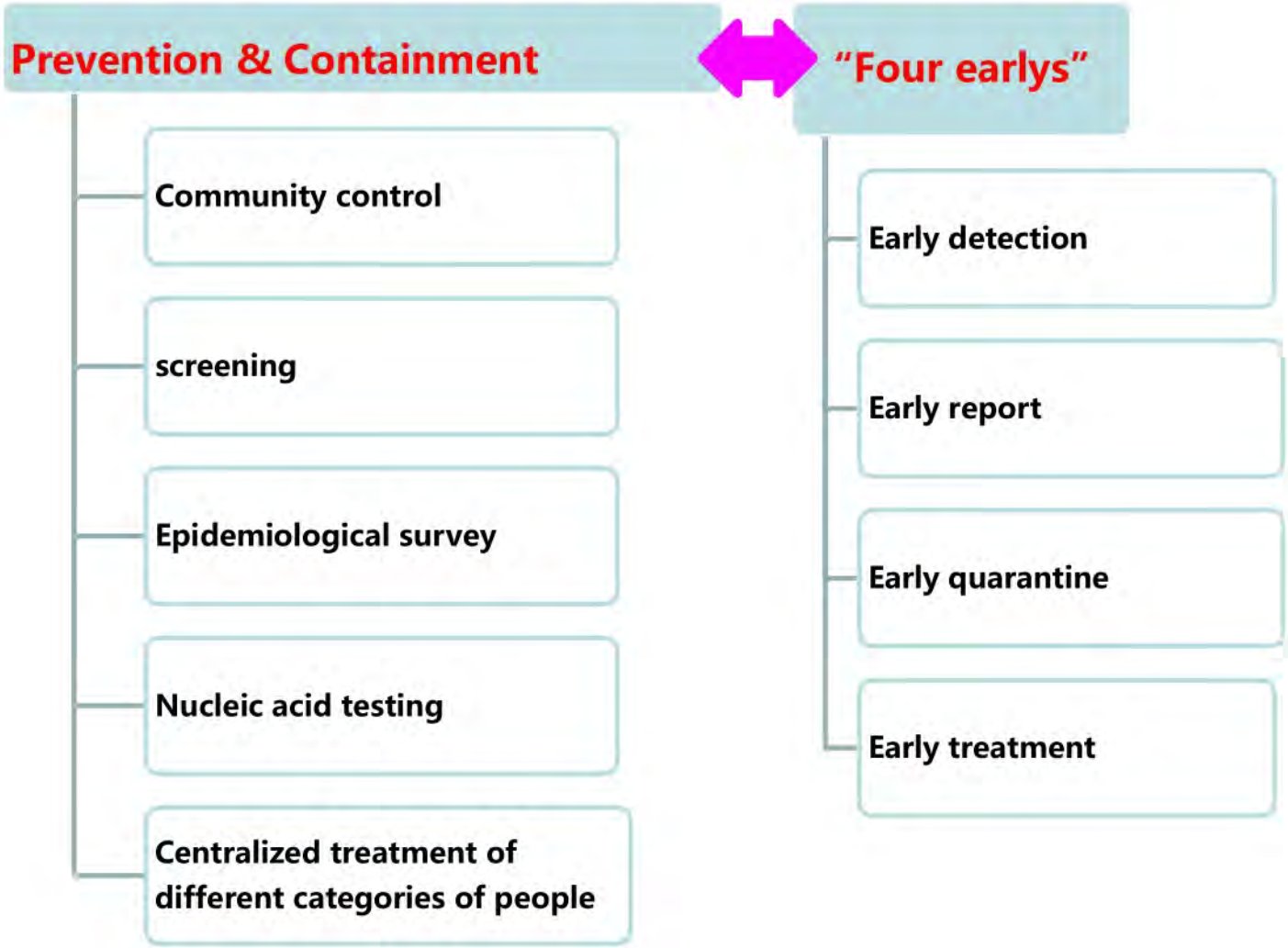
- The number of low-risk districts is 45, increasing from 11 in late February.
- Low and medium-risk districts account for 84 percent of all districts.






Two key procedures:
Prevention&
Containment
Treatment&
Medical rescue
"Three full coverages"
• Screening
• Sealing residential complexes
• Control of public places
"Two closed cycles"
• Data information
• Admission and treatment
"Four ensures"
• Ensure every suspected case is quarantined
• Ensure every confirmed case is hospitalized
• Ensure everyone needs to be tested could be tested
• Ensure every patient is attended to

Prevention and containment in full force on the principle of "four earlys"



villages

settlements

24/7 self-isolation management

communities

residential compounds

Asymptomatic cases

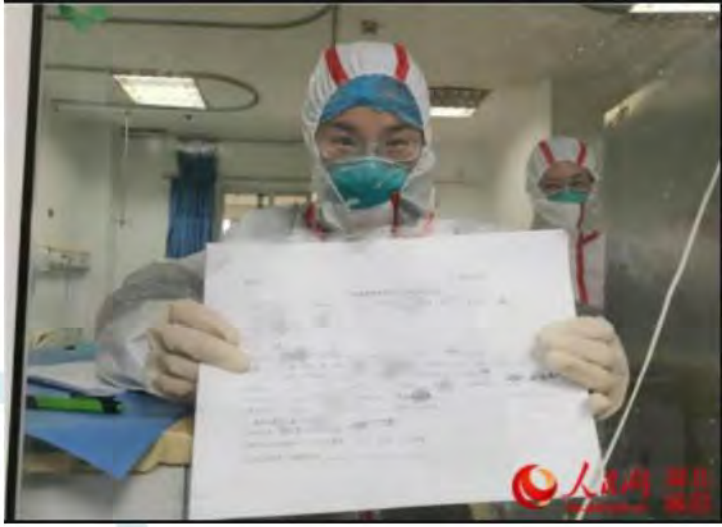
Close contacts

Individual-based comprehensive check and screening

Suspected cases

Confirmed cases

Case investigation of 67781 person



Activities

Community

Epidemiological survey

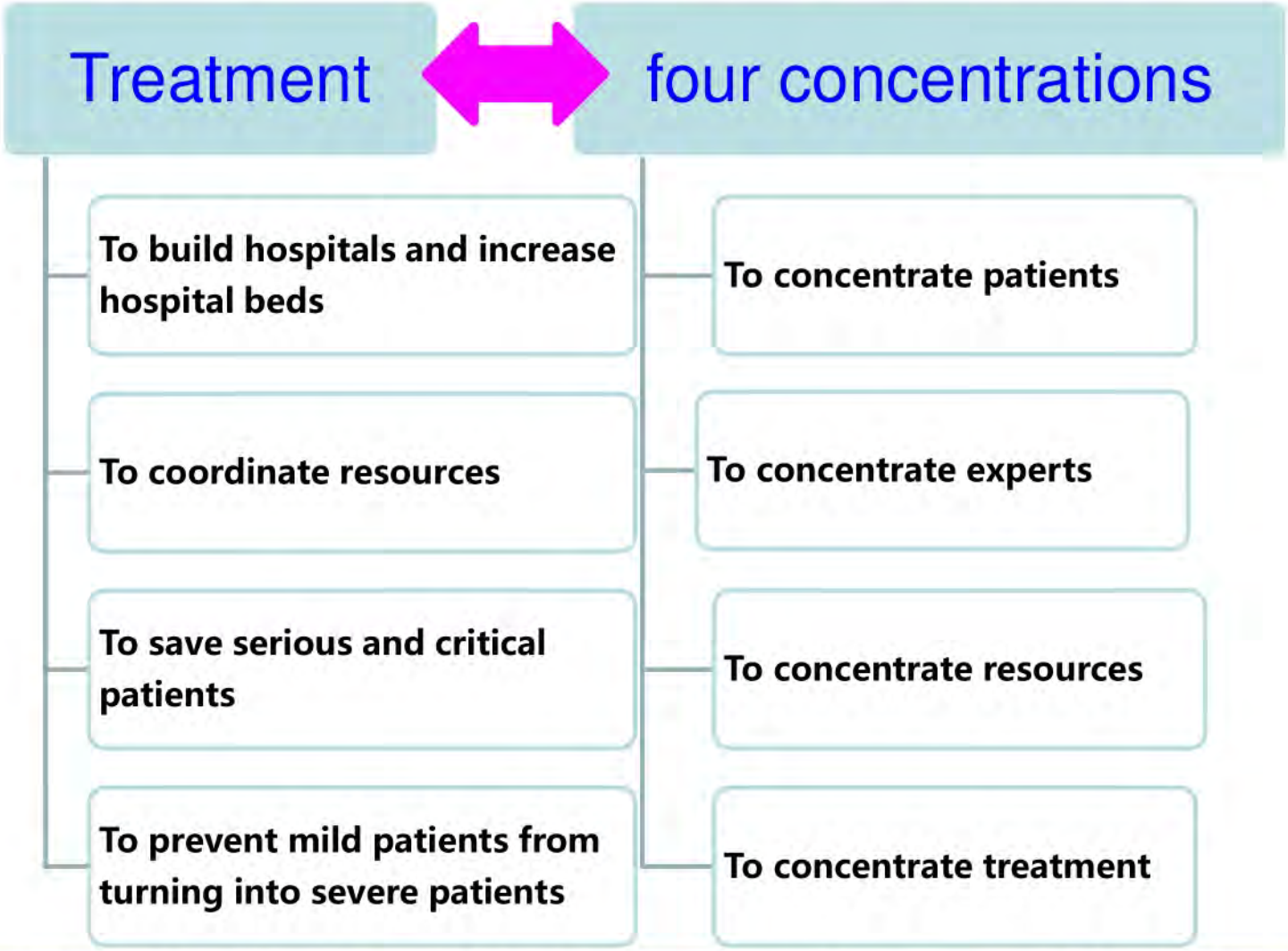
Disease control and prevention

Close contacts

Trail management of 274790 people

- Nucleic acid testing for all the "four categories of people”.
- An accumulated total of 1,215,690 people were tested in Hubei province.
- "four categories of people ” receive different levels of centralized treatment: all confirmed cased are centralized admitted; all suspected case are centralized treated; all patients with fever are centralized isolated for observation; and all close contacts are centralized quarantined for observation.

Treatment and medical rescue with full efforts on the principle of "four concentrations"



238
designated
hospitals

16
temporary
hospitals

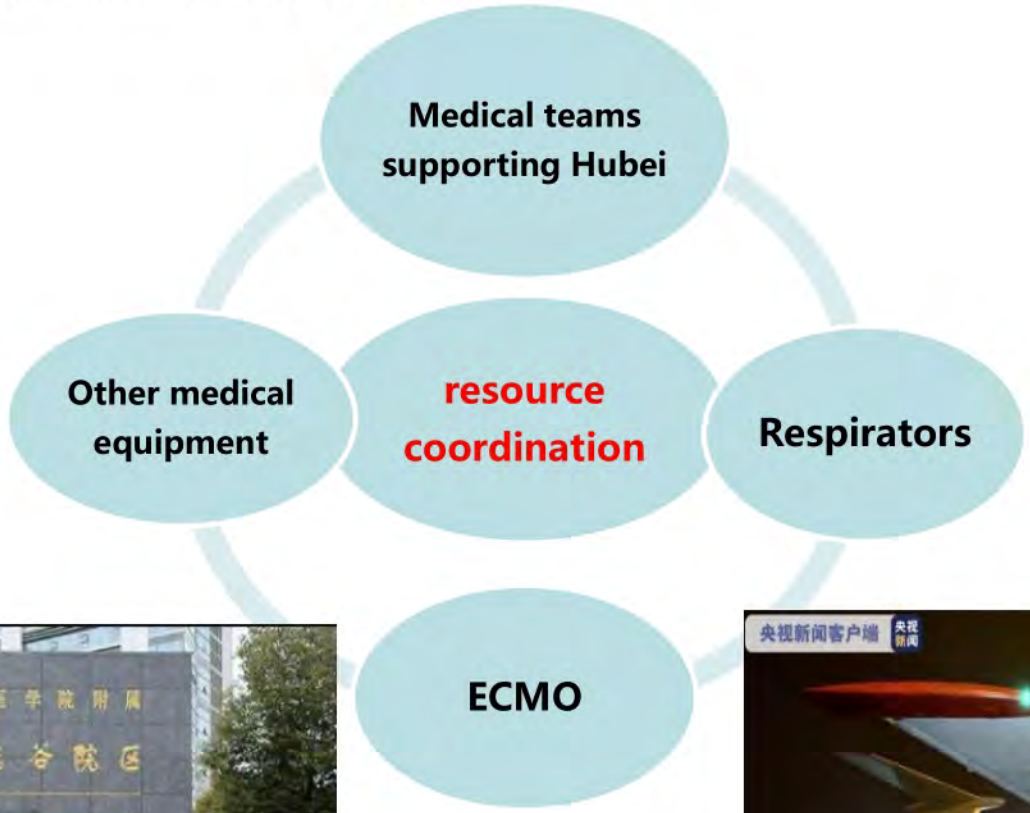
3920
isolated
sites

To build hospitals
and increase
hospital beds

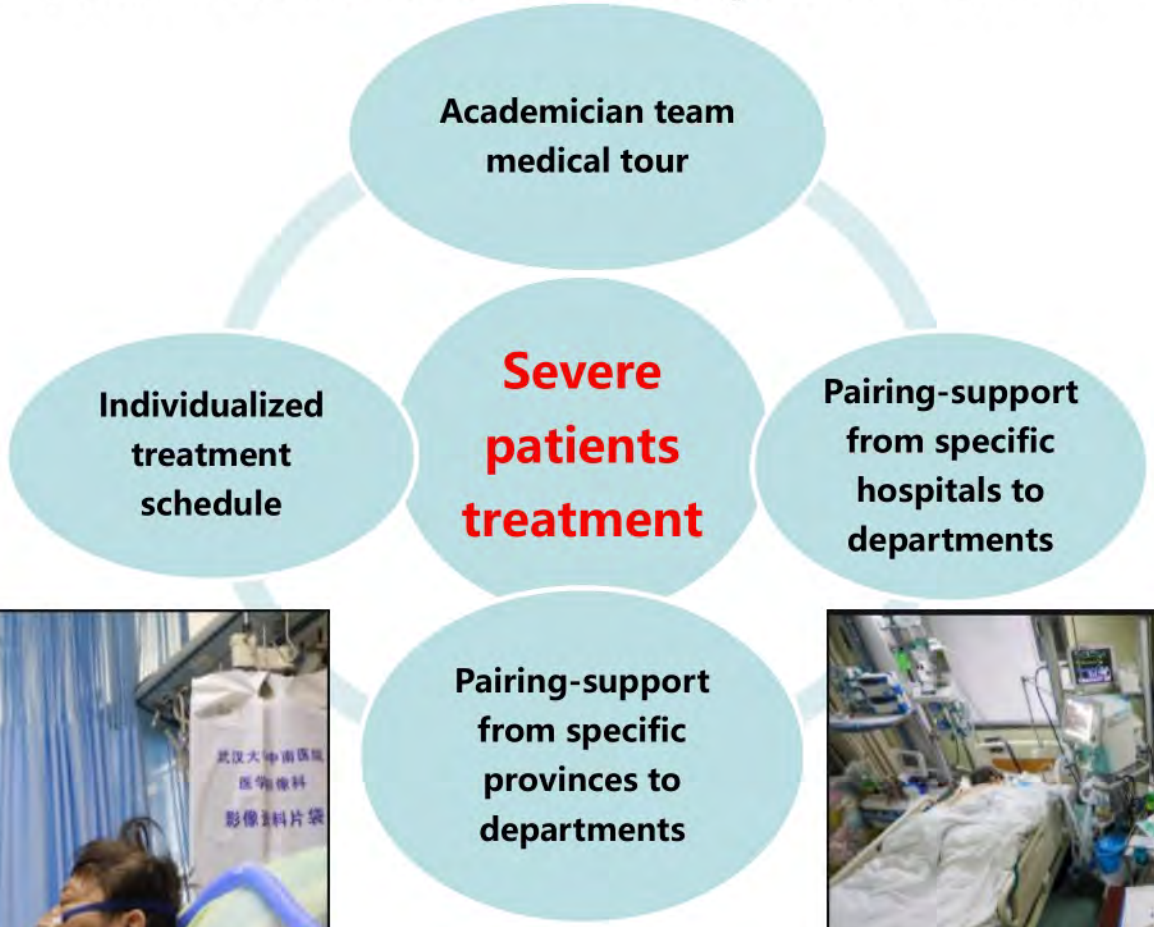
91143
hospital beds

湖北省卫生健康委员会 Health Commission of Hubei Province

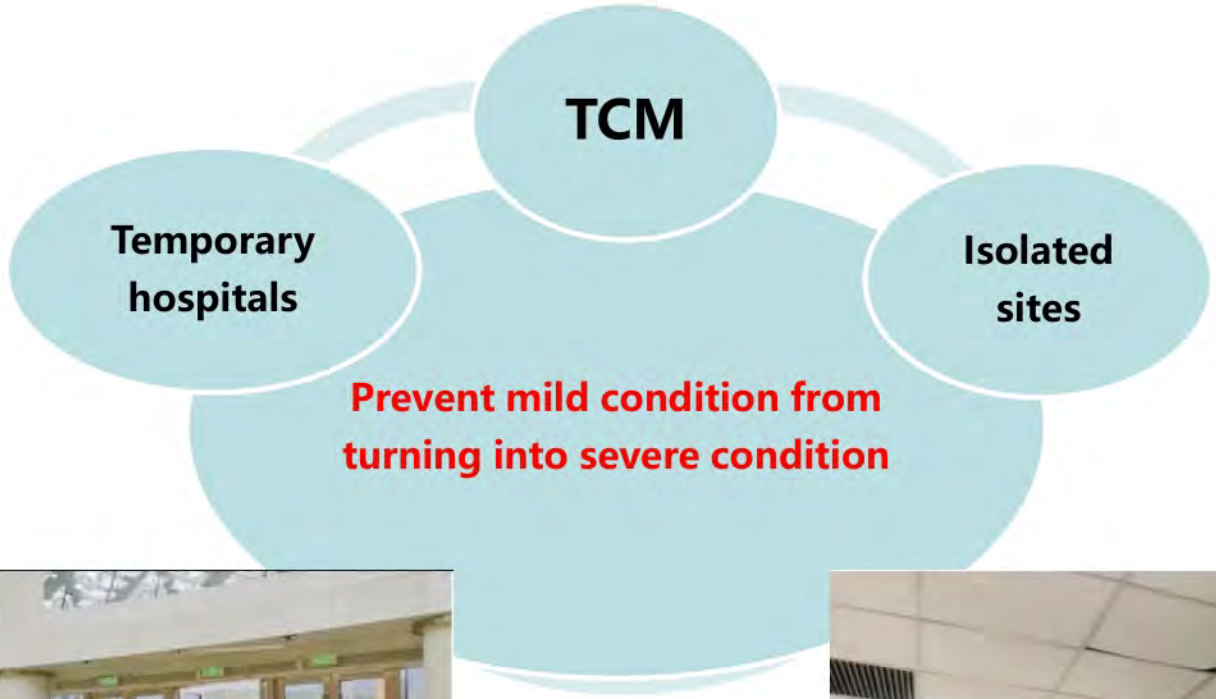
- A total of 395 batches of medical teams and 42,821 medical personnel are dispatched to Hubei Province, mainly supporting the key area of Wuhan, helping other cities and counties at the same time.



- **Severe patients are concentrated in top comprehensive hospitals, with about 9,000 beds open for them.**



- To make full use of TCM and promote the three agreed prescriptions
- The usage rate of TCM exceeds 99.93% in temporary hospitals

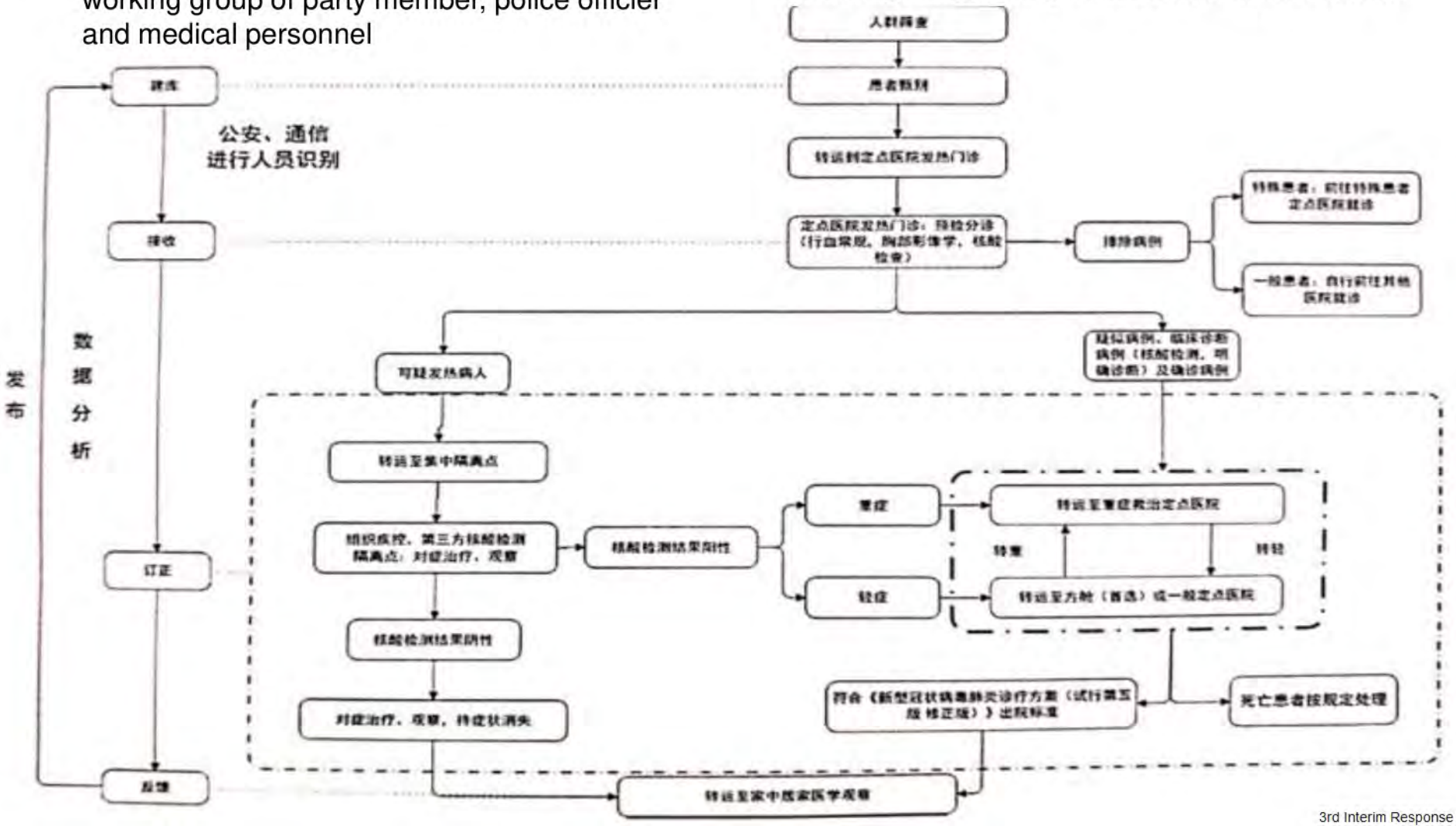


To fully construct the closed cycles of information and work

Information and work flow chart

Info closed cycle: setting up a three-member working group of party member, police officier and medical personnel

work closed cycle: centering on the four links of screening, transferring, admission, and treatment



To proactively build epidemic-free communities

135，9.6%

epidemic-free communities

as of 18:00, Mar. 8

3021，42.5%

epidemic-free residential compounds

as of 16:00, Mar. 8

1350，69.5%

epidemic-free villages

as of 16:00, Mar. 8.

湖北省卫生健康委员会 Health Commission of Hubei Province

Thanks for listening

AGENDA

COVID-19

Joint HHS / FEMA Interagency VTC

3/29/2020 at 12:30 p.m. ET

Call-in Number: 1-800-320-4330; Muted PIN: (b)(6)

Closed captioning available.

(Complete connection instructions provided below.)

BLUF:

1. **Situation Update** (Centers for Disease Control and Prevention)
    a. US Domestic: 123,942 cases/19,748 new, 2,139 deaths/466 new
        i. New York State: 22,552 cases/3,315, 107 deaths/11 new
        ii. New York City: 30,756 cases/4059 new, 672 deaths/222 new
            1. 13-14% hospitalizations
    b. Globally: 571,876 cases/62,514 new, 26,494 deaths/3,159 new

2. **Lines of Effort**
    a. Medical Countermeasures (BARDA)
        i. Driving partnerships with industry for diagnostics and vaccine
        ii. Progress on several clinical studies
            1. Remdesivir, 100 patients this week
            2. Vaccine study: 20 patients this week
    b. Medical Diagnostics
        i. 895,000 samples have been tested, looking at major biotech platform and acquiring data on burn rate.
    c. Modeling
        i. New model coming online with new assumptions and more data about the pandemic and resources
            1. Including worldwide and US state by state data
            2. Tracking PPEs, ventilators, hospitalizations, bed use, and ICU
                a. Modeling when these will peak out and decrease
                b. Daily death rates will inform the model

3. **Interagency Support**
    a. Prepared guidance (Questions & Answers) about beds and ventilators for Regions
        i. HHS/FEMA representatives need to follow this guidance and respond accordingly to state and local reps requesting excess numbers of ventilators

4. **WH National Security Council (NSC)**
    a. Also urges Region managers to speak directly with governors

AGENDA

Objective

- To discuss COVID-19 and related Federal response operations

Opening Comments

- HHS / FEMA

Situation Update (Centers for Disease Control and Prevention)

- US Domestic: 123,942 cases/19,748 new, 2,139 deaths/466 new
  - New York State: 22,552 cases/3,315, 107 deaths/11 new
  - New York City: 30,756 cases/4059 new, 672 deaths/222 new
    - 13-14% hospitalizations
- Globally: 571,876 cases/62,514 new, 26,494 deaths/3,159 new

Lines of Effort

- Community Based Testing
  - Tested 29,000 people, 18% COVID-19 positive
  - Moving CBT tests to the states by April 8th
- Healthcare Systems Resilience
  - Pushing out pre-decisional tool for low and medium acuity alternative care sites
- Supply Chain
  - Sending more PPEs to states
- Medical Countermeasures (BARDA)
  - Driving partnerships with industry for diagnostics and vaccine
  - Progress on several clinical studies
    - Remdesivir, 100 patients this week
    - Vaccine study: 20 patients this week
- Medical Diagnostics
  - 895,000 samples have been tested
  - looking at a major biotech platform and acquiring data on burn rate
- Data Analytics
  - Model on ventilators obtained information from New York City and tracking the curve
    - And have data on bed use and hospitalizations
  - Hospitalizations are higher than predicted
- Communications/Messaging (National Joint Information Center)
  - Pushed out press release on National Guard Title 32 status
  - Pushing out details on supply chain
  - Driving protective messaging to new hotspot areas in the US
- Modeling
  - New model coming online with new assumptions and more data about the pandemic and resources (including worldwide data)
    - And state by state data
    - PPEs, ventilators, hospitalizations, bed use, ICU
      - When they will peak out and when they will decrease
      - Daily death rate will inform the model

HHS/FEMA Regional Priorities/Concerns

- Region II
  - Mortuary response team arrived in New York
  - CDC recommend everyone in the tri state area to avoid non-essential travel for the next 14 days.
  - New York State asked for 80,000 medical personnel but withdrew request following consultation with FEMA officials
- Region X
  - Finalizing contract to set up Field Medical Hospital with DoD

    - Working Title 32 requests for Washington State, Oregon, and Alaska
    - Coordinating with states for final push of SNS
- Region IX
    - 1st day average % increase is lower than the national average
    - SNS for outer islands will arrive in Hawaii today and later to outer islands
    - Navajo Nation and the Tuba Title 638 medical facility had a substantial increase of ICU patients
        - Staffing shortfalls with medical staff diagnosed with COVID-19
- Region IV
    - Number of confirmed cases and fatalities across region increased over 20%
    - Completing site assessments for ACSs
    - 142 active RRFs
    - More Title 32 requests in process
- Region VI
    - Cases increased 24% region wide
    - Title 32 processed for Louisiana
    - Working with governors on availability of test kits and reagent
        - Monitoring burn rate of test kits and PPE
- Region III
    - Processing requests from DC and Pennsylvania
    - Sorting out test kit issues in Maryland
    - Looking for guidance on CBT
    - All jurisdictions received supplies
- Region I
    - Connecticut understand to submit request when they are critical within 72 hours
    - Tribal concerns about purchasing supplies ahead of model
    - Working with models for supplies
    - 8 PHS officers began working with Region I team today
- Region V
    - Working with Governors about PPEs and respirator technology needing FDA approval
    - Request from Ohio for disaster declaration
    - Working with state and jurisdictions on RRFs and SNS
        - Chicago in need of medical personnel
- Region VIII
    - Colorado major declaration last night. Working with North Dakota and Montana now
    - Working with other states in the Region on unmet needs
    - ACF are being established
    - Acute and critical bed needs are essential and the Region is requesting guidance
- Region VII
    - Number of cases increase 25%, consistent with national average
    - Missouri is main effort now and Title 32 request is still pending
    - Proceeding with site inspections

Interagency Support

- Prepared guidance (Questions and Answers) about beds and ventilators for Regions
    - HHS/FEMA representatives need to follow this guidance and respond accordingly to state and local reps requesting excess numbers of ventilators
- Emergency Support Functions (by exception)
    - ESF 3: completing assessments across the nation
- Veterans Affairs
    - New York Harbor health system is providing additional beds
    - Finalizing MAs for VA support to Javid center, including telehealth and pharmacy assistance
- Department of Defense, Office of the Secretary of Defense
    - Providing details on medical capabilities to HHS/FEMA

- U.S. Northern Command
  - Focus on deployment of Navy medical facilities to New Orleans and Dallas
  - Deploying mortuary affairs company
  - Washington State event center has been established
- National Guard Bureau
  - 15,000 soldiers supporting COVID-19
  - Thank you to FEMA for pushing out Title 32 guidance today
- Defense Logistics Agency
  - Tracking arrival of 300,000 commercial shelves

WH National Security Council (NSC)

- Monitoring actions with international partners
- Urge Region managers to speak directly with governors

Closing Comments

- FEMA / HHS
  - Thank you to everyone for all of your efforts.

From:	Ventura, Christy (OS/ASPR/BARDA) (CTR) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=9BB949CACA464329823CA3CF77654A06-VENTURA, CH <Christy.Ventura@hhs.gov>
To:	Bright, Rick (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=53034752f35a4317aa74f46348442d39-Bright, Ric <Rick.Bright@hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0fd5845defda4dc0bb45f8fac629cf09-Disbrow, Ga <Gary.Disbrow@hhs.gov>; Lambert, Linda (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ce6824b6a92a4a4e893ea7b54e17eb3c-Lambert, Li <Linda.Lambert@hhs.gov>
CC:	MCM Task Force /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=49010f8ab3ab4aed868a72c707c08d08-MCM Task Fo <MCMTaskForce@hhs.gov>
Subject:	MCM Task Force updates for Thursday
Date:	2020/04/15 19:32:57
Priority:	Normal
Type:	Note

Rick, Gary, Linda,

Tomorrow's updates for the MCM Task Force are shown here. I will update the enrollment numbers for the ACTT trial when I receive them. Please let us know if you have any concerns.

Accomplishments

- ACTT1 clinical trial to test remdesivir for treatment of COVID-19: 759 (+55) new patients at 67 (+2) sites, including 9 patients at 5 military treatment facilities, in last 24 hrs (target = 700)
- New award to initiate a Phase 3 clinical trial to test hydroxychloroquine and intravenous famotidine (Pepcid) for treatment of hospitalized COVID-19 patients
- 2230 (+34) market research submissions and 215 (+5) CoronaWatch meetings held

Currently working:

- Continuing to enroll patients in clinical trials to evaluate vaccines and therapeutics for COVID-19
- Accelerating vaccine manufacturing efforts to ensure rapid delivery of vaccines
- Continuing to identify lead antibody treatment candidates for further development and manufacturing

Thanks
Christy

--
Christy L. Ventura, Ph.D.
Tunnell Government Services
Executive Secretary, SARS-CoV-2 Medical Countermeasures Task Force
Project Manager, CBRN/BARDA/ASPR/HHS

O'Neill 23L05
Office: 202-730-8643
Cell: (b)(6)

Sender:	Ventura, Christy (OS/ASPR/BARDA) (CTR) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=9BB949CACA464329823CA3CF77654A06-VENTURA, CH <Christy.Ventura@hhs.gov>
Recipient:	Bright, Rick (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=53034752f35a4317aa74f46348442d39-Bright, Ric <Rick.Bright@hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0fd5845defda4dc0bb45f8fac629cf09-Disbrow, Ga <Gary.Disbrow@hhs.gov>; Lambert, Linda (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ce6824b6a92a4a4e893ea7b54e17eb3c-Lambert, Li <Linda.Lambert@hhs.gov>; MCM Task Force /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=49010f8ab3ab4aed868a72c707c08d08-MCM Task Fo <MCMTaskForce@hhs.gov>
Sent Date:	2020/04/15 19:32:55
Delivered Date:	2020/04/15 19:32:57
Message Flags:	Unread

From:	Erlandson, Karl (OS/ASPR/BARDA) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7F0EF5014C63481787389EB185DA5E5F-ERLANDSON, <Karl.Erlandson@hhs.gov>
To:	Johnson, Robert (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0851e89240324306b78740a4a60745e2-Johnson, Ro <Robert.Johnson@hhs.gov>
CC:	Donis, Ruben (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=af00dcf720cb429f8e2accbe06ee32ff-Donis, Rube <Ruben.Donis@hhs.gov>; Armstrong, Kimberly (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5b778c7e17734740b14fbae4d3ed652c-Armstrong, <Kimberly.Armstrong@hhs.gov>; Oshansky, Christine (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d7bd764440b44b06af644cdcd22e42d6-Oshansky, C <Christine.Oshansky@hhs.gov>; Bright, Rick (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=53034752f35a4317aa74f46348442d39-Bright, Ric <Rick.Bright@hhs.gov>
Subject:	RE: Response on sequencing question from Dr. Kadlec
Date:	2020/03/08 10:12:59
Priority:	Normal
Type:	Note

I am speaking directly with Natalie Thornburg and Sue Tong (who do the virology and the sequencing, but only have clinical data from the time the sample was taken). Based on our discussions, the CDC lab teams in Atlanta are now working with the CDC response teams on the ground to collect current data on patients who have been sequenced. They will also prioritize samples from fatal cases and those that received remdesivir.

From Natalie:
"My lab personally does not receive patient outcome when we receive a specimen, but I believe that data is being aggregated by our response teams. I can specifically ask them to alert me if we have specimens from fatalities and prioritize those. I can not promise having that in 3-4 weeks, though.

Our sequencing lab is working on collecting the sequencing serially drawn specimens from the first dozen or more cases. Some of them did receive remdesivir. We can provide that information once it's generated."

Cell: (b)(6)
Work: 202 692-4676

FOUO, Procurement Sensitive

From: Johnson, Robert (OS/ASPR/BARDA) <Robert.Johnson@hhs.gov>
Sent: Sunday, March 8, 2020 8:31 AM
To: Erlandson, Karl (OS/ASPR/BARDA) <Karl.Erlandson@hhs.gov>
Cc: Donis, Ruben (OS/ASPR/BARDA) <Ruben.Donis@hhs.gov>; Armstrong, Kimberly (OS/ASPR/BARDA)

<Kimberly.Armstrong@hhs.gov>; Oshansky, Christine (OS/ASPR/BARDA) <Christine.Oshansky@hhs.gov>
Subject: FW: Response on sequencing question from Dr. Kadlec

fyi

Robert Johnson, Ph.D.
Director, Influenza and Emerging Infectious Diseases Division
Biomedical Advanced Research and Development Authority
BARDA
Assistant Secretary for Preparedness and Response ASPR
Department of Health and Human Services
330 Independence Avenue, S.W. Room 640 G
Washington, D.C. 20201
Office: 202-401-4680
Cell: (b)(6)
email: Robert.Johnson@HHS.gov

From: Marble, Eric S. (CDC/DDPHSIS/CPR/DEO) <mre3@cdc.gov>
Sent: Friday, March 6, 2020 7:54 PM
To: Knutson, Donna (CDC/DDNID/NCEH/OD) <dbk2@cdc.gov>; Imbriale, Samuel (OS/ASPR/SIIM) <Samuel.Imbriale@hhs.gov>; Bright, Rick (OS/ASPR/BARDA) <Rick.Bright@hhs.gov>
Cc: Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Lambert, Linda (OS/ASPR/BARDA) <Linda.Lambert@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) <Robert.Johnson@hhs.gov>
Subject: Re: Response on sequencing question from Dr. Kadlec

Hi Donna,
Sure. I will go back to lab TF with the detailed request below. Also include science team for input.
Eric

Eric S. Marble
Global Emergency Management Capacity Development Branch
Center for Preparedness and Response
Centers for Disease Control and Prevention
1600 Clifton Road NE, Bldg 21, Mail Stop D-75, Atlanta, GA 30333
Work Phone: +1 (404) 639-2597

Mobile: +(b)(6)
Email: emarble@cdc.gov

From: Knutson, Donna (CDC/DDNID/NCEH/OD) <dbk2@cdc.gov>
Sent: Friday, March 6, 2020 7:42:44 PM
To: Imbriale, Samuel (OS/ASPR/SIIM) <Samuel.Imbriale@hhs.gov>; Bright, Rick (OS/ASPR/BARDA) <Rick.Bright@hhs.gov>
Cc: Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Lambert, Linda (OS/ASPR/BARDA) <Linda.Lambert@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) <Robert.Johnson@hhs.gov>; Marble, Eric S. (CDC/DDPHSIS/CPR/DEO) <mre3@cdc.gov>
Subject: Re: Response on sequencing question from Dr. Kadlec

Eric - can you ask Lia if they could share new data that is in the data set they review as it become available? Also, we might need to ask the science desk to examine the ability to review the metadata as requested from Dr Bright. Can you work on that one, too?

Donna Knutson, PhD
Centers for Disease Control and Prevention
(b)(6)

From: Imbriale, Samuel (OS/ASPR/SIIM) <Samuel.Imbriale@hhs.gov>
Sent: Friday, March 6, 2020 7:38:21 PM
To: Bright, Rick (OS/ASPR/BARDA) <Rick.Bright@hhs.gov>
Cc: Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Lambert, Linda (OS/ASPR/BARDA) <Linda.Lambert@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) <Robert.Johnson@hhs.gov>; Knutson, Donna (CDC/DDNID/NCEH/OD) <dbk2@cdc.gov>; Marble, Eric S. (CDC/DDPHSIS/CPR/DEO) <mre3@cdc.gov>
Subject: Re: Response on sequencing question from Dr. Kadlec

Copy, Rick.

Donna and Eric - see below. Looks like this was helpful but need to figure out recurring info stream. Can you assist?

Sam

V/r,

Sam Imbriale, MPH
Director, Information Management Division
Director (Acting), Secretary's Operations Center
Cell:(b)(6)
Samuel.imbriale@hhs.gov
Sent from mobile device - please excuse typos.

On: 06 March 2020 19:32,
"Bright, Rick (OS/ASPR/BARDA)" <Rick.Bright@hhs.gov>wrote:

SAM, thank you. We greatly appreciate your assistance.

I'll get a detailed read from our sme in the morning.

We are asking for access to sequences in real time as the are created by cdc and other labs (shared with cdc) to be able to review for evolutionary changes that could have a significant impact on mcm development.

We are especially interested in sequences from recently deceased patients.

Most critically, we are asking cdc to link sequences (GISAID ID) to metadata (age, sex, outcome, etc) from US cases.

We are still not getting this information that is extremely critical to assist us in design, development and risk management for dx, rx and vx mcms.

If they can have senior clearance to share all such data with our sme, I'm confident the working teams can communicate effectively.

Thanks for helping us to bridge a solid working relationship and open exchange of data. It is all kept very confidential; fouo and not shared externally.

Much appreciated. Rick.

On Mar 6, 2020, at 6:59 PM, Imbriale, Samuel (OS/ASPR/SIIM)
<Samuel.Imbriale@hhs.gov>wrote:

BARDA - is this what you wanted?

V/r,

Sam Imbriale, MPH
Director, Information Management Division
Director (Acting), Secretary's Operations Center
Cell: (b)(6)
Samuel.imbriale@hhs.gov

Sent from mobile device - please excuse typos.

From: "Marble, Eric S. (CDC/DDPHSIS/CPR/DEO)" <mre3@cdc.gov>
Subject: Response on sequencing question from Dr. Kadlec
Date: 06 March 2020 18:36
To: "Imbriale, Samuel (OS/ASPR/SIIM)" <Samuel.Imbriale@hhs.gov>, "Greene, Jonathan (OS/ASPR/EMMO)" <Jonathan.Greene@hhs.gov>

Sam / Jonathan,

In the 0800 briefing, Dr. Kadlec discussed the need for a copy CDC results (sequencing) for the Washington cases; I believe it was BARDA that needed the results.

I shared this request with Atlanta and received the following response below from the Lab Task Force along with the diagram attached.

When you have the opportunity, please look this over and let me know if this meets his needs, or forward for his review.

Thank you,
Eric

Eric S. Marble
Center for Preparedness and Response (CPR) | Division of Emergency Operations (DEO)
Centers for Disease Control and Prevention
1600 Clifton Rd NE, Bldg 21, Mail Stop H21-4, | Atlanta, GA 30333
Work Phone: +1 (404) 639-2597 | Mobile: (b)(6) Email: mre3@cdc.gov

---

From: Haynes, Lia (CDC/DDPHSIS/CPR/OD) <loh5@cdc.gov>
Sent: Friday, March 6, 2020 6:26 PM
To: Dreyzehner, John (CDC/DDPHSIS/CPR/OD) <PWN3@cdc.gov>; Marble, Eric S. (CDC/DDPHSIS/CPR/DEO) <mre3@cdc.gov>; Frank, Mark (CDC/DDPHSIS/CPR/DEO) <mqf1@cdc.gov>
Cc: Kennedy, David N. (CDC/DDPHSIS/CPR/DEO) <guf5@cdc.gov>; Bermingham, John (CDC/DDPHSIS/CPR/DEO) <uvk7@cdc.gov>; CDC IMS Planning Section Chief (CDC) <eocplans@cdc.gov>; Kuhnert-Tallman, Wendi (CDC/DDID/OD) <wdk1@cdc.gov>
Subject: RE: 0815 SOC OPS brief

Good evening Eric,

I spoke with our Pathogen Discovery Team Leader, Dr. Sue Tong, regarding your request. Her sequencing lab has not received the recent WA samples yet. She submitted the whole genome sequence for the first WA case to GenBank and GISAID. Dr. Tong searched through GISAID and it looks like there are sequences from recent WA cases (EPI413458, EPI 413457, EPI 413486, EPI 412970, EPI 413456, EPI 413487, EPI 413455, EPI 413025). All those WA sequences were submitted by local labs in WA. Dr. Tong has provided the attached tree with all WA case sequences except the EPI 413025 and it shows that the sequences are clustered together.

Respectfully,

Lia

Lia Haynes Smith, PhD
Lab Task Force Co-Lead
<176seq_HKY_03052020.pdf>

Sender:	Erlandson, Karl (OS/ASPR/BARDA) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7F0EF5014C63481787389EB185DA5E5F-ERLANDSON, <Karl.Erlandson@hhs.gov>
Recipient:	Johnson, Robert (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0851e89240324306b78740a4a60745e2-Johnson, Ro <Robert.Johnson@hhs.gov>; Donis, Ruben (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=af00dcf720cb429f8e2accbe06ee32ff-Donis, Rube <Ruben.Donis@hhs.gov>; Armstrong, Kimberly (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5b778c7e17734740b14fbae4d3ed652c-Armstrong, <Kimberly.Armstrong@hhs.gov>; Oshansky, Christine (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d7bd764440b44b06af644cdcd22e42d6-Oshansky, C <Christine.Oshansky@hhs.gov>; Bright, Rick (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=53034752f35a4317aa74f46348442d39-Bright, Ric <Rick.Bright@hhs.gov>
Sent Date:	2020/03/08 10:12:58
Delivered Date:	2020/03/08 10:12:59

BCCI

Digital Guide

MARCH 2020

BIO ANTITRUST STATEMENT

All BIO meeting activities shall be conducted to abide strictly by all applicable antitrust laws. The antitrust principles discussed below apply to every meeting or conference call, no matter how informal, in which BIO members and staff gather under BIO auspices. Antitrust violations do not require proof of a formal agreement. A violation may be alleged based upon the mere appearance of unlawful activity. For example, discussion of a sensitive topic, such as price, followed by parallel action by those involved or present at the discussion, may be sufficient to show a price-fixing conspiracy. It is therefore important for speakers and attendees at BIO meetings to avoid discussing confidential business plans or information that is competitively sensitive, including:

- Company-specific current or future prices, including discounts, rebates, and pricing plans or policies;
- Sales or research in particular markets or sales to particular customers, including whether or how to sell in specific markets, whether to bid for specific business or participate in specific programs, conditions (such as resale restrictions) applicable to particular private or governmental customers, and whether to conduct research in particular areas;
- Advertising and promotion plans, including expected levels of advertising, which products to advertise, content of advertising, and future plans for the number of sales representatives and levels of expenditure on sales activities; and
- How companies might or should respond in the marketplace (such as by changing pricing, sales, distribution, or advertising policies) in light of existing or pending laws or regulations or current business or policy climates, including the suggestion of boycotts, or refusals to deal with, particular markets or customers

This list of generally prohibited topics is not exhaustive. By the same token, it is generally fine to discuss the nature of government regulations or policies on pricing, advertising and other aspects of pharmaceutical or biotechnology company business and advocacy efforts to address these government regulations or policies, as long as the discussions are limited to matters of public policy and advocacy.

Criminal prosecution by federal or state authorities is a very real possibility for violations of the antitrust laws. Imprisonment, fines or treble damages may ensue. BIO, its members and guests must conduct themselves in a manner that avoids even the perception or slightest suspicion that antitrust laws are being violated. Whenever uncertainty exists as to the legality or propriety of conduct, including during any meeting or discussion, promptly obtain legal advice by contacting Peter McHugh, BIO's General Counsel, (202) 312-9285.

The antitrust laws do not prohibit meetings among members of a trade association in order to petition government or respond to government initiatives, to educate and inform the public, or to suggest quality and safety standards, thereby promoting economic welfare and the vitality of our several industries. It is in this spirit that BIO conducts its meetings and conferences.

OVERVIEW OF THE BIO CORONAVIRUS COLLABORATION INITIATIVE ("BCCI")

With the expanding novel Coronavirus outbreak, many experts in the biotechnology industry have independently, or as part of a collaboration(s), gone beyond watching. They are actively developing products and services to address the crisis. They are heroes for doing this work.

BIO wants to help them, and other experts, bring forward the needed expertise and passion to help solve this crisis.

To this end, BIO has been working closely with U.S. government agencies, the World Health Organization, and authoritative bodies to identify the most pressing needs in the areas of vaccination, diagnostics, and antivirals and other treatments, and to facilitate collaborations with industry. BIO is now taking these efforts one step further – by bringing together the brightest minds in our member organizations, along with government and public health agency thought leaders and other experts, to exponentially amplify what is currently being done individually.

Among other goals, BIO and the experts it retains will help those who want to get involved find potential collaborations and make their way through the various government agencies and programs to get to solutions for patients as quickly as possible.

The companies BIO is bringing together are those that have demonstrated excellence relevant to the Coronavirus on three fronts: 1. Scientific Foundation; 2. Development Expertise; and 3. Manufacturing Capabilities.

BIO has done extensive outreach and a survey to invite anyone who believes she/he can help. So BIO is now convening a series of fora for expert groups, including scientists, public health/government leaders, and other experts.
BIO is undertaking these preliminary steps, which may ultimately result in joint research, because the world health situation associated with the Coronavirus (or COVID 19) is both urgent and compelling. If an opportunity for joint research presents itself to meet this threat, the research will be both necessary and constructive. BCCI will help determine and define the following factors that often compel such joint research: 1) the kind(s) of problem(s) being investigated; 2) the state of the art; 3) the resources available to individual firms; 4) the anticipated costs; and 4) the need for fast action. Participation in this initiative is open to all firms in the biotech industry, and it is envisioned that the results of any joint research efforts would be available on a nondiscriminatory basis.
While many scientific issues and challenges will be addressed, legal counsel will be present should there be a need, if any, for the sharing of confidential information, especially if such confidential information is about costs, productivity, prices, and similar matters that could lead to the reduction or elimination of competition. Ideally, no such conversations will be needed. Therefore, eventually, the BCCI may lead to separate and independent groups forming that may take advantage of protections of joint research under the National Cooperative Research and Production Act of 1993, which amended the National Cooperative Research Act of 1984, as well as possibly the Standards Development Organization Advancement Act of 2004.

For any questions about this BCCI or BIO's role in trying to meet this urgent health crisis, please contact **Phyllis Arthur**, at **parthur@bio.org**.

Contents

Introduction

Welcome to BCCI

This digital booklet will provide you with information to enrich your understanding of the current treatments, vaccines and diagnostics landscape vis-à-vis COVID-19 efforts. It also includes supplemental information—such as the details of major funding outlets

Please review these materials in order to ensure a productive conversation during the break-out sessions

Attendees

Complete list of attendees: Treatments

Facilitator	Organization	Role
Gerald W. Parker Jr., DVM, PhD	Texas A&M University	Associate Dean, Global One Health
Richard Whitley, MD	University of Alabama at Birmingham	Professor of Pediatrics, Vice Chair of Dept. of Pediatrics, and Co-Division Director of Pediatric Infectious Diseases

Attendee	Company	Role
Abigail Keller	American Enterprise Institute	Research Assistant
Bryan Strouse	Sierra Oncology	Associate Director, Scientific Affairs
Carla Cartwright	Johnson & Johnson	Senior Director, Global Digital & Regulatory Policy
Chad Wessel	BIO	Director, Industry Research
Chan Harjivan	BCG	Dr
Chris Healey	Grifols	President, Corporate Affairs
Christian Peters MD, PhD	Pinpoint Therapeutics	CEO
Claire Brandewie	Biotechnology Innovation Organization	Director, Federal Government Relations
Claudia Carravetta	AbbVie	Senior Director, External Affairs
Cristina Cassetti	NIAID/NIH	Division Deputy Director
Dan Durham	BIO	EVP Health Policy
Debbie Hart	BioNJ	President and CEO
Donovan Yeates	KAER Biotherapeutics Corporation	CEO

Complete list of attendees: Treatments

Attendee	Company	Role
Dr. David Chernoff	Nuritas	Chief Medical Officer
Dr. Brian Keogh	Nuritas	Head of early biology
Dr. Ian Holyer	Nuritas	Head of Preclinical Development
Dr. Nora Khaldi	Nuritas	CEO and acting CSO
Eddie J . Sullivan, Ph.D.	SAB Biotherapeutics, Inc.	President and CEO
Erika Smith	ReNetX Bio	CEO
Evan Loh	Paratek Pharmaceuticals	CEO
Hans Sauer	BIO	Deputy General Counsel
Hansilla Alaigh	Emergent Biosolutions	Director, Strategy & External Development
Jackie	Sen-Jam Pharmaceutical	Founder/Head of Clinical Development
James Mayne	PhRMA	VP, Science & Regulatory Advocacy
Janet Hammond	AbbVie	VP, Clinical Development, Virology & General Medicine
Jim Iversen	Sen-Jam Pharmaceutical	CEO
John Murphy	BIO	VP & Deputy General Counsel, Health
Julie Tierney	Food and Drug Administration	Chief of Staff, Center for Biologics Evaluation & Research
Ken Kelley	Halozyme	Director

Complete list of attendees: Treatments

Attendee	Company	Role
Kenji Cunnion	ReAlta Life Sciences	Chief Medical Officer
Krishnan Nandabalan	InveniAI	President and CEO
Liza Herschel	SDI-JMW Consulting	Partner
Madan Anant	InveniAI	Senior Director, Strategic Alliances
Marina Kozak	DHHS	Health Scientist
Mark Pruzanski	Intercept Pharmaceuticals	President and CEO
Mark Trudeau	Mallinckrodt Pharmaceuticals	President & CEO
Melissa Brand	Biotechnology Innovation Organization	Assistant General Counsel, IP
Michael J. LaBarre	Halozyme	Senior Vice President, Chief Technical Officer
Michelle Drozd	Gilead Sciences	Executive Director, Reimbursement Policy
Michelle Rozo	Department of Defense	Deputy Assistant Director for Biotechnology
Missy Banashak	Takeda	Federal Affairs
Nathan Fisher	Southern Research Institute	Senior Business Development Executive
Neel Krishna, PhD	ReAlta Life Sciences	Chief Scientific Officer
Nicole Selenko- Gebauer	AbbVie	Vice President, Global Medical Affairs
Nicolette Louissaint, PhD	Healthcare Ready	Executive Director, President
Pooja Chatley	InveniAI	Assistant Director, Medical Affairs

Complete list of attendees: Treatments

Attendee	Company	Role
Rachel Dorin	TeraPore Technologies	President
Rick E WInningham	Theravance Biopharma	CEO
Sanjeev Munshi	InveniAI	Senior VP, Healthcare Business & Alliance Managemen
Spencer Robbins	TeraPore Technologies	Director of Intellectual Property
Steven Gelone	Nabriva Therapeutics	President
Sue Washer	AGTC	President & CEO
Theodore Tsai MD	Takeda Vaccines	Head, Immunization Science and Policy
Ulo Palm	Allergan	Senior VP Digital Sciences
Ulrich Thienel	ReAlta Life Sciences	CEO
Wei He, Ph.D.	DTRM Biopharma	Inventor, Founder & CEO

Complete list of attendees: Vaccines

Facilitator	Organization	Role
David Noll, PhD	Tiber Creek Partners	Senior Vice President
Gigi Kwik Gronvall, PhD	Johns Hopkins University	Senior Scholar, John Hopkins Center for Health Security

Attendee	Company	Role
Alessandra Nardin	immunoSCAPE	COO
Alexander Koglin	NTx Inc.	President / CSO
Amy Redl	Sanofi	Senior Director, Federal Government Relations
Andrea Masciale	Johnson & Johnson	VP, Regulatory Policy
Andrew Emmett	Pfizer	FDA Liaison & Head of US Regulatory Policy
Angela Riemer	Pfizer	Senior Director, Government Relations
Anjana Narain	CSL	EVP and General Manager, Seqirus
Anne De Groot, MD	EpiVax, Inc.	CEO-CSO
Anthony Macaluso	Tonix Pharmaceuticals Holding Corp.	Executive VP, Strategic Development
Bill Kridel	Ferghana Partners/Emergex Vaccines	Mr
Brant Biehn	Vaxart	VP Commercial Operations
Brian Rosen	Novavax	SVP, Public Policy and Commercial Strategy
Carsten Brunn	Selecta Biosciences	CEO
Charlie Villanueva	NTx	Product Manager
Chris Gibson	Recursion Pharmaceuticals	-

Complete list of attendees: Vaccines

Attendee	Company	Role
Chris Twitty	OncoSec Medical, Inc.	Chief Scientific Officer
Christine Boyle	EpiVax, Inc.	Director of Projects
Clem Lewin	Sanofi Pasteur	AVP Head BARDA Office NV Stakeholder Engagement
Daniel Mangelsdorf	SDI-JMW Consulting	Partner
Dave Hanaman	Curavit	CCO
David Dodd	Geovax	Chairman, CEO
David Giljohann	Exicure	CEO
David Novack	Dynavax	President & COO
David Spiwack	SDI - JMW Consulting	Partner
Debra Yeskey	CEPI	Head of Regulatory Affairs, North America
Douglas Bryce	JPEO-CBRND	Joint Program Exec Off. for Chem., Biol., Radiological and Nuclear Defense
Ethan Settembre	Seqirus	VP, Research, Research Development, & Sciences
Farshad Guirakhoo	geovax	CSO
Greg Meiselbach	Tonix Pharmaceuticals	Senior Advisor
Hayley Alexander	BIO	Director, Federal Government Relations
In-Kyu Yoon	Coalition for Epidemic Preparedness Innovations	Vaccine Development Project Leader
Jeff Kindler	Centrexion Therapeutics	CEO

Complete list of attendees: Vaccines

Attendee	Company	Role
John Mascola	Vaccine Research Center, NIAID, NIH	Director, Vaccine Research Center
Jonathan Edelman	Seqirus	VP, Clinical Development
Julian Ritchey	Sanofi Pasteur	VP, Head of Public Affairs and Patient Advocacy
Julie Gerberding	Merck & Co.	Executive Vice President and Chief Patient Officer
Karin Bok	Vaccine Research Center, NIAID	Senior Advisor
Kei Kishimoto	Selecta Biosciences	CSO
Keir Loiacono	OncoSec Medical, Inc.	General Counsel, VP Corporate Development
Kim Jaffe	OncoSec Medical, Inc.	Senior Director, Operations
Kizzmekia Corbett	National Institutes Of Health	Research Fellow, Scientist Lead
Landon Westfall	Southern Research	Associate Director Influenza, Infectious Disease Research
Laura Efros	Bavarian Nordic	VP, US Government Affairs
Lenny Moise	EpiVax, Inc.	Senior Director, Vaccine Research
Marion Gruber, PhD	FDA/.CBER	Director, Office of Vaccines Reserach & Review
Mark Reynolds	GeoVax Labs, Inc.	CFO
Matthew Hepburn	JPEO CBRND DoD	Joint Product Lead, Enabling Biotechnologies
Melissa Malhame	Adjuvance Technologies	Policy Consultant
Michael Fehlings	immunoSCAPE	Dir. Scientific Affairs

Complete list of attendees: Vaccines

Attendee	Company	Role
Michelle Pernice	Dynavax	Senior Director, Head of Regulatory Affairs
Monica He	BIO	Director, Intl Affairs
Nathalie Charland	Medicago Inc.	Sr Director, Scientific & Medical Affairs
Neda Safarzadeh	Arcturus Therapeutics	Director, Head of Investor Relations/Public Relations/Marketing
Pad Chivukula	Arcturus Therapeutics	CSO/COO
Peter Marks	U.S. FDA	Director, Center for Biologics Evaluation and Research
Phyllis Frosst	Seqirus	Director, Health Policy
Punit Dhillon	Emerald Pharmaceuticals	CEO
Rob Janssen	Dynavax Technologies	Chief Medical Officer
Ruben Donis	BARDA	Dr.
Ryan Muldoon	PrEP Biopharm	CEO
Seth Lederman	Tonix Pharmaceuticals	CEO
Thomas Hess	Medicago	Senior Director, Commercial Development
Thomas Rademacher	Emergex Vaccines Holding Ltd	Professor
Tommi Kainu	Bavarian Nordic	Executive Vice President & Chief Business Officer
William Kridel	Ferghana Partners	Managing Partner
Wouter Latour	Vaxart Inc.	CEO

Complete list of attendees: Diagnostics

Facilitator	Organization	Role
Chris Hoefler, PhD	Draper Labs	Computational Biologist
Luciana Borio	In-Q-Tel	VP, Technical Staff

Attendee	Company	Role
Cartier Esham	BIO	Executive Vice President Emerging Companies
Cristina Tato	Chan Zuckerberg Biohub	Director, Rapid Response
Crystal Kuntz	BIO	VP Policy
David Spiegel	IES Life Sciences, Inc.	CEO and co-Founder
Dr. Jason W. Roos	Joint Program Executive Office for Chemical, Biological, Radiological and Nuclear Defense	Deputy Joint Program Executive Officer
Hilary Stiss	BIO	Senior Manager
Jay West	BioSkryb	President
Jim Stewart	Abbott Laboratories	Director Assay Development
Joseph Hamel	HHS ASPR	Strategic Innovation Manager
Laura Biesiadecki	NACCHO	Senior Director, Preparedness
Libby Mullin	Mullin Strategies	President
Patrick Ayscue	Chan Zuckerberg Biohub	Senior Biosecurity Fellow
Rangarajan Sampath	FIND	Chief Scientific Officer
Susan Van Meter	AdvaMedDx	Executive Director
Timothy Stenzel	Food and Drug Administration (FDA)	Director, In Vitro Diagnostics and Radiological Health

Background on the outbreak

COVID-19 outbreak continues to accelerate globally

World-wide COVID-19 Cases

(Animated map of daily movement)

US cases

35K
Total
Cases

470
Total
Deaths

Source: Johns Hopkins CSSE

Insights from survey: Manufacturing capacity available in US

Company	US	Europe	Canada	LatAm	Asia
ADMA Biologics	■				
AIM ImmunoTech Inc.	■				
Arcturus Therapeutics	■	■			
Clene Nanomedicine, Inc.	■				
Dynavax	■				
Emergent Biosolutions	■	■	■		
EpiVax	■				
Exicure		■			
Lumos Diagnostics	■				
Medicago	■				
Nabriva Therapeutics		■			■
NanoViricides	■				
Novavax	■				
OncoSec	■				
ReAlta Life Sciences	■				
SAB Biotherapeutics, Inc.	■				
Sanofi	■				
Takeda Pharmaceuticals	■				
Vaxart	■				

■ Indicates mfg capacity exists based on survey responses

Source: BCCI summit participant survey

SARS-CoV2 Product Development Landscape: Treatments, Vaccines and Diagnostics

Treatments

Info as of March 20, not exhaustive

Organizations involved in Anti-Viral treatment development (I/V)

Company	Technology	Summary
AbbVie	HIV protease inhibitor	- **Partnering with Global Authorities** to determine antiviral activity as well as efficacy & safety of HIV drug against COVID-19 - China's National Health Commission authorized Kaletra to treat pneumonia caused by SARS-CoV-2; AbbVie has donated RMB 10 million ($1.4 million) of Kaletra to Chinese authorities "as an experimental option to support this growing public health crisis." - The Health Commission of Henan Province announced January 31 that three confirmed cases of patients diagnosed with new coronavirus infections recovered after taking Kaletra, a combination of ritonavir and lopinavir.
ADMA Biologics	Immuno-globulin	- ADMA focuses on manufacturing, marketing and developing **specialty plasma-derived biologics**, especially immunoglobulin plasma pool compositions such as ASCENIV (IVIG) - ADMA has committed to generating immunotherapeuti, immunoglobulin (IG & IVIG) compositions for the prevention and treatment of a wide variety of respiratory infections, including certain strains of coronavirus
AIM ImmunoTech	Double-stranded RNA	- Approved for chronic fatigue syndrome in various countries, rintatolimod entered discovery for use as a prophylactic/early-onset therapeutic against COVID-19 in February 2020 - **Rinatolimod achieved a 100% survival rate**, as compared to 100% mortality in the untreated control animals, in SARS animal experiments after the outbreak in 2003; the Company believes it may provide similarly effective prophylaxis against COVID-19, as both coronaviruses are extremely similar in key regulatory RNA sequences essential for coronaviral replication - Rinatolimod has a well-developed safety profile based on approximately 100,000 IV doses administered to humans and is ready to deploy for clinical trials in China if trials are approved by the PRC authorities
Alnylam / Vir	RNAi	- Alnylam Pharmaceuticals and Vir Biotechnology have expanded their existing collaboration to include the development and commercialization of **RNAi therapeutics** targeting SARS-CoV-2, the virus that causes COVID-19 - The companies will utilize Alnylam's recent advances in lung delivery of novel conjugates of siRNA – the molecules that mediate RNAi – together with Vir's infectious disease expertise and established capabilities, to bring forward one or more siRNAs to treat SARS-CoV-2 - Alnylam has designed and synthesized over 350 siRNAs targeting all available SARS-CoV and SARS-CoV-2 genomes, which will be screened

Info as of March 20, not exhaustive

Organizations involved in Anti-Viral treatment development (II/V)

Company	Technology	Summary
Clene Nanomedicine	Nanocrystal	- Clene clean surface nanocrystal (CSN) treatments to **improve bioenergetics processes that impact disease** - CSN silver-zinc is an ionic solution of zinc and silver in pre-clinical development for wound healing and for use as an anti-infective
DTRM Biopharma	BTK inhibitor	- Develops, produces, and sells bruton's tyrosine kinase inhibitor for the treatment of cancer in China
Eli Lilly	Immuno-globulin	- **AbCellera and Lilly** entered into an agreement to co-develop antibody products for the treatment and prevention of COVID-19 - Collaboration will leverage AbCellera's rapid pandemic response platform to identify anti-SAR-CoV-2 antibodies, and Lilly's global capabilities for rapid development, manufacturing and distribution of therapeutic antibodies - Lilly scientists are **partnering with the Indiana State Department of Health (ISDH),** with support from the FDA, to accelerate testing in Indiana for SARS-CoV-2
Emergent Biosolutions	Polyclonal hyperimmune globulin (H-IG)	- Initiated development of candidates to treat and prevent COVID-19, using its hyperimmune platforms; COVID-HIG, manufactured from **human plasma with antibodies to SARS-CoV-2**, will be developed as a treatment for severe hospitalized patients and to protect at-risk individuals; COVID-EIG, manufactured from plasma of immunized horses with antibodies to SARS-CoV-2, will be developed as a treatment for severe hospitalized patients
Genentech	Interleukin-6 (IL-6) blocker	- Working with the FDA to initiate a randomized, double-blind, placebo-controlled Phase III clinical trial of Actemra In hospitalized patients with severe COVID-19 Pneumonia in collaboration with the Biomedical Advanced Research and Development Authority (BARDA) - First global study of Actemra in this setting and is expected to begin enrolling as soon as possible in early April with a target of approximately 330 patients globally

Info as of March 20, not exhaustive

Organizations involved in Anti-Viral treatment development (III/V)

Company	Technology	Summary
Gilead / University of Alabama at Birmigham	Nucleoside analog	- **Remedesivir** is an investigational intravenous anti-viral (nucleoside analog) treatment **undergoing Phase III clinical trials** in China and Nebraska as a potential treatment for COVID-19; it was already used to treat one infected patient in the US for "compassionate use" - Remdesivir has demonstrated in vitro and in vivo activity in animal models against the viral pathogens MERS and SARS, which are coronaviruses that are structurally similar to SARS-CoV-2 - Initiation of **two Phase 3 clinical studies** to evaluate the safety and efficacy of remdesivir in adults diagnosed with COVID-19
Grifols	Immuno-globulin	- Shared its broad knowledge and technology in convalescent plasma (plasma with antibodies against the virus) with their partner-to-be in China, Shanghai RAAS, and intl. health authorities to develop potential antiviral with immunoglobulins
InveniAI	Multiple anti-virals	- InveniAI uses AlphaMeld analysis to identify human genes that interact with COVID-19 and then determine how those genes play a role in infection (viral entry, replication, etc.) before then identifying drug candidates that have the potential to be re-purposed to treat COVID-19 - Its AI-powered platform, VaxMeld™, has **found 10 genes that play a direct role in Coronavirus**, and identified over 100 drug candidates that can be repurposed to potentially treat COVID19 - Classes of drugs identified to have high potential include inhibitors for proteases, RNA processing, membrane fusion, and pathogenesis
J&J	Multiple anti-virals	- Expanded its **collaboration with the federal Biomedical Advanced Research and Development Authority** enhance to screen a library of existing antiviral molecules, with the aim of identifying compounds which show promise against COVID-19 - HIV protease inhibitor, Prezcobix, **donated to Shanghai Public Health Clinical Center and Zhongnan Hospital of Wuhan Univ.** for studies
KAER Biotherapeutics	Aerosol Generation Technology	- KAER provides **new treatments for respiratory diseases** through the inhalation of therapeutic aerosols using its proprietary SUPRAER technology
Nabriva	Semi-synthetic pleuromutilin	- Biopharma company engaged in the commercialization and development of innovative anti-infective agents to treat serious infections; **monitoring efforts by the U.S. BARDA** in its preparation for the potential need for widespread CABP and XENLETA treatment to treat patients infected with coronavirus with suspected/documented secondary bacterial pneumonia

Info as of March 20, not exhaustive

Organizations involved in Anti-Viral treatment development (IV/V)

Company	Technology	Summary
Nabriva	Semi-synthetic pleuromutilin	- Biopharmaceutical company engaged in the commercialization and development of innovative anti-infective agents to treat serious infections - **Monitoring efforts by the U.S. BARDA** in its preparation for the potential need for widespread CABP and XENLETA treatment to treat patients infected with the coronavirus with suspected or documented secondary bacterial pneumonia
NanoViricides	Nanoviricide	- Recently completed synthesis of a number of **nanoviricide drug candidates** for testing in just a few weeks after identification of virus-binding ligands; these will now be tested in cell culture studies against coronaviruses - Presently, the Company does not have any collaboration established for further testing of its drug candidates against COVID-19
Pfizer	Multiple anti-virals	- Pfizer has identified **several antiviral compounds, already in development,** with potential to block coronaviruses, and has initiated efforts to advance these therapies - Pfizer has also committed to sharing its clinical development and regulatory expertise to support the most promising candidates that smaller biotech companies may bring forward; many of these companies are screening compounds or existing therapies but lack experience in late stage development and navigating complex regulatory system
PhRMA	Multiple anti-virals	- PhRMA (Pharmaceutical Research and Manufacturers of America) **represents the country's leading innovative biopharmaceutical research companies** - Currently rapidly screening their vast global libraries of medicines to identify potential treatments and have numerous clinical trials underway to test new and existing therapies
Premas	3-D cell models	- Continuing research on viral surface proteins to find a potential candidate for developing vaccines
Regeneron	Monoclonal Antibody	- Regeneron Pharmaceuticals is developing **multiple monoclonal antibodies** that, individually or in combination, could be used to treat COVID-19. Under its expanded agreement with BARDA, Regeneron will leverage its existing monoclonal antibody discovery platform called VelocImmune, to develop therapeutic products to treat COVID-19 infections

Organizations involved in Anti-Viral treatment development (V/V)

Company	Technology	Summary
Roivant	Monoclonal Antibody	- Developed Gimsilumab to prevent and treat Acute Respiratory Distress Syndrome (ARDS) in patients with COVID-19 - Gimsilumab is a monoclonal antibody that targets GM-CSF, a pro-inflammatory cytokine found to be up-regulated in COVID-19 patients - Emerging clinical evidence in COVID-19 patients suggests that GM-CSF contributes to immunopathology caused by SARS CoV-2 in patients with or at risk of developing ARDS
SAB Biotherapeutics	Immuno-globulin	- SAb is focused on producing a **polyclonal antibody therapeutic** for the SARS-CoV-2 virus - Polyclonal antibodies are the proteins created by the body to fight invading diseases by creating an immune response that attacks and ideally kills the invading pathogen; SAB expects to be ready for the pre-clinical and clinical-trial evaluations by the end of the summer
Takeda	Polyclonal hyperimmune globulin (H-IG)	- Takeda is initiating the development of an anti-SARS-CoV-2 polyclonal **hyperimmune globulin (H-IG)** to treat high-risk individuals with COVID-19; Hyperimmune globulin is a plasma derived-therapy that has previously been shown to be effective in the treatment of severe acute viral respiratory infections and could be a treatment option for patients with COVID-19 - Takeda believes the therapy will be among the first approved treatments - H-IG works by concentrating the pathogen-specific antibodies from plasma collected from recovered patients or vaccinated donors - Takeda is **collaborating with several health and regulatory agencies and health care partners** across the globe to move the research forward; scientists need to have access to source plasma from people who have successfully recovered from COVID-19 - Also studying whether Takeda's currently marketed and pipeline products may be effective treatments for infected patients
Vir	Immuno-globulin	- Vir Biotechnology is **partnering with Biogen** to develop and manufacture an experimental treatment for COVID-19 - Vir is working with antibodies isolated from people who had previously survived an infection with the SARS virus, which shares genetic similarities to SARS-CoV-2; they are looking at these antibodies, and possibly ones identified in the future, as the potential foundation for a treatment against the newer coronavirus

Info as of March 20, not exhaustive

Organizations involved in symptomatic treatment development (I/II)

Company	Technology	Summary
Bayer	Chloroquine	• Evaluated in clinical trials in over 10 hospitals in Beijing, Guangdong Province, and Hunan Province; China's National Health Commission included **chloroquine phosphate in its latest treatment guidelines for COVID-19 pneumonia** • **Highly effective in control of COVID-19 infection in vitro**
Bellerophon	Inhaled nitric oxide	• FDA has granted "emergency expanded access" to Bellerophon Therapeutics' inhaled nitric oxide delivery system for treating the novel coronavirus- opening up its INOpulse system for use at high-doses in ventilated COVID-19 patients, immediately
Emerald Pharma-ceuticals	ECS	• Developing new pharmaceutical drug candidates by enhancing the known benefits of **cannabinoid interactions** with the human endocannabinoid system (ECS)
Mallinckrodt	Inhaled nitric oxide	• Currently evaluating potential role for **inhaled nitric oxide (iNO) as a supportive measure** in treating patients infected with coronavirus and having associated pulmonary complications
Nabriva Therapeutics	Anti-bacterial	• Lefamulin is an antibacterial agent indicated approved in 2019 for the treatment of **community-acquired pneumonia** • Lefamulin is a treatment option in the up to 15% of COVID-19 infected patients who develop secondary bacterial pneumonia and is being pursued for such indications with the US government and a partner in China
Paratek	Anti-bacterial	• Submitted a pre-EUA application to FDA for **NUZYRA for treatment of COVID-19** • NUZYRA is a once-daily oral and intravenous antibiotic available in the U.S. for the treatment of adults with community-acquired bacterial pneumonia and acute bacterial skin and skin structure infections

Info as of March 20, not exhaustive

Organizations involved in symptomatic treatment development (II/II)

Company	Technology	Summary
Pinpoint Therapeutics	Chloroquine	- Spun out from the University of Pennsylvania, Pinpoint Therapeutics **produces DC661, a potent chloroquine** (commonly used to treat malaria - Chloroquine can inhibit viral/host cell fusion and inhibit viral RNA polymerases
ReAlta Life Sciences	Complement C1 inhibitor	- ReAlta makes a peptide **Inhibitor of complement C1 called (PIC1)** - PIC1 belongs to a family of novel anti-inflammatory peptides that can rapidly attenuate acute inflammatory reactions such as Coronavirus Related Acute Lung Injury (CRALI) which is the proximate cause of mortality and morbidity
Regeneron / Sanofi	Interleukin-6 (IL-6) inhibitor	- Regeneron and Sanofi are set to begin a clinical programme evaluating the efficacy of **Kevzara (sarilumab), an interleukin-6 inhibitor (IL-6), as a treatment for severely ill**, hospitalized COVID-19 patients - The IL-6 pathway is thought to play a role in the overactive inflammatory response observed in the lungs of severely and critically ill COVID-19 patients; China has already approved Roche's rival IL-6 inhibitor Actemra (tocilizumab) for the treatment of coronavirus patients with lung complications
Sierra Oncology	JAK1, JAK2 & ACVR1 inhibitor	- Late stage drug development company focused on advancing targeted therapeutics for the treatment of patients with significant unmet medical needs in hematology and oncology - **Momelotinib**, lead drug candidate, is a potent, selective and orally-bioavailable JAK1, JAK2 & ACVR1 inhibitor with a **differentiated therapeutic profile in myelofibrosis** encompassing robust constitutional symptom improvements, a range of meaningful anemia benefits, including eliminating or reducing the need for frequent blood transfusions, and comparable spleen control to ruxolitinib

Vaccines

Organizations involved in vaccine development – Protein sub-unit vaccines (I/II)

Company	Technology	Summary	Phase
CSL Behring	Protein subunit	• Partnered with the University of Queensland's COVID-19 vaccine development program to provide technical expertise as well as a donation of Seqirus' **proprietary adjuvant technology**, MF59®, to their pre-clinical development program • Adjuvants are used in vaccines to create a stronger immune response and to speed vaccine production and output; the University of Queensland will use the adjuvant to test the viral protein they are developing with their molecular clamp technology	Pre-clinical
Dynavax	Protein subunit	• Developing a novel **single-dose, intranasal vaccine** using Altimmune's proprietary technology to protect against COVID-19 • Collaborating with the university of Queensland as part of a Coalition for Epidemic Preparedness (CEPI) to develop a vaccine to prevent COVID-19 consisting of the **spike antigen of SARS-CoV-2 and CpG 1018 as adjuvant** • Dynavax is providing technical expertise and the company's proprietary toll-like receptor 9 **(TLR9) agonist adjuvant, CpG 1018 (an FDA approved adult hepatitis B vaccine)**	Not yet initiated
Emergex	Syntentic T-Cell	• Developing a first generation vaccine based on experimentally-validated viral codes from closely related coronaviruses and **predicted SARS-CoV-2 sequences** and a universal coronavirus vaccine based on viral codes derived from **SARS-CoV-2-infected human cells** and confirmed in convalescent patients • Vaccines use synthetic components to **"program" T-cells** that destroy infected human cells- T-cells are composed of: an established library of universal coronavirus peptide "codes" and a gold nanoparticle carrier system to deliver viral code • The company **has already begun manufacturing vaccine components** and could have a vaccine ready to **test by May 2020**	Pre-clinical

Organizations involved in vaccine development — Protein sub-unit vaccines (II/II)

Company	Technology	Summary	Phase
EpiVax	Virus-like particles (VLPs)	• Collaboration to develop a vaccine with University of Georgia vaccine expert Ted Ross (Director, Center for Vaccines and Immunology (CVI)) • EpiVax has proprietary in **silico (computational) tools** that identify the key regions of viral sequences that should be included in vaccines to keep individuals safe from infection, while excluding other sequences that make the vaccine less effective or safe	Pre-clinical
Medicago	Virus-like particles (VLPs)	• Medicago produced **Virus-Like Particle (VLPs)** of the coronavirus just 20 days after obtaining the SARS-CoV-2 gene- VLPs mimic the native structure of viruses, allowing them to be easily recognized by the immune system. However, they lack core genetic material which makes them non-infectious & unable to replicate; VLP vaccine candidate will now undergo preclinical testing for safety and efficacy	Pre-clinical
Novavax	Protein subunit	• Novavax has produced and is currently assessing **multiple recombinant nanoparticle vaccine** candidates in animal models prior to advancing to clinical trials. Initiation of Phase 1 clinical testing is expected in late spring of 2020. Novavax' COVID-19 vaccine candidates were created with its proprietary recombinant protein nanoparticle technology platform to generate antigens derived from the coronavirus spike (S) protein. • Novavax also expects to utilize its proprietary Matrix-M™ adjuvant with its COVID-19 vaccine candidates to enhance immune responses • Coalition for Epidemic Preparedness Innovations (CEPI) awarded an initial funding of $4 million to support Novavax' efforts to develop a COVID-19 vaccine	Pre-clinical
SAB Biothera-peutics	Protein subunit	• **SAB Biotherapeutics' SAB-301** is in Phase 1 as a candidate vaccine to COVID-19	Clinical
Selecta Biosciences	Virus-like particles (VLPs)	• Clinical stage biotechnology company developing a novel class of targeted antigen-specific immune therapies using **synthetic vaccine particles** (SVP)	Clinical

Info as of March 20, not exhaustive

Organizations involved in vaccine development—Nucleic acid sub-unit vaccines (I/III)

Company	Technology	Summary	Phase
Altimmunne	Non-replicating Viral Vector	• Developing a novel **single-dose, intranasal vaccine** using Altimmune's proprietary technology to protect against COVID-19 • New intranasal vaccine is based on the same platform vaccine technology as NasoVAX, the company's influenza vaccine candidate • Completed the design and synthesis of the vaccine and is now advancing it toward animal testing and manufacturing; **clinical testing to begin Aug 2020**	Pre-clinical
AnGes	DNA	• **Partnering with Osaka University** to develop a DNA vaccine; however, to date DNA vaccines have yet to be commercialized for human use • Vaccine will produce antibodies against the new coronavirus inside a person's body through the use of synthetic DNA • AnGes has **started joint manufacturing** of the DNA vaccine for the new coronavirus **with Takara Bio Inc**., a leading reagent company	Pre-clinical
Arcturus Therapeutics	RNA	• **Received a grant of $10M** from Singapore government agency to co-develop a vaccine • Work on the vaccine will occur in partnership with the Duke-National University of Singapore Medical School • Researchers will tap Arcturus's self-replicating RNA platform, known as STARR, and nanoparticle lipid delivery system	Pre-clinical
Bavarian Nordic	Non-replicating smallpox	• International biotechnology company developing and manufacturing novel cancer immunotherapies and vaccines for infectious diseases • Partnership with Janssen, under which the company has outlicensed MVA-BN vaccine technology for Ebola, HPV, HIV and Hepatitis B vaccines	Pend

Info as of March 20, not exhaustive

Organizations involved in vaccine development—Nucleic acid sub-unit vaccines (II/III)

Company	Technology	Summary	Phase
GeoVax	Non-replicating Viral Vector	• Developing human immunotherapies and vaccines against infectious diseases and cancer, together with BravoVax, a vaccine developer in Wuhan, China, are working to jointly develop a vaccine • GeoVax will use its MVA-VLP vaccine platform and expertise to design and construct the vaccine candidate using genetic sequences from the coronavirus; BravoVax will provide further development, including testing and manufacturing support, as well as interactions with Chinese authorities	Pre-clinical
Inovio	DNA	• A leader in coronavirus vaccine development and the only company with a Phase 2 vaccine for a related coronavirus that causes MERS • Inovio leveraged its modern DNA medicines platform to design a DNA vaccine INO-4800 three hours after the publication of the genetic sequence of the novel coronavirus that causes COVID-19; the team then immediately began preclinical testing and small-scale manufacture • Plan to begin human clinical trials in the U.S. in April and soon thereafter in China and South Korea • $5m grant from Gates Foundation to accelerate testing and scale up of CELLECTRA® 3PSP proprietary smart device for intradermal delivery of INO-4800	Pre-clinical
J&J	Non-replicating viral vector	• Operating a **coronavirus vaccine program** via collaboration with the Biomedical Advanced Research and Development Authority (BARDA), part of the Office of the Assistant Secretary for Preparedness and Response (ASPR) at the U.S. Department of Health & Human Services • BARDA will help fund the phase 1 trials of the vaccine candidate, with an option to extend that further if the initial studies are positive. Meanwhile, J&J has agreed to ramp up production and manufacturing capacity for the candidate	Pre-clinical

Info as of March 20, not exhaustive

Organizations involved in vaccine development—Nucleic acid sub-unit vaccines (III/III)

Company	Technology	Summary	Phase
Moderna	RNA	• Developing a novel **single-dose, intranasal vaccine** using Altimmune's proprietary technology to protect against COVID-19 • NIH and Moderna's infectious disease research team finalized the sequence for mRNA-1273 vaccine, 2 days after Chinese shared genetic sequence- First clinical batch, including fill and finishing of vials, was completed, a total of 25 days from sequence selection to vaccine manufacture • On March 16, the NIH announced the **first participant in Phase 1** study for mRNA-1273 was dosed, 63 days from sequence selection to first human dosing	Phase 1
Multimeric Biothera-peutics	DNA	• Advancing a new vaccine platform, MagaVax, that uses the company's technology to **generate CD8+ T cell responses** strong enough to protect against HIV, influenza, and malaria, making quarantine unnecessary for vaccinated subjects	Pre-Clinical
OncoSec	DNA	• Identified a novel SARS-CoV-2 vaccine which is augmented by the company's **existing IL-12 immunotherapy** platform- OncoSec's proprietary gene delivery system uses established reversible electroporation technology to deliver a plasmid-based DNA immunogen and well as potent immune stimulating cytokine, collectively known as CORVax-12	Clinical
Pfizer	RNA	• Pfizer signed a deal with Germany's BioNTech SE to co-develop a potential vaccine for the coronavirus using BioNTech's **mRNA-based drug development** platform (vaccine candidate BNT162); the drug-makers will start the collaboration immediately and have signed a letter of intent for the vaccine's distribution outside China	Pre-clinical
PrEP Biopharm	RNA	• Development stage biopharmaceutical company focused on the prevention of respiratory infections with a once-daily, nasal spray containing PolyIC, **an RNA-based viral mimic (PrEP-001)** • **Human phase 2a challenge studies** demonstrating prophylactic efficacy against influenza and the common cold	Clinical

Organizations involved in vaccine development - Adjuvants

Company	Technology	Summary	Phase
Adjuvance Technologies	Adjuvant	• Privately held biopharmaceutical company dedicated to empowering health through fundamental breakthroughs in vaccine adjuvant design and manufacturing • Advancing in synthetic **saponin vaccine adjuvants for infectious disease**, immuno-oncology and other applications with an optimized analogue of the saponin adjuvant QS-21: TQL1055, which is a critical component of the AS01 adjuvant used in the zoster vaccine commercialized by GSK • Adjuvance has received $4M of NIH funding to date, and recently closed a $20M Series A round which will enable to get **1055 through a phase 1/2 clinical trial in infectious disease**	Clinical
Exicure	Adjuvant	• Broad pipeline of proprietary SNA1 (Spherical Nucleic Acid) based treatments, with a **TLR9 agonist in phase 2** • TLR9 agonist SNAs are a promising approach to cancer immunotherapy, asthma treatment, and **vaccine adjuvant applications**	Clinical
GSK	Adjuvant	• Working with Coalition for Epidemic Preparedness Innovations to **support COVID-19 vaccine** development - will make its established pandemic vaccine **adjuvant platform technology** available to enhance the development of an effective vaccine against 2019-nCoV • Also lending its technology to Clover Biopharmaceuticals, a Chinese biotech firm at work on a coronavirus vaccine; Clover's approach involves injecting proteins that spur an immune response, thereby priming the body to resist infection	Pre-clinical

Diagnostics

Info as of March 20, not exhaustive

Organizations involved in diagnostic development – IVD

Company	Test type	Summary
Abbott	Lab-based IVD	• Received FDA EUA to use the test on **m2000 RealTime system** that is currently available **in hospitals and molecular labs in US** • Shipping **150K lab tests immediately**; test already sent to hospital and academic medical center **labs in 18 states** • Scaling up production at its U.S. manufacturing location to **reach capacity for 1 million tests per week** by end of march
CDC	Lab-based IVD	• **First diagnostic to be deployed in US**. On a applied Biosystems7500 fast diagnostics platform • Can process up to **20 samples per 4 hours** with **~3-4 hours test run time**
Hologic	Lab-based IVD	• Received FDA **EUA for Panther Fusion SARS-CoV-2 test** on 03/16/20 • Targeting to make **~600K tests per month** starting in April; can process up to **1150 samples daily** with **3 hour test run time**
Quidel	Lab-based IVD	• Received FDA **EUA approval** on 03/17/20 • Same platform as CDC test, which is widely available especially in mi-sized and smaller hospitals and labs; **4 hour test run time**
Roche	Lab-based IVD	• Received EUA to ship 400K test kits across US; aim to send **additional 400K test per week to 30 lab testing** sites across the US • Run on Roche's fully automated Cobas 6800 and 8800 and has the capacity to process **384 and 960 results in an 8 hour shift** • After the lab starts the test, **results are available in ~3.5 hours**
Thermo Fisher Scientific Inc.	Lab-based IVD	• Received EUA for diagnostic test on 03/13/20 that can be **used immediately by high-complexity laboratories** in the US • Designed to **provide patient results within four hours of a sample being received** by a lab • Currently have **1.5 million devices available** with a goal of producing **5 million per week by April**

Info as of March 20, not exhaustive

Organizations involved in diagnostic development – LDT (I/II)

Company	Test type	Summary
NY Department of Health	LDT	• Launched February 29th, 2020 • Tested at NY PH high-complexity labs and have a **turnaround time of 2~4 days**
Stanford Health Care	LDT	• Launched February 29th, 2020 • Tested at Stanford health Care and Stanford Children's health, and expected to **deliver results within 12-24 hours**
UW Medicine	LDT	• Launched March 4th, 2020 and tested only at UW Medicine clinics, with **turnaround time of 8 hours** • Also offering appointment-only **drive through clinic** for UW medicine
BioReference Laboratories	LDT	• Launched March 5th, 2020 and tested only at BioReference high-complexity labs • Can accommodate up to **15,000 tests per day**
BWH / MGH	LDT	• Launched March 7th and tested only at MGH/Brigham's network • Can accommodate up to **130 tests per day**
Northwell Health	LDT	• Launched semi-automated testing, and seeking FDA approval to fully automate the process • Once automated, they can process **1,000 tests daily**
Quest Diagnostics	LDT	• Reveived FDA EUA on 03/17/20 to start testing at Quest Diagnostic's high-complexity labs • Can test up to **5,000 samples per day** with turn around time of **~3 days**
Solaris diagnostics	LDT	• Launched March 9th, 2020 and tested at Solaris diagnostics high-complexity labs
Avellino Labs	LDT	• Launched March 10th, 2020 and tested at Avellion's CLIA certified labs, which takes from **1.5 to 3 hours to perform**
Viracor	LDT	• Launched March 10th, 2020 and can be turned around within **12-18 hours**
ARUP Laboratories	LDT	• Launched March 12th, 2020; temporarily halted national orders due to supply constraints on March 16th
Hackensack Meridian Health	LDT	• Launched March 12th, 2020; can process **24 patients every 8 hours**

Note: ordered by launch date

Info as of March 20, not exhaustive

Organizations involved in diagnostic development – LDT (II/II)

Company	Test type	Summary
TriCore	LDT	• Launched March 12th, 2020 to be tested at TriCore Patient Care Centers
Mayo Clinic	LDT	• Launched March 12th, 2020 and submitted for FDA EUA; patient can receive **results within 24 hours**
Univ. of California	LDT	• UC health systems launched in-house testing on March 12th, 2020; **turnaround time ~24 hours**
LabCorp	LDT	• Received FDA EUA for COVID-19 RT-PCR test on 03/16/20 • Announced that it will be able to **perform more than 20K COVID-19 tests per day** beginning 03/20/20
Cleveland Clinic	LDT	• Cleveland Clinic, University hospitals launched in-house testing on March 13th, 2020 • Turnaround time is expected **between 12 and 24 hours**
Johns Hopkins	LDT	• Launched March 13th, 2020 and aims to **test up to 1K per day with 24 hours turnaround time**
UPMC	LDT	• Launched March 14th, 2020 with **24 hour turnaround time**
NewYork Presbyterian	LDT	• Launched March 15th, 2020 to test patients at NY Presbyterian network (**~200/day**)
UNC Health	LDT	• Began testing at UNC Medical center on March 16th, 2020
Diagnostic solutions	LDT	• Launched March 16th, 2020 with **~24 hour turnaround time**
NorthShore Univ. health system	LDT	• Launched March 16th, 2020 and testing **~500 patients daily**
Assurance scientific labs	LDT	• Launched March 16th, 2020 and also offering **drive-thru testing** with **72 hours turnaround time**
Yale NewHaven	LDT	• Launched March 16th, 2020 and testing **~200 samples daily**

Note: ordered by launch date

Info as of March 20, not exhaustive

Other organizations involved in diagnostic development

Company	Summary
AdvaMedDx	• AdvaMedDx supports the establishment, through legislation, of a modernized and predictable, risk-based diagnostics regulatory framework under the Food and Drug Administration (FDA) to which all developers of in vitro clinical tests (IVCTs) would be subject
Chan Zuckerberg Biohub	• Working with UCSF and Stanford to **quadruple the Bay Area's testing and diagnostics capacity** • Funding the acquisition of state-of-the-art FDA approved COVID-19 diagnostic machines • **Bridging connections between clinical labs** at Stanford and UCSF to help distribute the testing load throughout the area
FIND	• Launched an **expression of interest for test developers of in vitro diagnostics** for COVID-19, and received 200+ submissions • Launched a second **EOI for test developers interested in having their immunoassays** (manual ELISA, machine-based or lateral flow, rapid tests specific for SARS-CoV-2 antigen or antibodies) evaluated • **Compiled a list of COVID-19 diagnostics** in commercialization and in development across the globe
Gates Foundation	• Partner with the University of Washington to **offer home testing kits for COVID-19 in the Seattle area** • Test package to include nose swabs that can be mailed to the University of Washington for analysis, (target 1,000s of tests per day) • The home testing will use **resources from the Gates-funded Seattle Flu Study**, which conducts at-home testing for influenza
Grifols	• **Shared knowledge and technology** in convalescent plasma (plasma with antibodies against the virus) with their partner in China, Shanghai RAAS, and international health authorities to accelerate the development of diagnostic tests for the detection of COVID-19
IES Life Sciences, Inc.	• IES has co-developed, with leading FDA scientists, the first and only comprehensive test to accurately and reliably identify the **IFN signature** for a disease and **can identify contagious diseases immediately** following exposure with a simple blood test
Lumos Diagnostics	• **Raised $15M** for rapid, in-office diagnostic testing • Once developed, FebriDx test is designed to take only 10 minutes and can be done during an outpatient visit

Other organizations

Organizations offering services

Company	Summary
Aequor	- Aequor offers a large portfolio of **non-toxic, "green," eco-friendly, and sustainable chemicals**: dispersants, cleaning and freshening agents & antibiofilm, antifouling, antimicrobial agents - The company has advanced its "green" surface cleaners to stop the spread of COVID-19
Curavit	- "Next Generation" clinical trial enterprise that provides d**ecentralized clinical trial execution** - Through formal partnerships with Medical Practices and Specialty Healthcare Entities, patients enroll into clinical trials that are appropriate given their individual health situation
DOD	- On March 19 the department of Health and Human Services (HHS) and the Department of Defense (DOD) coordinated an emergency international airlift of **500,000 swabs and sample kits used in the COVID-19 testing** process in an effort to increase diagnostic testing for Americans
Emergent Biosolutions	- **Drug substance and drug manufacturing support** including fill/finish
EpiVax	- We can do **T cell assays with naive blood** at our facility in Providence. This service can be useful for confirming immune responses in Vaccinees, and to explore response to candidate vaccine antigens in Naive donors
HHS	- HHS health centers can provide with an on-the-ground-perspective on the response to the COVID-19 pandemic and what stresses our healthcare system is experiencing as a result. Health centers are on the frontlines of **providing accessible, affordable care** in many of our communities, and play a vital role in our response efforts
Johnson & Johnson	- To screen potential compounds, Janssen will work with the Rega Institute for Medical Research (KU Leuven), in Belgium. The arrangement couples the Institute's infrastructure, breadth of high throughput screening experience, and capabilities for studying special pathogens with Janssen's **drug development resources and antiviral expertise**.

Info as of March 20, not exhaustive

Organizations offering services

Company	Summary
Mullin Strategies	• Providing health care organizations with strategic advice related to **government relations, policy, board development, alliance development and fundraising**
NanoViricides	• Pilot scale (up to 2kg batches) **clinical product manufacture**
Nuritas	• Nuritas artificial intelligence platform provides **the largest peptide database in the world** for our drug hunters to explore, and offers the potential to expand and enhance the scope, efficacy and accuracy of discovery in the biopharmaceutical industry
Recursion Pharma-ceuticals	• Combines artificial intelligence and machine learning with automation and wet lab validation to conduct experimental biology at unprecedented scale - conducting more than 800,000 experiments every week • Only company with a massive **dataset of biological images** generated entirely **in-house** on our platform and fit for the purpose of machine learning
Southern Research	• **In vitro and in vivo support for antiviral and vaccine developers**

Info as of March 20, not exhaustive

Other relevant organizations

Company	Summary
BARDA	- Providing funding for clinical trials e.g., antibody medicine to treat severe COVID-19 cases and rapid diagnostic tool to detect novel coronavirus infections
BioNJ	- Network of 400 Member companies representing research-based life sciences companies and stakeholders, dedicated to propelling an innovation ecosystem and serving as a clearinghouse of information and intelligence, as convener of valuable networking and partnering programs, and as an advocate for capital formation
CEPI	- The Coalition for Epidemic Preparedness Innovations (CEPI) is looking to invest up to $2 billion to develop a COVID-19 vaccine - The $2 billion funding call will enable CEPI to expand the number of vaccine candidates to increase the chances of success and fund clinical trials for these candidates
FDA	- Issued first Emergency Use Authorization for Point of Care diagnostic on March 21, 2020; test believed to provide results within hours vs. days and roll-out now expected ~March 30, 2020
Healthcare Ready	- Healthcare Ready helps to **strengthen healthcare supply chains** through collaboration with public health and private sectors by addressing pressing issues before, during, and after disasters - Closely monitoring the following areas related to the COVID-19 outbreak: Supply chain operations, response of the US health system, global response efforts and humanitarian assistance efforts
JPEO-CBRND	- Joint Program Executive Office for **Chemical, Biological, Radiological and Nuclear Defense** (JPEO-CBRND) to manage our nation's investments in chemical, biological, radiological, and nuclear (CBRN) defense equipment
NACCHO	- Activated Level 3 and full Incident Command Structure to **enable staff members to prioritize COVID-19 related activities**
NIH	- Began clinical trial of investigational vaccine for COVID-19 in Seattle as of March 16, 2020 - In late February 2020, began clinical trial of remdesivir to treat COVID-19 patients based in Nebraska

COVID-19 Disclaimer

The situation surrounding COVID-19 is dynamic and rapidly evolving, on a daily basis. Although we have taken great care prior to producing this presentation, it represents BCG's view at a particular point in time. This presentation is not intended to: (i) constitute medical or safety advice, nor be a substitute for the same; nor (ii) be seen as a formal endorsement or recommendation of a particular response. As such you are advised to make your own assessment as to the appropriate course of action to take, using this presentation as guidance. Please carefully consider local laws and guidance in your area, particularly the most recent advice issued by your local (and national) health authorities, before making any decision.

Appendix

Funding Sources and Supplemental Information

Contents

HHS

ASPR/BARDA

FOR IMMEDIATE RELEASE
March 18, 2020

Contact: ASPR Press Office
202-205-8117
asprmedia@hhs.gov

HHS Announces New Public-Private Partnership to Develop U.S.-Based, High-Speed Emergency Drug Packaging Solutions

The U.S. Department of Health and Human Services (HHS) has launched a public-private partnership to create a U.S.-based, high-speed, high-volume emergency drug packaging solution using low-cost prefilled syringes.

Working with HHS' Office of the Assistant Secretary for Preparedness and Response (ASPR), the new consortium for Rapid Aseptic Packaging of Injectable Drugs, or RAPID, will enable the Strategic National Stockpile (SNS) to fill and finish, on a rapid basis, hundreds of millions of prefilled syringes to respond quickly and efficiently to widespread health emergencies, such as the novel coronavirus outbreak. Projects are under evaluation to expedite this process and could yield results within six months.

"The ability to deliver vaccines and therapeutic drugs when they are needed the most is among our top priorities. As vaccines and therapeutics become available, we must not be caught short on our capacity to deliver emergency drugs to Americans in need," said HHS Secretary Alex Azar. "The creation of RAPID is the right move at the right time, both for immediate and longer-term national public health emergency needs."

The RAPID consortium is being launched to build a surge capacity network of up to eight domestic facilities for the manufacture of prefilled syringes using a well-established process called Blow-Fill-Seal (BFS). The BFS process features a low cost, high volume, sterile plastic container that holds a pre-filled volume of medicines. This technology is already used for the delivery of billions of doses annually of sterile medicines such as eye drops, nasal sprays, and rotavirus oral vaccines. The RAPID consortium will combine well-established BFS technology with an innovative interlocking needle hub that eliminates the inefficiencies and difficulties of drawing medicines from glass vials. This will help the SNS to reduce its reliance on existing glass vial manufacturing and filling technology with very limited surge capacity.

HHS Assistant Secretary for Preparedness and Response Robert Kadlec commented, "We have been working over the past year on the creation of the RAPID consortium as an essential element of our nation's ability to deliver medicines quickly to large and wide-spread populations affected by a health emergency."

ASPR awarded Apiject Systems America, the public benefit corporation leading RAPID, with an award valued up to $456 million for research and development of BFS prefilled syringes, rapid prototyping and stability testing of select medical countermeasures from the SNS in these devices. Apiject Systems America will recruit the private and philanthropic investment necessary to create year-round domestic manufacturing facilities of aseptic BFS prefilled syringes for population-scale surge response capacity during health emergencies.

About HHS, ASPR and SNS

HHS works to enhance and protect the health and well-being of all Americans, providing for effective health and human services and fostering advances in medicine, public health, and social services. The mission of ASPR is to save lives and protect Americans from 21st century health security threats. ASPR leads the federal government's healthcare and public health preparedness, response, and recovery efforts.

The SNS is the nation's largest supply of potentially life-saving pharmaceuticals and medical supplies for use in a public health emergency severe enough to cause local supplies to run out. When state, local, tribal, and territorial responders request federal assistance to support their response efforts, the stockpile ensures that the right medicines and supplies get to those who need them most during an emergency. Organized for scalable response to a variety of public health threats, this repository contains enough supplies to respond to multiple large-scale emergencies simultaneously.

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Note: All HHS press releases, fact sheets and other news materials are available at https://www.hhs.gov/news.

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Last revised: March 18, 2020

FOR IMMEDIATE RELEASE
March 6, 2020

Contact: ASPR Press Office
202-205-8117
asprmedia@hhs.gov

HHS solicits proposals for development of medical products for novel coronavirus

As part of the government-wide effort to mitigate the spread of COVID-19 in U.S. communities, the U.S. Department of Health and Human Services (HHS) has updated a broad agency announcement (BAA) to focus specifically on products to diagnose, prevent or treat coronavirus infections.

The Biomedical Advanced Research and Development Authority (BARDA), part of the HHS Office of the Assistant Secretary for Preparedness and Response (ASPR), issued the BAA, BAA-18-100-SOL-00003-Amendment 13, to solicit proposals for advanced development and licensure of COVID-19 diagnostics, vaccines, or medicines such as therapeutics or antivirals.

“Amid the expanding global outbreak of COVID-19, Americans need diagnostics, vaccines, and medicines to mitigate the potential impact of this virus”, said BARDA Director Rick Bright, Ph.D. “To accelerate the availability of these lifesaving tools, BARDA took an important step today to request proposals for development of COVID-19 diagnostics, vaccines, or therapeutics, many of which will be developed using existing platform technologies to permit rapid development.”

BARDA will provide funding as well as expertise and core services to support development projects selected through this BAA. These products include diagnostic tests (assays); vaccines; therapeutics; medications to help regulate or normalize the immune system (immunomodulators); therapeutics targeting lung repair; medicines that prevent infections either before or after exposure to the virus (pre-exposure or post-exposure prophylaxis); respiratory protective devices; and ventilators.

There are currently no approved diagnostics, vaccines or treatments for COVID-19 infections. However, the U.S. Food and Drug Administration (FDA) issued two emergency use authorization of diagnostic tests from the Centers for Disease Control and Prevention (CDC) and other authorized public health laboratories, and for use of New York State's Wadsworth diagnostics test. In addition, FDA also issued a new policy Feb. 29 to help expedite the availability of diagnostics.

HHS continues to work across the U.S. government, including with the Department of Defense, to review potential products from public and private sectors to identify promising candidates that could detect or protect against or treat COVID-19 for development and licensure. HHS divisions, including the National Institutes of Health (NIH) and ASPR, have begun supporting development of multiple vaccines and treatments for COVID-19.

To obtain information about any potential products in development in the private sector that could be used in responding to the novel coronavirus outbreak, the U.S. government launched a single point-of-entry website for innovators and product developers to submit brief descriptions of their diagnostics, therapeutics, vaccines, and other products or technologies being developed for COVID-19.

To shorten the time to apply for product licensure and to reduce the spread of COVID-19, federal agencies are particularly interested in identifying products and technologies that have progressed beyond non-clinical studies, have established domestic large-scale commercial Good Manufacturing Practices (cGMP) manufacturing capability, and have utilized a platform used to manufacture a product already approved by the FDA.

In addition, BARDA opened an easy broad agency announcement, an EZ-BAA, seeking diagnostics that utilize platforms already cleared by the FDA, with a viable plan to meet requirements for the FDA to consider emergency use authorization within 12 weeks.

About HHS, ASPR, and BARDA

HHS works to enhance and protect the health and well-being of all Americans, providing for effective health and human services and fostering advances in medicine, public health, and social services. The mission of ASPR is to save lives and protect Americans from 21st century health security threats. Within ASPR, BARDA invests in the innovation, advanced research and development, acquisition, and manufacturing of medical countermeasures – vaccines, drugs, therapeutics, diagnostic tools, and non-pharmaceutical products needed to combat health security threats. To date, 54 BARDA-supported products have achieved regulatory approval, licensure or clearance.

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Office of Biomedical Advanced Research and Development Authority (BARDA) Division of Research, Innovation & Ventures (DRIVe)

Special Instructions 001 Issuance for Easy Broad Agency Announcement (EZ-BAA) BAA-20-100-SOL-0002

Area of Interest (AOI) #4: 2019-nCoV

DRIVe Contracting Office
200 C Street SW
Washington, DC 20201

I. INTRODUCTION AND OVERVIEW INFORMATION

A. Development Opportunity Objective:

Under these Special Instructions, BARDA is temporarily suspending AOIs 1-3 as part of its EZ-BAA (BAA-20-100-SOL-0002), but is pleased to announce that it is now accepting abstract submissions for AOI #4: 2019-nCoV. We are seeking abstracts for the following under this focus area:

1. The development and Emergency Use Authorization (EUA) of an *in vitro* diagnostic assay for the detection of 2019-nCoV RNA in clinical specimens, including upper (e.g, nasopharyngeal and oropharyngeal swabs, nasopharyngeal wash/aspirate, or nasal aspirate) and lower (e.g., bronchoalveolar lavage, tracheal aspirate, or sputum) respiratory tract specimens.

   The assay must be developed for use with an existing FDA-cleared molecular platform that is currently widely placed in U.S. healthcare settings. Respondents should present a viable plan that achieves an EUA submission milestone within 12 weeks of award. As part of the abstract submission, respondents should describe the current development status of their 2019-nCoV assay, including *in silico* analysis of targets, access to validation materials to support EUA submission, and contacts with the FDA.

B. Eligible Respondents & Scope Parameters:

These Special Instructions are open to all responsible sources as described in the EZ-BAA. Preliminarily, a call with the relevant technical team is strongly encouraged prior to any submission to better understand the program objectives for AOI #4. The point of contact for AOI #4 is the following:

John Lee – john.lee@hhs.gov

AOI #4 will be open for abstract submissions until 1700 HRS ET on 18 March 2020, unless otherwise extended. Additionally, award(s) expected to be made under these Special Instructions will be less than $750,000 in total government funding.

Abstract submissions that do not conform to the requirements outlined in the EZ-BAA (BAA-20-100-SOL-0002) may be considered non-responsive and will not be reviewed.

C. Number of Awards:

Multiple awards are anticipated and are dependent upon the program priorities, scientific/technical merit of submissions, how well submissions fit within the area of interest, and the availability of funding. The program funding is subject to change based on the government's discretion.

D. Special Instructions Application Process:

These Special Instructions will follow the same submission process and review procedures as those established under the EZ-BAA (BAA-20-100-SOL-00002). For complete details, please read the EZ-BAA solicitation in its entirety.

Office of Biomedical Advanced Research and Development Authority (BARDA) Division of Research, Innovation & Ventures (DRIVe)

Special Instructions 002 Issuance for Easy Broad Agency Announcement (EZ-BAA) BAA-20-100-SOL-0002

New Topic under Area of Interest (AOI) #4: 2019-nCoV

DRIVe Contracting Office
200 C Street SW
Washington, DC 20201

I. INTRODUCTION AND OVERVIEW INFORMATION

A. Development Opportunity Objective:

Under these Special Instructions 002, BARDA is adding a new topic under its temporary AOI #4: 2019-nCoV as part of its EZ-BAA (BAA-20-100-SOL-0002). We are now seeking abstract submissions for the following:

AOI #4.1: Molecular Diagnostic Assay for 2019-nCoV

The development and Emergency Use Authorization (EUA) of an *in vitro* diagnostic assay for the detection of 2019-nCoV RNA in clinical specimens, including upper (e.g, nasopharyngeal and oropharyngeal swabs, nasopharyngeal wash/aspirate, or nasal aspirate) and lower (e.g., bronchoalveolar lavage, tracheal aspirate, or sputum) respiratory tract specimens.

The assay must be developed for use with an existing FDA-cleared molecular platform that is currently widely placed in U.S. healthcare settings. Respondents should present a viable plan that achieves an EUA submission milestone within 12 weeks of award. As part of the abstract submission, respondents should describe the current development status of their 2019-nCoV assay, including *in silico* analysis of targets, access to validation materials to support EUA submission, and contacts with the FDA.

AOI #4.2: Nonclinical Model Development and Screening for 2019-nCoV

The development of an *in vitro* assay and *in vivo* 2019-nCoV nonclinical model(s) for screening potential medical countermeasures for the treatment of 2019-nCoV.

Respondents must possess a 2019-nCoV strain, hold a Select Agent Permit, and have access to a nonclinical BSL-3 laboratory capable of performing mouse therapeutic studies of 2019-nCoV. As part of the abstract submission, respondents should describe the current development status of their 2019-nCoV assay, justify species to be used for *in vivo* screening, and demonstrate recent *in vivo* work with therapeutics for SARS-CoV and MERS-CoV.

B. Eligible Respondents & Scope Parameters:

These Special Instructions 002 are open to all responsible sources as described in the EZ-BAA. Preliminarily, a call with the relevant Program Manager is strongly encouraged prior to any submission to better understand the program objectives for AOI #4. The points of contact for each topic under AOI #4 are the following:

AOI #4.1: John Lee, john.lee@hhs.gov
AOI #4.2: Brian Tse, brian.tse@hhs.gov

AOI #4 will be open for abstract submissions until 1700 HRS ET on 18 March 2020, unless otherwise extended. Additionally, award(s) expected to be made under these Special Instructions 002 will be less than $750,000 in total government funding.

Abstract submissions that do not conform to the requirements outlined in the EZ-BAA may be considered non-responsive and will not be reviewed.

NOTE: Funding is limited, so we encourage any interested vendors to reach out to the appropriate Program Manager listed above before submitting an abstract as soon as possible.

C. Number of Awards:

Multiple awards are anticipated and are dependent upon the program priorities, scientific/technical merit of submissions, how well submissions fit within the AOI, and the availability of funding. The program funding is subject to change based on the government's discretion.

D. Special Instructions Application Process:

These Special Instructions 002 will follow the same submission process and review procedures as those established under the EZ-BAA. For complete details, please read the EZ-BAA solicitation in its entirety.

Office of Biomedical Advanced Research and Development Authority (BARDA) Division of Research, Innovation & Ventures (DRIVe)

Special Instructions 003 Issuance for Easy Broad Agency Announcement (EZ-BAA) BAA-20-100-SOL-0002

New Topic under Area of Interest (AOI) #4: COVID-19

DRIVe Contracting Office
200 C Street SW
Washington, DC 20201

I. INTRODUCTION AND OVERVIEW INFORMATION

A. Development Opportunity Objective:

Under these Special Instructions 003, BARDA is adding a new topics under its temporary AOI #4: COVID-19 as part of its EZ-BAA (BAA-20-100-SOL-0002). We are now seeking abstract submissions for the following:

AOI #4.1-A: Molecular Diagnostic Assay for SARS-CoV-2 virus on existing FDA-cleared platform

The development and Emergency Use Authorization (EUA) of an *in vitro* diagnostic assay for the detection of SARS-CoV-2 (2019-nCoV) RNA in clinical specimens, including upper (e.g, nasopharyngeal and oropharyngeal swabs, nasopharyngeal wash/aspirate, or nasal aspirate) and lower (e.g., bronchoalveolar lavage, tracheal aspirate, or sputum) respiratory tract specimens.

The assay must be developed for use with an existing FDA-cleared molecular platform that is currently widely placed in U.S. healthcare settings. Preference will be given to respondents who present a viable plan that achieves an EUA submission milestone within 12 weeks of award. As part of the abstract submission, respondents should describe the current development status of their SARS-CoV-2 (2019-nCoV) assay, including *in silico* analysis of targets, access to validation materials to support EUA submission, and contacts with the FDA. Priority will be given to products manufactured in the United States.

AOI #4.1-B: Point-of-Care Diagnostic Assay for detection of SARS-CoV-2 virus

The development and Emergency Use Authorization (EUA) of an *in vitro* diagnostic test for the detection of SARS-CoV-2 (i.e., virus, viral RNA, or viral antigens) in respiratory specimens that has a small footprint (e.g., hand-held), is easy to use at the point of care (i.e., suitable for use in CLIA-waived settings) and produces results in less than 30 minutes (less than 15 minutes preferred). While there is no minimum Technology Readiness Level (TRL) required, Respondents should describe the platform, proposed detection targets, development status of the test, information to support clinical utility claims, and proposed plan to achieve EUA submission. Priority will be given to products manufactured in the United States.

AOI #4.1-C: Diagnostic Assay for detection of COVID-19 disease

The development and Emergency Use Authorization (EUA) of an *in vitro* diagnostic test for COVID-19 disease that has a small footprint (e.g., hand-held) and is easy to use at the point of care (i.e., suitable for use in CLIA-waived settings). Assays should detect host or pathogen biomarkers specific for COVID-19 disease in non-invasive specimens that can be easily collected in CLIA-waived settings, and provide results in less than 30 minutes (less than 15 minutes preferred). While there is no minimum Technology Readiness Level (TRL) required, Respondents should describe the platform, proposed detection targets, development status of the test, information to support clinical utility claims, and proposed plan to achieve

EUA submission. Priority will be given to products manufactured in the United States.

AOI #4.2: Nonclinical Model Development and Screening for SARS-CoV-2 virus

The development of an *in vitro* assay and *in vivo* SARS-CoV-2 nonclinical model(s) for screening potential medical countermeasures for the treatment of SARS-CoV-2.

Respondents must possess a SARS-CoV-2 strain, hold a Select Agent Permit, and have access to a nonclinical BSL-3 laboratory capable of performing mouse therapeutic studies of SARS-CoV-2. As part of the abstract submission, respondents should describe the current development status of their SARS-CoV-2 assay, justify species to be used for *in vivo* screening, and demonstrate recent *in vivo* work with therapeutics for SARS-CoV and MERS-CoV.

AOI #4.3: COVID-19 Vaccine

The development of "ready to use", rapid response platform technologies, alternative vaccine administration/delivery, and adjuvants for application to the production of COVID-19 vaccines on an accelerated timeline. Priority given to platforms that offer an integrated approach to the full spectrum of vaccine development; from creation of candidate vaccines through testing, selection and regulatory approval, to full-scale manufacturing capability with the fewest adjustments and refinements necessary for a vaccine for COVID-19. Priority will be given to products manufactured in the United States.

AOI #4.4: Advanced Manufacturing Technologies

The development and demonstration of innovations and enhancements to manufacturing platforms to support the development of necessary medical countermeasures including vaccines and therapeutics in prevention, preparation, and response to COVID-19. The purpose of the innovations and enhancement to advanced manufacturing technologies may include, but are not limited to, improving pharmaceutical quality, rapidly scaling manufacturing capabilities, shortening supply chains, increasing manufacturing resilience to disruption, accelerating availability of emerging therapies/vaccines, or reducing the risk of pharmaceutical shortages. Advanced manufacturing technologies may include, but are not limited to, continuous manufacturing and additive manufacturing (including 3D printing). Priority will be given to products manufactured in the United States.

B. Eligible Respondents & Scope Parameters:

These Special Instructions 003 are open to all responsible sources as described in the EZ-BAA. Preliminarily, a call with the relevant Program Manager is strongly encouraged prior to any submission to better understand the program objectives for AOI #4. The points of contact for each topic under AOI #4 are the following:

AOI #4.1-A: Justin Yang, Ge.Yang@hhs.gov
AOI #4.1-B: Justin Yang, Ge.Yang@hhs.gov

AOI #4.1-C: Justin Yang, Ge.Yang@hhs.gov
AOI #4.2: Brian Tse, brian.tse@hhs.gov
AOI #4.3: Armen Donabedian, armen.donabedian@hhs.gov
AOI #4.4: Timothy Belski, Timothy.Belski@hhs.gov

AOI #4 will be open for abstract submissions until 1700 HRS ET on 30 June 2020, unless otherwise extended. Additionally, award(s) expected to be made under these Special Instructions 003 will be less than $750,000 in total government funding.

Abstract submissions that do not conform to the requirements outlined in the EZ-BAA may be considered non-responsive and will not be reviewed.

NOTE: Funding is limited, so we encourage any interested vendors to reach out to the appropriate Program Manager listed above before submitting an abstract as soon as possible.

C. Number of Awards:

Multiple awards are anticipated and are dependent upon the program priorities, scientific/technical merit of submissions, how well submissions fit within the AOI, and the availability of funding. The program funding is subject to change based on the government's discretion.

D. Special Instructions Application Process:

These Special Instructions 003 will follow the same submission process and review procedures as those established under the EZ-BAA. For complete details, please read the EZ-BAA solicitation in its entirety.

FDA

Contains Nonbinding Recommendations

FDA Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Pandemic

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Guidance for Industry, Investigators, and Institutional Review Boards

March 2020

Comments may be submitted at any time for Agency consideration. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. Submit electronic comments to https://www.regulations.gov. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions on clinical trial conduct during the COVID-19 pandemic, please email Clinicaltrialconduct-COVID19@fda.hhs.gov.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)
Office of Good Clinical Practice (OGCP)

FDA U.S. FOOD & DRUG ADMINISTRATION

Preface

Public Comment

You may submit electronic comments and suggestions at any time for Agency consideration to https://www.regulations.gov. Submit written comments to the Dockets Management Staff, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD 20852. Identify all comments with the docket number FDA 2020-D-1106. Comments may not be acted upon by the Agency until the document is next revised or updated.

Additional Copies

Additional copies are available from https://www.fda.gov/regulatory-information/search-fda-guidance-documents. You may also send an e-mail request to Clinicaltrialconduct-COVID19@fda.hhs.gov to receive a copy of the guidance. Please include the document number FDA-2020-D-1106 and complete title of the guidance in the request.

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FDA Guidance on Conduct of Clinical Trials of Medical Products during the COVID-19 Pandemic

Guidance for Industry, Investigators, and Institutional Review Boards

I. Introduction

The Food and Drug Administration (FDA or Agency) plays a critical role in protecting the United States from threats including emerging infectious diseases, including the Coronavirus Disease 2019 (COVID-19) pandemic. FDA is committed to providing timely guidance to support continuity and response efforts to this pandemic.

FDA is issuing this guidance to provide general considerations to assist sponsors in assuring the safety of trial participants, maintaining compliance with good clinical practice (GCP), and minimizing risks to trial integrity during the COVID-19 pandemic.

Given this public health emergency, this guidance is being implemented without prior public comment because the FDA has determined that prior public participation for this guidance is not feasible or appropriate (see section 701(h)(1)(C)(i) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) and 21 CFR 10.115(g)(2)). This guidance document is being implemented immediately, but it remains subject to comment in accordance with the Agency's good guidance practices.

In general, FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidance means that something is suggested or recommended, but not required.

II. Background

There is currently an outbreak of respiratory disease caused by a novel coronavirus that was first detected in Wuhan City, Hubei Province, China, and that has now been detected in many locations internationally, including cases in the United States. The virus has been named "SARS-CoV-2" and the disease it causes has been named "Coronavirus Disease 2019" (COVID-19). On January 31, 2020, the Department of Health and Human Services (HHS) issued a declaration of a public health emergency related to COVID-19 and mobilized the Operating Divisions of HHS.[1] In addition, on March 13, 2020, the President declared a national emergency in response to COVID-19.[2]

FDA recognizes that the COVID-19 pandemic may impact the conduct of clinical trials of medical products. Challenges may arise, for example, from quarantines, site closures, travel limitations, interruptions to the supply chain for the investigational product[3], or other considerations if site personnel or trial subjects become infected with COVID-19. These challenges may lead to difficulties in meeting protocol-specified procedures, including administering or using the investigational product or adhering to protocol-mandated visits and laboratory/diagnostic testing. FDA recognizes that protocol modifications may be required, and that there may be unavoidable protocol deviations due to COVID-19 illness and/or COVID-19 control measures. Although the necessity for, and impact of, COVID-19 control measures on trials will vary depending on many factors, including the nature of disease under study, the trial design, and in what region(s) the study is being conducted, FDA outlines the following general considerations to assist sponsors in assuring the safety of trial participants, maintaining compliance with good clinical practice (GCP), and minimizing risks to trial integrity.

III. Discussion

A. Considerations for ongoing trials:

- Ensuring the safety of trial participants is paramount. Sponsors should consider each circumstance, focusing on the potential impact on the safety of trial participants, and modify study conduct accordingly. Study decisions may include those regarding continuing trial recruitment, continuing use of the investigational product for patients already participating in the trial, and the need to change patient monitoring during the trial. In all cases, it is critical that trial participants are kept informed of changes to the study and monitoring plans that could impact them.

- Sponsors, in consultation with clinical investigators and Institutional Review Boards (IRBs)/Independent Ethics Committees (IECs), may determine that the protection of a

[1] Secretary of Health and Human Services Alex M Azar, Determination that a Public Health Emergency Exists. Jan. 31, 2020. (Accessible at https://www.phe.gov/emergency/news/healthactions/phe/Pages/2019-nCoV.aspx).
[2] [Placeholder for official link to announcement]
[3] For the purposes of this guidance, the term *investigational product* refers to human drugs and biological products, and medical devices.

participant's safety, welfare, and rights is best served by continuing a study participant in the trial as per the protocol or by discontinuing the administration or use of the investigational product or even participation in the trial. Such decisions will depend on specific circumstances, including the nature of the investigational product, the ability to conduct appropriate safety monitoring, the potential impact on the investigational product supply chain, and the nature of the disease under study in the trial.

- Since trial participants may not be able to come to the investigational site for protocol-specified visits, sponsors should evaluate whether alternative methods for safety assessments (e.g., phone contact, virtual visit, alternative location for assessment, including local labs or imaging centers) could be implemented when necessary and feasible, and would be sufficient to assure the safety of trial participants. Sponsors should determine if in-person visits are necessary to fully assure the safety of trial participants (for example to carry out procedures necessary to assess safety or the safe use of the investigational product appropriately); in making the decision to continue use or administration of the investigational product, the sponsor should consider whether the safety of trial participants can be assured with the implementation of the altered monitoring approach.

- In some cases, trial participants who no longer have access to investigational product or the investigational site may need additional safety monitoring (e.g. withdrawal of an active investigational treatment).

- The need to put new processes in place or to modify existing processes will vary by the protocol and local situation. For example, this assessment could include consideration of whether it is appropriate to delay some assessments for ongoing trials, or, if the study cannot be properly conducted under the existing protocol, whether to stop ongoing recruitment, or even withdraw trial participants.

- COVID-19 screening procedures that may be mandated by the health care system in which a clinical trial is being conducted do not need to be reported as an amendment to the protocol even if done during clinical study visits unless the sponsor is incorporating the data collected as part of a new research objective.

- Changes in a protocol are typically not implemented before review and approval by the IRB/IEC, and in some cases, by FDA. Sponsors and clinical investigators are encouraged to engage with IRBs/IEC as early as possible when urgent or emergent changes to the protocol or informed consent are anticipated as a result of COVID-19. Such changes to the protocol or investigational plan to minimize or eliminate immediate hazards or to protect the life and well-being of research participants (e.g., to limit exposure to COVID-19) may be implemented without IRB approval or before filing an

amendment to the IND or IDE, but are required to be reported afterwards.[4] FDA encourages sponsors and investigators to work with their IRBs to prospectively define procedures to prioritize reporting of deviations that may impact the safety of trial participants.

- The implementation of alternative processes should be consistent with the protocol to the extent possible, and sponsors and clinical investigators should document the reason for any contingency measures implemented. Sponsors and clinical investigators should document how restrictions related to COVID-19 led to the changes in study conduct and duration of those changes and indicate which trial participants were impacted and how those trial participants were impacted.

- Changes in study visit schedules, missed visits, or patient discontinuations may lead to missing information (e.g., for protocol-specified procedures). It will be important to capture *specific* information in the case report form that explains the basis of the missing data, including the relationship to COVID-19 for missing protocol-specified information (e.g., from missed study visits or study discontinuations due to COVID-19). This information, summarized in the clinical study report, will be helpful to the sponsor and FDA.

- If scheduled visits at clinical sites will be significantly impacted, certain investigational products, such as those that are typically distributed for self-administration, may be amenable to alternative secure delivery methods. For other investigational products that are normally administered in a health care setting, consulting FDA review divisions on plans for alternative administration (e.g., home nursing or alternative sites by trained but non-study personnel) is recommended. In all cases, existing regulatory requirements for maintaining investigational product accountability remain and should be addressed and documented.

- With respect to efficacy assessments, FDA recommends consultation with the appropriate review division regarding protocol modifications for the collection of efficacy endpoints, such as use of virtual assessments, delays in assessments, and alternative collection of research-specific specimens, if feasible. For individual instances where efficacy endpoints are not collected, the reasons for failing to obtain the efficacy assessment should be documented (e.g., identifying the specific limitation imposed by COVID-19 leading to the inability to perform the protocol-specified assessment).

- If changes in the protocol will lead to amending data management and/or statistical analysis plans, the sponsor should consider doing so in consultation with the applicable

[4] See 21 CFR 56.108(a)(4), 21 CFR 56.104(c), 21 CFR 312.30(b)(2)(ii), and 21 CFR 812.35(a)(2).

FDA review division. Prior to locking the database, sponsors should address in the statistical analysis plan how protocol deviations related to COVID-19 will be handled for the prespecified analyses.

- If planned on-site monitoring visits are no longer possible, sponsors should consider optimizing use of central and remote monitoring programs to maintain oversight of clinical sites.

B. In general, and if policies and procedures are not already in place for applicable trials:

- Sponsors, clinical investigators, and IRBs should consider establishing and implementing policy and procedures, or revise existing policy and procedures, to describe approaches to be used to protect trial participants and manage study conduct during possible disruption of the study as a result of COVID-19 control measures at study sites. Changes to policy and procedures could address, but not be limited to, impact on the informed consent process, study visits and procedures, data collection, study monitoring, adverse event reporting, and changes in investigator(s), site staff, and/or monitor(s) secondary to travel restrictions, quarantine measures, or COVID-19 illness itself. Policy and procedures should be compliant with applicable (regional or national) policy for the management and control of COVID-19. Depending upon the nature of the changes described above, a protocol amendment may be required under the applicable regulations.[5]

C. For all trials that are impacted by the COVID-19 pandemic:

Sponsors should describe in appropriate sections of the clinical study report (or in a separate study-specific document):

1. Contingency measures implemented to manage study conduct during disruption of the study as a result of COVID-19 control measures.
2. A listing of all participants affected by the COVID-19 related study disruption by unique subject number identifier and by investigational site, and a description of how the individual's participation was altered.
3. Analyses and corresponding discussions that address the impact of implemented contingency measures (e.g., trial participant discontinuation from investigational product and/or study, alternative procedures used to collect critical safety and/or efficacy data) on the safety and efficacy results reported for the study.

Robust efforts by sponsors, investigators, and IRBs/IECs to maintain the safety of trial participants and study data integrity are expected, and such efforts should be documented. As stated above, FDA recognizes that protocol modifications may be required, including unavoidable protocol deviations due to COVID-19 illness and/or COVID-19 control measures. Efforts to minimize impacts on trial integrity, and to document the reasons for protocol deviations, will be important.

[5] See 21 CFR 312.30(b) and 21 CFR 812.35(a).

IV. Additional Resources

For further questions on clinical trial conduct during the COVID 19 pandemic, please email Clinicaltrialconduct-COVID19@fda.hhs.gov.

Contact information for FDA's review divisions is as follows:

CDER: https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/office-new-drugs

CBER: https://www.fda.gov/about-fda/center-biologics-evaluation-and-research-cber/contacts-center-biologics-evaluation-research-cber#indcont

CDRH: https://www.fda.gov/about-fda/cdrh-offices/cdrh-management-directory-organization

Bill and Melinda Gates Foundation

Bill & Melinda Gates Foundation, Wellcome, and Mastercard Launch Initiative to Speed Development and Access to Therapies for COVID-19

COVID-19 Therapeutics Accelerator will coordinate R&D efforts and remove barriers to drug development and scale-up to address the epidemic

Bill & Melinda Gates Foundation
206-709-3400
media@gatesfoundation.org
follow @gatesfoundation

SEATTLE, March 10, 2020 – The Bill & Melinda Gates Foundation, Wellcome, and Mastercard today committed up to $125 million in seed funding to speed-up the response to the COVID-19 epidemic by identifying, assessing, developing, and scaling-up treatments. The partners are committed to equitable access, including making products available and affordable in low-resource settings. The COVID-19 Therapeutics Accelerator will play a catalytic role by accelerating and evaluating new and repurposed drugs and biologics to treat patients with COVID-19 in the immediate term, and other viral pathogens in the longer-term. Currently there are no broad-spectrum antivirals or immunotherapies available for the fight against emerging pathogens, and none approved for use on COVID-19.

The Gates Foundation and Wellcome are each contributing up to $50 million, and the Mastercard Impact Fund has committed up to $25 million to catalyze the initial work of the accelerator. The Gates Foundation's funding is part of its up to $100 million commitment to the COVID-19 response announced last month.

"Viruses like COVID-19 spread rapidly, but the development of vaccines and treatments to stop them moves slowly," said Mark Suzman, chief executive officer of the Bill & Melinda Gates Foundation. "If we want to make the world safe from outbreaks like COVID-19, particularly for those most vulnerable, then we need to find a way to make research and development move faster. That requires governments, private enterprise, and philanthropic organizations to act quickly to fund R&D."

The COVID-19 Therapeutics Accelerator will work with the World Health Organization, government and private sector funders and organizations, as well as the global regulatory and policy-setting institutions. The Accelerator will have an end-to-end focus, from drug pipeline development through manufacturing and scale-up. By sharing research, coordinating investments, and pooling resources, these efforts can help to accelerate research. This kind of collaboration was a key lesson from the 2014 Ebola outbreak. By providing fast and flexible funding at key stages of the development process, the Accelerator will de-risk the pathway for new drugs and biologics for COVID-19 and future epidemic threats, ensuring access in lower-resource countries.

The COVID-19 Therapeutics Accelerator will operate jointly as an initiative of the funders, drawing on expertise from inside and outside their organizations. The Accelerator will pursue several aspects of the development cycle to streamline the pathway from candidate product to clinical assessment, use, and manufacturing. To identify candidate compounds, the Accelerator will take a three-pronged approach: testing approved drugs for activity against COVID-19, screening libraries of thousands of compounds with confirmed safety data, and considering new investigational compounds and monoclonal antibodies. Drugs or monoclonal antibodies that pass initial screening would then be developed by an industry partner. The biotech and pharmaceutical industries will be critical partners, bringing their compound libraries and clinical data to the collaboration and lending commercialization and other expertise that will be required to scale up successful drugs and monoclonal antibodies. In parallel to the development of the COVID-19 drug pipeline, the Accelerator will work with regulators to align criteria and develop manufacturing capacity with industry. An accelerated pathway to bringing effective treatments to patients is around one year for products that have current regulatory approval or candidates with existing clinical data. The timeline would be longer for compounds further upstream in the pipeline that have limited existing clinical data.

Dr. Jeremy Farrar, director of Wellcome said, "This virus is an unprecedented global threat, and one for which we must propel international partnerships to develop treatments, rapid diagnostics, and vaccines. Science is moving at a phenomenal pace against COVID-19, but to get ahead of this epidemic we need greater investment and to ensure research co-ordination. The Therapeutics Accelerator will allow us to do this for potential treatments with support for research, development, assessment, and manufacturing. COVID-19 is an extremely challenging virus, but we've proved that through collaborating across borders we can tackle emerging infectious diseases. We must strive to strengthen efforts in the face of COVID-19, and in doing so, continue to make sure advances are accessible and affordable to all. Investing now, at scale, at risk and as a collective global effort is vital if we are to change the course of this epidemic. We welcome others to join us in this effort."

While antiviral drugs are approved to lessen the severity of seasonal flu and treat HIV, among other viral diseases, none have demonstrated efficacy against the current epidemic. One reason for the lack of effective treatments is that products may not have an immediate market, which can slow or prevent their research and commercial development. The COVID-19 Therapeutics Accelerator is designed to help by bringing together resources and expertise to lower the financial and technical risk for academia, biotech, and pharmaceutical companies, while ensuring that these products are accessible and affordable to people in low-resource settings. The expertise of pharmaceutical companies will be critical in identifying, researching, and commercializing successful drugs.

"We're proud to join this crucial effort to combat COVID-19 in furtherance of our commitment to inclusive growth," said Mike Froman, vice chairman of Mastercard. "This global challenge not only represents a risk to the health and safety of populations all over the world, but also poses a potential disruption to the economic vitality of millions of people, businesses, and organizations worldwide. Our experience with financial inclusion shows us the importance of building a network of parties who bring not only their capital, but complementary assets and skill sets to the table, and we welcome other partners concerned about inclusive growth to join this effort."

About the Bill & Melinda Gates Foundation

Guided by the belief that every life has equal value, the Bill & Melinda Gates Foundation works to help all people lead healthy, productive lives. In developing countries, it focuses on improving people's health and giving them the chance to lift themselves out of hunger and extreme poverty. In the United States, it seeks to ensure that all people—especially those with the fewest resources—have access to the opportunities they need to succeed in school and life. Based in Seattle, Washington, the foundation is led by CEO Mark Suzman and Co-chair William H. Gates Sr., under the direction of Bill and Melinda Gates and Warren Buffett.

About Wellcome

Wellcome exists to improve health by helping great ideas to thrive. We support researchers, we take on big health challenges, we campaign for better science, and we help everyone get involved with science and health research. We are a politically and financially independent foundation.

About Mastercard

Mastercard is a global technology company in the payments industry. Our mission is to connect and power an inclusive, digital economy that benefits everyone, everywhere by making transactions safe, simple, smart, and accessible. Using secure data and networks, partnerships and passion, our innovations and solutions help individuals, financial institutions, governments, and businesses realize their greatest potential. Our decency quotient, or DQ, drives our culture

and everything we do inside and outside of our company. With connections across more than 210 countries and territories, we are building a sustainable world that unlocks priceless possibilities for all. Mastercard is the sole corporate donor to the Mastercard Impact Fund.

Media Contacts:

For the Bill & Melinda Gates Foundation: media@gatesfoundation.org
For Wellcome: Maggie Stratton +44(0)20 7611 8609, m.stratton@wellcome.ac.uk
For Mastercard: Casey Stavropoulos +1 914 414 5291, casey.stavropolous@mastercard.com

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Bill & Melinda Gates Foundation, Wellcome, and Mastercard Launch Initiative to Speed Development and Access to Therapies for COVID-19

COVID-19 Therapeutics Accelerator will coordinate R&D efforts and remove barriers to drug development and scale-up to address the epidemic

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SEATTLE, March 10, 2020 – The Bill & Melinda Gates Foundation, Wellcome, and Mastercard today committed up to $125 million in seed funding to speed-up the response to the COVID-19 epidemic by identifying, assessing, developing, and scaling-up treatments. The partners are committed to equitable access, including making products available and affordable in low-resource settings. The COVID-19 Therapeutics Accelerator will play a catalytic role by accelerating and evaluating new and repurposed drugs and biologics to treat patients with COVID-19 in the immediate term, and other viral pathogens in the longer-term. Currently there are no broad-spectrum antivirals or immunotherapies available for the fight against emerging pathogens, and none approved for use on COVID-19.

The Gates Foundation and Wellcome are each contributing up to $50 million, and the Mastercard Impact Fund has committed up to $25 million to catalyze the initial work of the accelerator. The Gates Foundation's funding is part of its up to $100 million commitment to the COVID-19 response announced last month.

"Viruses like COVID-19 spread rapidly, but the development of vaccines and treatments to stop them moves slowly," said Mark Suzman, chief executive officer of the Bill & Melinda Gates Foundation. "If we want to make the world safe from outbreaks like COVID-19, particularly for those most vulnerable, then we need to find a way to make research and development move faster. That requires governments, private enterprise, and philanthropic organizations to act quickly to fund R&D."

The COVID-19 Therapeutics Accelerator will work with the World Health Organization, government and private sector funders and organizations, as well as the global regulatory and policy-setting institutions. The Accelerator will have an end-to-end focus, from drug pipeline development through manufacturing and scale-up. By sharing research, coordinating investments, and pooling resources, these efforts can help to accelerate research. This kind of collaboration was a key lesson from the 2014 Ebola outbreak. By providing fast and flexible funding at key stages of the development process, the Accelerator will de-risk the pathway for new drugs and biologics for COVID-19 and future epidemic threats, ensuring access in lower-resource countries.

The COVID-19 Therapeutics Accelerator will operate jointly as an initiative of the funders, drawing on expertise from inside and outside their organizations. The Accelerator will pursue several aspects of the development cycle to streamline the pathway from candidate product to clinical assessment, use, and manufacturing. To identify candidate compounds, the Accelerator will take a three-pronged approach: testing approved drugs for activity against COVID-19, screening libraries of thousands of compounds with confirmed safety data, and considering new investigational compounds and monoclonal antibodies. Drugs or monoclonal antibodies that pass initial screening would then be developed by an industry partner. The biotech and pharmaceutical industries will be critical partners, bringing their compound libraries and clinical data to the collaboration and lending commercialization and other expertise that will be required to scale up successful drugs and monoclonal antibodies. In parallel to the development of the COVID-19 drug pipeline, the Accelerator will work with regulators to align criteria and develop manufacturing capacity with industry. An accelerated pathway to bringing effective treatments to patients is around one year for products that have current regulatory approval or candidates with existing clinical data. The timeline would be longer for compounds further upstream in the pipeline that have limited existing clinical data.

Dr. Jeremy Farrar, director of Wellcome said, "This virus is an unprecedented global threat, and one for which we must propel international partnerships to develop treatments, rapid diagnostics, and vaccines. Science is moving at a phenomenal pace against COVID-19, but to get ahead of this epidemic we need greater investment and to ensure research co-ordination. The Therapeutics Accelerator will allow us to do this for potential treatments with support for research, development, assessment, and manufacturing. COVID-19 is an extremely challenging virus, but we've proved that through collaborating across borders we can tackle emerging infectious diseases. We must strive to strengthen efforts in the face of COVID-19, and in doing so, continue to make sure advances are accessible and affordable to all. Investing now, at scale, at risk and as a collective global effort is vital if we are to change the course of this epidemic. We welcome others to join us in this effort."

While antiviral drugs are approved to lessen the severity of seasonal flu and treat HIV, among other viral diseases, none have demonstrated efficacy against the current epidemic. One reason for the lack of effective treatments is that products may not have an immediate market, which can slow or prevent their research and commercial development. The COVID-19 Therapeutics Accelerator is designed to help by bringing together resources and expertise to lower the financial and technical risk for academia, biotech, and pharmaceutical companies, while ensuring that these products are accessible and affordable to people in low-resource settings. The expertise of pharmaceutical companies will be critical in identifying, researching, and commercializing successful drugs.

"We're proud to join this crucial effort to combat COVID-19 in furtherance of our commitment to inclusive growth," said Mike Froman, vice chairman of Mastercard. "This global challenge not only represents a risk to the health and safety of populations all over the world, but also poses a potential disruption to the economic vitality of millions of people, businesses, and organizations worldwide. Our experience with financial inclusion shows us the importance of building a network of parties who bring not only their capital, but complementary assets and skill sets to the table, and we welcome other partners concerned about inclusive growth to join this effort."

About the Bill & Melinda Gates Foundation

Guided by the belief that every life has equal value, the Bill & Melinda Gates Foundation works to help all people lead healthy, productive lives. In developing countries, it focuses on improving people's health and giving them the chance to lift themselves out of hunger and extreme poverty. In the United States, it seeks to ensure that all people—especially those with the fewest resources—have access to the opportunities they need to succeed in school and life. Based in Seattle, Washington, the foundation is led by CEO Mark Suzman and Co-chair William H. Gates Sr., under the direction of Bill and Melinda Gates and Warren Buffett.

About Wellcome

Wellcome exists to improve health by helping great ideas to thrive. We support researchers, we take on big health challenges, we campaign for better science, and we help everyone get involved with science and health research. We are a politically and financially independent foundation.

About Mastercard

Mastercard is a global technology company in the payments industry. Our mission is to connect and power an inclusive, digital economy that benefits everyone, everywhere by making transactions safe, simple, smart, and accessible. Using secure data and networks, partnerships and passion, our innovations and solutions help individuals, financial institutions, governments, and businesses realize their greatest potential. Our decency quotient, or DQ, drives our culture and everything we do inside and outside of our company. With connections across more than 210 countries and territories, we are building a sustainable world that unlocks priceless possibilities for all. Mastercard is the sole corporate donor to the Mastercard Impact Fund.

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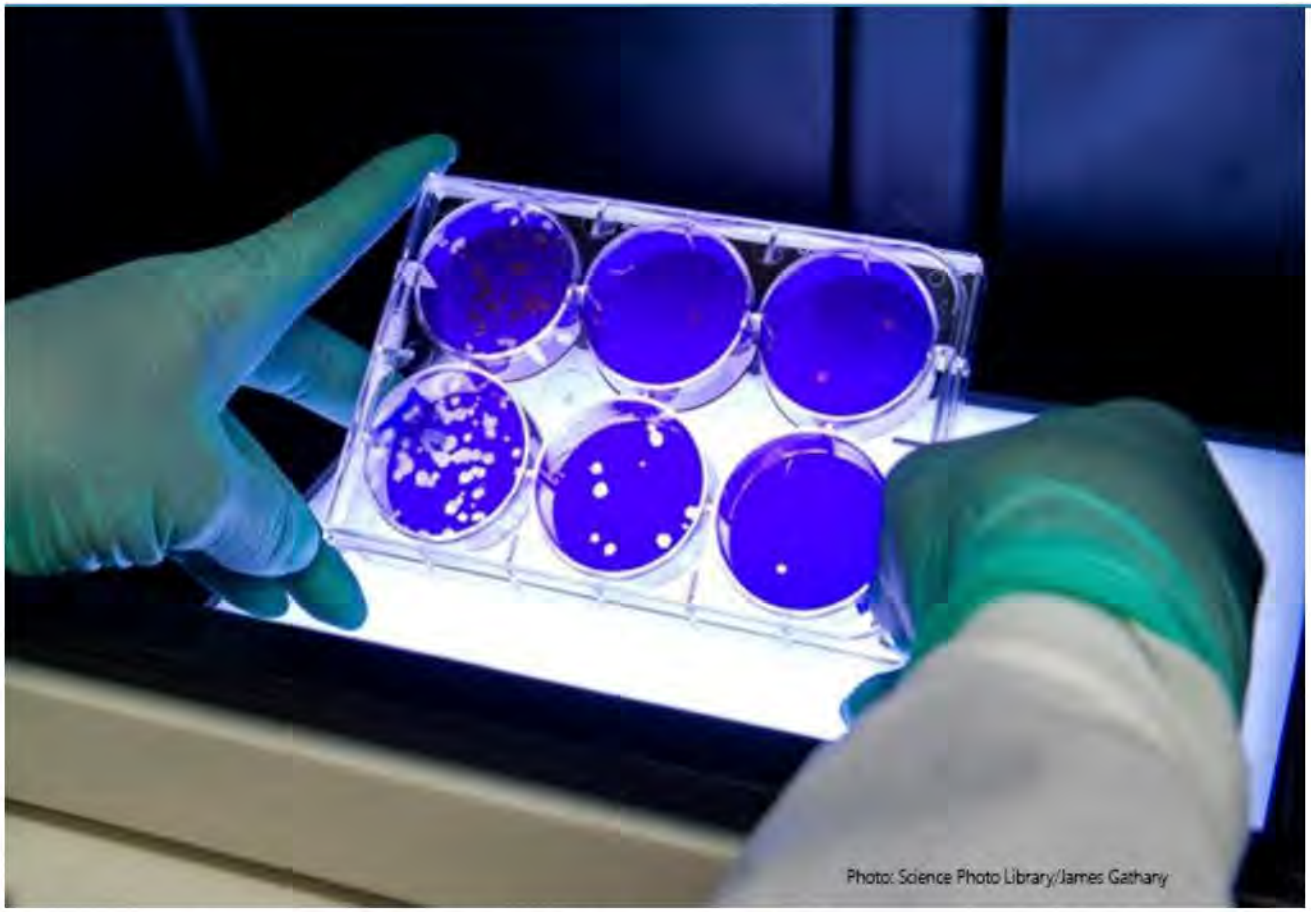


Announcing the COVID-19 Therapeutics Accelerator

The first time I ever wrote about global health was an article on the looming AIDS crisis in my native South Africa. My piece for the *Johannesburg Star* in 1991 reported dire predictions from experts about the potential of an epidemic. A major cause for pessimism was that, back then, HIV/AIDS could not be prevented or treated medically.

The same was true of the outbreaks of SARS in 2002, MERS in 2012, Ebola in 2014, and Zika in 2016. It is also the case with the previously unknown coronavirus, COVID-19, which has now reached more than 100,000 cases worldwide.

Any disease which threatens lives is disturbing, but one for which there is no treatment is especially alarming. And, as we've already seen with COVID-19, countries and communities bear immense human, economic, and social costs. At the Bill & Melinda Gates Foundation, we're committed to doing everything we can to ease that burden, especially for the world's poorest people who are often hardest hit by epidemics and their aftermath.

That is why today, we are joining forces with Wellcome and Mastercard to beef up our response—backed by $125 million in both new funding and money already earmarked to tackle this epidemic. The money will be used to identify potential treatments for COVID-19, accelerate their development, and prepare for the manufacture of millions of doses for use worldwide. The expertise of pharmaceutical companies will be critical to this endeavor, named the COVID-19 Therapeutics Accelerator.

Epidemics introduce a paradox to the world. Viruses like COVID-19 spread rapidly but developing vaccines and treatments to stop them moves slowly. If we want to make people, particularly the most vulnerable, safer from outbreaks then we need to find a way to unwind this paradox: to speed up R&D and slow down the spread.

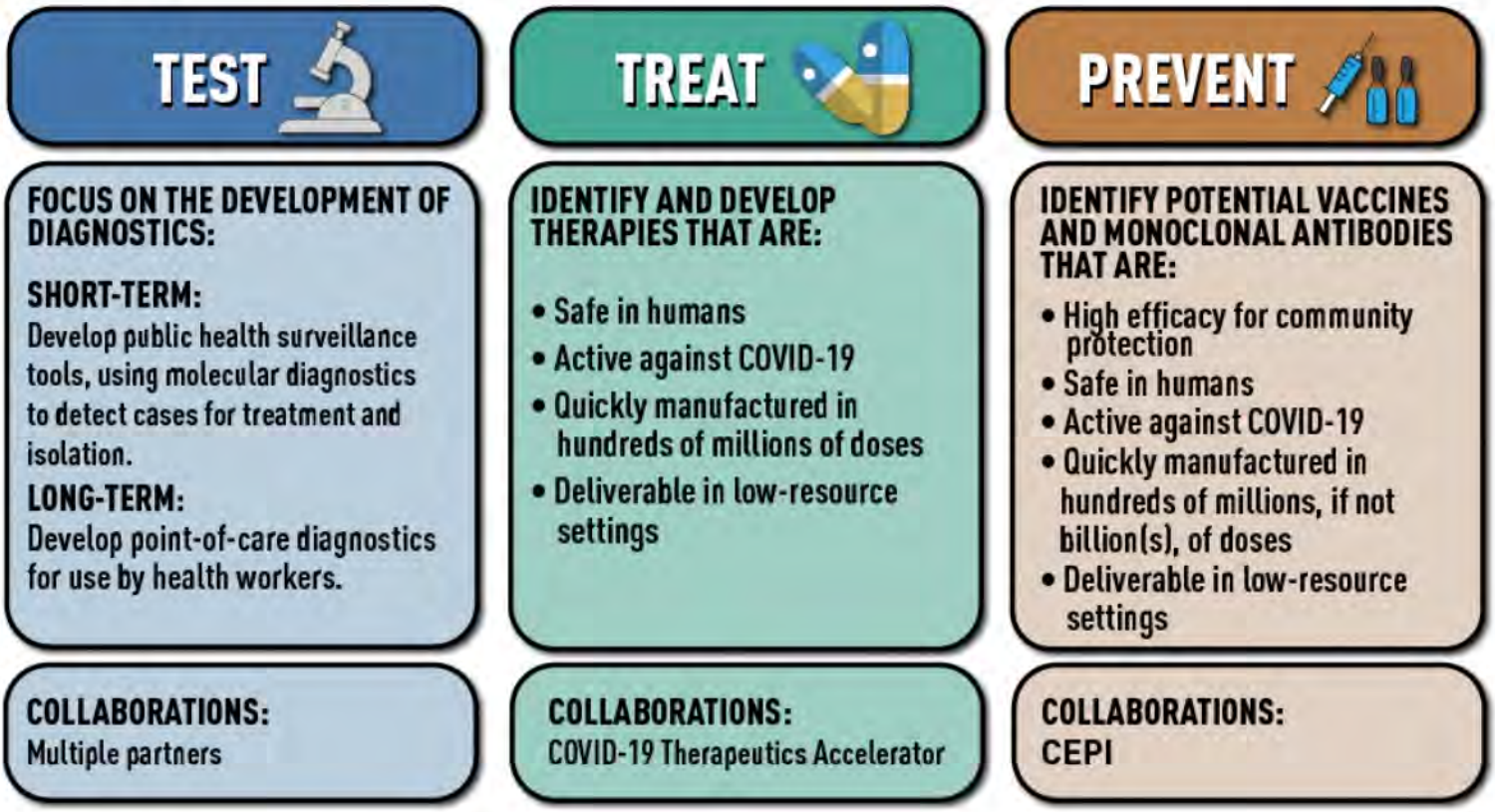
The only way to treat a viral infection, such as COVID-19, is with antiviral drugs. Right now, we can only treat the symptoms since there simply aren't antiviral medications that can treat a range of conditions in the same way that antibiotics do for bacterial infections. This is where we believe we can help by partnering with private and philanthropic enterprises to lower the financial risk and technical barriers for biotech and pharmaceutical companies developing antivirals for COVID-19.

We're optimistic about the progress that will be made with this new approach because we've seen what can come of similar co-operation and coordination in other parts of our work to combat epidemics.

The best way to prevent an infectious disease is with a vaccine. And in 2017, the Coalition for Epidemic Preparedness Innovations (CEPI) was created with nearly $650 million from Germany, Japan, Norway, Wellcome, and our foundation. Since then, others have come on board, including the UK, Canada, Ethiopia, Australia, Belgium, and the European Commission, to dramatically reduce the time it takes to develop vaccines for emerging epidemics, and ensure they are accessible, available, and affordable. The speed with which companies have begun working on a vaccine for COVID-19 is a result, in part, of CEPI.

R&D's ROLE IN A PANDEMIC

Developing New Tools in Response to COVID-19



Ultimately, our goal with the COVID-19 Therapeutics Accelerator is to do for treatment what CEPI does for vaccines. That requires governments, private enterprise, and philanthropic organizations to act urgently to fund innovation for drugs that can be developed, mass-produced and delivered rapidly.

As Bill Gates points out in his article for the *New England Journal of Medicine*, primary health care systems, which can monitor disease patterns and act as an early warning system, also need to be strengthened. And the world should invest in disease surveillance, including a case database that is instantly accessible to relevant organizations.

The *Johannesburg Star* was my very first job in journalism and I am proud of my article. I still have a copy of it. What I remember most is that it was headlined *Aids spectre must be tackled* –but for various reasons nothing happened for a long time. It would be unforgivable to make the same mistake with this epidemic. The need to act with urgency is critical. I'm fortunate to lead an organization that has the financial resources, technical experience and expertise, and the convening power to do just that.

Aids spectre must be tackled

Aids is regarded as one of the most serious health problems in South Africa today and, in the absence of a cure, the only way to limit the spread of the virus is through education and "safe" sexual practices.

But local anti-Aids campaigns have been severely limited in scope and appear to have had minimal impact.

Senior deputy Medical Officer of Health with Johannesburg City Council Dr Nicky Padayachee says there will be 315 000 Aids carriers in South Africa by the end of 1991 if present trends continue. This figure will balloon to between 2,5 and 7,5 million by the year 2005. More pessimistic researchers predict 10 million infected by the turn of the century.

Such figures have shaken the Government out of its lethargy in recent months and, according to Minister of Health and Population Development Dr Rina Venter, it now regards Aids as an "absolute priority".

Similarly, the ANC has also acknowledged the gravity of the threat after years of denying its existence, and declared "the entire democratic movement should make (Aids) a priority".

Such unprecedented consensus between the country's two main political groupings would seem to bode well for the rapid spread of Aids education programmes. The reality has fallen far short.

Working off a R5,4 million budget — far below international norms — the Government Aids education campaign has been largely confined to printing pamphlets and producing educational videos combined with an advertising media blitz. Similarly starved of funding, ANC input has been restricted to forming a few action committees.

Dr Padayachee that notes-

search shows that such methods are relatively successful in spreading awareness about Aids, but they fail to make people change sexual behaviour patterns.

This problem is exacerbated by the Government's lack of credibility among the black population, particularly the youth, who tend to regard the campaign as a plot to keep the black population down.

The Professor of Pathology at University of Natal Medical School, Dr Soromini Kalichurum, says the current campaign is almost completely ineffective in rural areas where most people are illiterate and lack access to the media.

In response, various groups have tried more uncoventional methods, including Aids comic books and dramatic presentations.

But the experience of fieldworkers round the world has found the best means of Aids education is through trained workers who can deal personally with different groups, preferably in their own language and with a knowledge of local sexual customs.

Most experts agree the Government alone cannot cope with Aids — education initiatives should be expanded through a combination of government, community and business resources.

The Director of the Aids Policy Research group and author of the manual "Facing Aids", Andre Spier, says the private sector could play an important role in working with and funding Aids education. It is in its own interests if the business community hopes to maintain a healthy labour force over the coming years.

Industry surveys show some groups, such as the Chamber of Mines, have launched extensive in-house Aids education programmes, but most major companies have yet to take action.

Aids education in schools is equally contentious.

The Government, held back by the NP's Calvinist heritage, has been reluctant to institute such programmes. Late last year Minister Venter conceded the need for such education and at a conference in Pretoria last week a strategy for Aids prevention in schools was set out.

This is encouraging, but the campaign is centered around the importance of abstinence and Dr Kalichurum notes such a policy ignores the reality of widespread sexual activity among school children.

Even more ridiculous, in an incident that revealed government ambivalence about Aids education, a pamphlet was recently banned for providing a too-graphic description of how to put on a condom.

But there are signs that the State is starting to make good its promises to take Aids more seriously. Last January it convened a a special intra-governmental task force to formulate and implement plans of action.

To complement these new strategies, the Department of Health is hoping to expand its Aids budget substantially this year and use it to fund Aids Education and Training Centres nationwide. A revised Aids prevention strategy now acknowledges non-governmental, community groups as "important partners in the fight against Aids".

Aids workers hope sch new initiatives will quickly expand and other groups, especially in the business community, will follow suit.

But even if the campaigns get off the ground, the sad truth is that they may still have little effect on people's sexual lifestyles.

"Until we see people start dying," laments Mr Spier, "the full message will not get through."

MARK SUZMAN

Tags:

Partnerships Private Sector Vaccines

About the Author

By Mark Suzman

Identifying therapeutics: The role of COVID-19 Therapeutics Accelerator

What role are you playing in the foundation's response to COVID-19?

I'm supporting the effort to identify therapeutics that could be used to treat moderate to severe cases of COVID-19.

What are your priorities right now?

Our first priority is to work with partners to test already approved drugs – drugs that could be available at your local pharmacy – to determine whether any are active against SARS-CoV-2, the virus that causes COVID-19. We're doing this because the safety profile of these medicines is well known, they're already being manufactured at scale, and they could be made immediately available to treat coronavirus patients through a simple off-label recommendation. Finding a drug that fits this profile could have a big impact in saving lives, protecting healthcare workers, and ultimately stopping this pandemic.

What are you currently doing to accelerate that work?

For the past two weeks, our focus has been looking closely at approved drugs and screening them for the properties they would need to have. Is there evidence that they're active against viruses? Is there evidence that they could be delivered to millions of people in the form of a pill? Do we have evidence that the compound

is easy to formulate and manufacture at scale? We have used published data from labs and computer modeling as well to explore these questions and narrow down our list to about 75 compounds worth exploring.

What other steps are you taking to accelerate the discovery of potential treatments?

With the launch of the new COVID-19 Therapeutics Accelerator, we are working with an array of pharmaceutical companies and academic researchers to examine their catalogs for potential treatments. One incredibly valuable resource is the ReFRAME catalog of the Scripps Research Institute in La Jolla, CA. ReFRAME is a collection of more than 10,000 small molecules and biologics that have already gone through safety testing in humans and have a well-characterized safety profile.

Researchers also know other important things about these compounds – such as how well they dissolve in water or in fats and how quickly the body processes them. This information is essential to understanding which compounds are likely to work as oral treatments versus which compounds would need to be delivered by injection or infusion.

What is the advantage of creating a treatment that people can take as a pill?

We're especially interested in compounds that can be delivered orally because that would dramatically expand the number of people who could have access to them, and it would also allow us to treat people who are in the early stages of infection. If someone needs to be hooked up to an IV drip to receive an antiviral, that means you need an in-patient hospital setting and a qualified healthcare provider to administer the treatment. It also means that infusions are likely to be prioritized for people who are critically ill as opposed to people who are just beginning to show symptoms.

If you can develop a pill-based treatment, however, that means you can deliver it to people via a pharmacist or a local clinic dispensary. And if you can treat people in the early stages of infection, you can also reduce the spread of the virus across the community, preventing other people from getting sick.

What other properties are important for the drugs you're seeking to develop?

Cost of manufacturing is obviously very important to ensure that we can design treatments that are

accessible to populations in low- and middle-income countries. And we also need formulations that are stable at ambient temperatures and have a long shelf life.

Tags:

Infectious Diseases Partnerships Vaccines

About the Interviewee

Monalisa Chatterji

Monalisa Chatterji, a senior program officer for the Bill & Melinda Gates Foundation's Discovery & Translational Sciences team, works on the discovery of novel candidate therapeutics.

More Stories Like This

DPA, CICP, PREP & EO

GUIDANCE FROM HOGAN LOVELLS ON DPA

With the rapidly changing circumstances surrounding COVID-19, there is no doubt that life sciences companies will be an active part of the solution, either by developing effective treatments and vaccines or by providing the medical supplies and devices needed to treat the expected influx of patients. Having already declared a National Emergency, yesterday President Trump invoked the Defense Production Act and issued an executive order delegating authority to the Secretary of Health and Human Services (HHS) as the lead Federal Department tasked with emergency procurement of health and medical resources. HHS already had taken action to declare COVID-19 a Public Health Emergency and issued a PREP Act declaration to facilitate expanded contracting to meet critical needs. Federal agencies are leveraging these new authorities to enhance access to needed medical items, and state and local governments are following suit.

Federal Contracting: Government needs are expanding rapidly and we expect they will continue to do so throughout this pandemic. Solicitations for products, services, and research and development efforts can be found at beta.SAM.gov using the search term COVID-19. In particular, the Biomedical Advanced Research and Development Authority (BARDA), which serves as the sole point of entry for product and technology development submissions pertaining to COVID-19, has posted an expedited request for submissions.

To facilitate purchasing during the pandemic, the Government has begun to utilize some of the multiple tools at its disposal for emergency purchasing:

- Defense Production Act ("DPA"): Yesterday, the President invoked the DPA for health and medical items, and by executive order designated HHS as the lead agency in carrying out the necessary contracting and allocation efforts under the statute. The DPA is the President's primary authority to mobilize resources and expedite acquisition of critical industrial items for national defense and emergency preparedness requirements.

  The DPA authorizes the Federal government to issue "rated orders," which are required to be prioritized. These orders can be issued against existing government contracts, but ***they also can be issued to companies that do not have government contracts in place***. Commercial businesses generally are required to accept these orders and are not permitted to discriminate in any manner against the procuring agency, such as by charging higher prices or by imposing different terms and conditions than for comparable commercial orders or non-rated Federal ones. Companies receiving rated orders must also provide preferential scheduling and must ensure delivery of all needed production items or services in a timely manner to satisfy contract requirements.

  The DPA also authorizes the Federal government to issue "allocation" orders, which may be placed when there is insufficient supply of a material, service, or facility to satisfy national defense supply requirements. There are three types of allocation orders:

  (a) ***Set-aside***. An official action that requires a company to reserve materials, services, or facilities capacity in anticipation of the receipt of rated orders;
  (b) ***Directive***. An official action that requires a company to take or refrain from taking certain actions. A directive can require a halt or reduction in production of an item; prohibit the use of selected materials, services, or facilities; or divert the use of materials, services, or facilities from one purpose to another; and

(c) ***Allotment***. An official action that specifies the maximum quantity of a material, service, or facility authorized for a specific use.

Orders and allocations can be postponed or adjusted in certain limited circumstances, but need to be addressed on a case-by-case basis. Given the expansive reach of the DPA into commercial business activity, its use can raise a wide variety of legal concerns, implicating regulatory, commercial, and intellectual property considerations.

- Increased Purchasing Thresholds: Federal Acquisition Regulation [FAR] Part 18 and FAR 13.500 provide contracting agencies with tools to expedite delivery of goods and services to support responses to emergency situations. Agencies may increase both the micro-purchase threshold and the simplified acquisition threshold, which allows for more streamlined procurement for higher dollar value acquisitions. In addition, agencies can simplify procedures for commercial items acquisition and even treat certain non-commercial items as commercial for purposes of procurement. Exercising this authority, earlier this week the Department of Veterans Affairs (VA) issued a memorandum increasing the micro-purchase threshold from $3,500 to $20,000, the simplified acquisition threshold (SAT) from $150,000 to $750,000, and the threshold for use of simplified acquisition procedures for commercial items – including drugs, medical devices, and supplies – for use in response to a national emergency to $13 million. We expect that other agencies will be taking similar steps.

- Non-Competed Solicitations: Under the Competition in Contract Act (CICA), Federal executive agencies cannot contract without providing for "full and open competition," unless a statutory exception applies. FAR Part 6 provides that the government may waive competition requirements where there is an unusual and compelling urgency, for national security reasons, and when waiver would be in the public interest. Additionally, under the waiver rules, the government can issue a contract to a single source where that source has submitted a proposal for an innovative product, service, or concept that is not otherwise available to the government.

- Application of Rules of Origin: Country of origin (COO) rules typically place restrictions on Federal procurements that operate to limit the ability of an offeror to supply foreign end products. These rules and any accompanying restrictions on procurement of non-U.S. items, can be waived under certain circumstances, including for national security purposes. Both the Buy American Act, which generally applies to purchases between $10,000 and $182,000, and the Trade Agreements Act (TAA), which applies to procurements over $182,000, may be "waived" upon a finding that the product being procured by the government is not available from TAA "compliant" countries in sufficient quantities to meet the government's needs. *It is also worth noting that Trump administration officials have signaled that additional "Buy American" incentives and, potentially, restrictions will be applied in the near future. It is possible that these will limit existing flexibility in procurement COO regulations.*

- PREP Act: The Public Readiness and Emergency Preparedness Act ("PREP Act") enables the Health and Human Services ("HHS") to issue declarations that provides Federal contractors immunity from claims resulting from the administration or use of countermeasures to address public health emergencies. On February 4, 2020, HHS issued a PREP Act declaration for medical countermeasures against COVID-19. "Covered countermeasures" include "qualified pandemic or epidemic products," or "security countermeasures," or drugs, biological products, or devices authorized for investigational or emergency use. The purpose of this declaration is to encourage the

development, testing, manufacture, and distribution of measures designed to combat the spread of COVID-19.

State and Local Government Purchasing: As the Federal government readies its procurement tools to optimize its response to the COVID-19 pandemic, state and local governments have been directed by President Trump to do the same. These governments may contract using their own vehicles or, in times of emergency, may access certain federal contracts, such as the VA Federal Supply Schedule (FSS) contracts.

Two separate FSS contract provisions provide for state and local government to access FSS contracts in emergency circumstances. First, based on the Secretary of HHS's January 31, 2020 declaration that COVID-19 is a Public Health Emergency, state and local governments were permitted to access FSS contracts held by contractors that opted to participate in expanded contracting efforts for emergency/disaster recovery. Additionally, when President Trump declared a National Emergency under the Robert T. Stafford Act, state and local governments were provided access to all FSS contracts. While there is some limited basis to reject orders, as a practical matter manufacturers may not have the ability to do so, because these orders generally are placed through third-party distributors and thus manufacturers will only learn of these sales after the fact. It is also worth noting that additional state/local government terms and conditions may apply to these transactions. And, manufacturers of innovator drugs should keep close track of FSS sales data and consider implications that these sales may have on government pricing (GP) calculations.

For companies selling to state and local governments outside of the FSS contract, it is important to understand that the various state and local governments have their own unique procurement processes, terms, and conditions. Despite the urgency of these purchases, companies should ensure that they closely review contract terms and understand associated obligations.

About CICP

About the Countermeasures Injury Compensation Program

CICP was created to provide compensation for serious countermeasure injuries. You can learn more about this program and the events leading to the creation of CICP by reading below or clicking on the following links:

CICP Rules

The CICP Administrative Implementation, Interim Final Rule and Final Rule with technical amendments allows the CICP to evaluate and process requests for benefits filed by individuals who experienced serious physical injuries as a direct result of the administration or use of covered countermeasures identified by the Secretary of the U.S. Department of Health and Human Services (HHS) in declarations issued under the PREP Act

PREP Act

The Public Readiness and Emergency Preparedness, or PREP Act, established liability protections to covered persons (as defined in section 319F-3(i)(2) of the Public Health Service Act (PHS Act)). In addition to liability protections, the PREP Act established the CICP to provide compensation to eligible individuals for serious physical injuries or death directly caused by the administration or use of pandemic, epidemic, or security countermeasures identified in declarations issued by the Secretary pursuant to section 319F-3(b) of the PHS Act (42 U.S.C. 247d-6d).

Declarations

The countermeasures covered by the CICP are determined through declarations issued by the Secretary of the U.S. Department of Health and Human Services.

The current declarations are listed here.

Date Last Reviewed: March 2020

Seasonal Flu

Seasonal influenza vaccines are not covered countermeasures under the CICP. If you received the seasonal influenza vaccine or other vaccines covered by the National Vaccine Injury Compensation Program (VICP) such as tetanus or the human papillomavirus vaccine and think that you had an adverse reaction from one or a combination of these covered vaccines, see the VICP.

CICP Fact Sheet

Download the CICP fact sheet (PDF - 82 KB)

Countermeasures Injury Tables

Pandemic Influenza Countermeasure Injury Table

Pandemic Influenza Countermeasure Injury Table Final Rule (PDF - 238 KB)

Frequently Asked Questions

General FAQs

FAQs for Individual Requesters/Recipients

FAQs for Representatives

FAQs for Administrators or Executors of Estates

FAQs for Survivors

Ohio, Court of Federal Claims No: 20–0225V
71. Shannon Pyers, Dresher, Pennsylvania, Court of Federal Claims No: 20–0231V
72. Lisa Macon, Englewood, New Jersey, Court of Federal Claims No: 20–0232V

[FR Doc. 2020–05525 Filed 3–16–20; 8:45 am]

BILLING CODE 4165–15–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Office of the Secretary

Declaration Under the Public Readiness and Emergency Preparedness Act for Medical Countermeasures Against COVID–19

ACTION: Notice of declaration.

SUMMARY: The Secretary is issuing this Declaration pursuant to section 319F–3 of the Public Health Service Act to provide liability immunity for activities related to medical countermeasures against COVID–19.

DATES: The Declaration was effective as of February 4, 2020.

FOR FURTHER INFORMATION CONTACT: Robert P. Kadlec, MD, MTM&H, MS, Assistant Secretary for Preparedness and Response, Office of the Secretary, Department of Health and Human Services, 200 Independence Avenue SW, Washington, DC 20201; Telephone: 202–205–2882.

SUPPLEMENTARY INFORMATION: The Public Readiness and Emergency Preparedness Act (PREP Act) authorizes the Secretary of Health and Human Services (the Secretary) to issue a Declaration to provide liability immunity to certain individuals and entities (Covered Persons) against any claim of loss caused by, arising out of, relating to, or resulting from the manufacture, distribution, administration, or use of medical countermeasures (Covered Countermeasures), except for claims involving ''willful misconduct'' as defined in the PREP Act. This Declaration is subject to amendment as circumstances warrant.

The PREP Act was enacted on December 30, 2005, as Public Law 109–148, Division C, Section 2. It amended the Public Health Service (PHS) Act, adding Section 319F–3, which addresses liability immunity, and Section 319F–4, which creates a compensation program. These sections are codified at 42 U.S.C. 247d-6d and 42 U.S.C. 247d–6e, respectively.

The Pandemic and All-Hazards Preparedness Reauthorization Act (PAHPRA), Public Law 113–5, was enacted on March 13, 2013. Among other things, PAHPRA added sections 564A and 564B to the Federal Food, Drug, and Cosmetic (FD&C) Act to provide new authorities for the emergency use of approved products in emergencies and products held for emergency use. PAHPRA accordingly amended the definitions of ''Covered Countermeasures'' and ''qualified pandemic and epidemic products'' in Section 319F–3 of the Public Health Service Act (PREP Act provisions), so that products made available under these new FD&C Act authorities could be covered under PREP Act Declarations. PAHPRA also extended the definition of qualified pandemic and epidemic products that may be covered under a PREP Act Declaration to include products or technologies intended to enhance the use or effect of a drug, biological product, or device used against the pandemic or epidemic or against adverse events from these products.

COVID–19 is an acute respiratory disease caused by the SARS-CoV-2 betacoronavirus or a virus mutating therefrom. This virus is similar to other betacoronaviruses, such as Middle Eastern Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS). Although the complete clinical picture regarding SARS-CoV-2 or a virus mutating therefrom is not fully understood, the virus has been known to cause severe respiratory illness and death in a subset of those people infected with such virus(es).

In December 2019, the novel coronavirus was detected in Wuhan City, Hubei Province, China. Today, over 101 countries, including the United States have reported multiple cases. Acknowledging that cases had been reported in five WHO regions in one month, on January 30, 2020, WHO declared the COVID–19 outbreak to be a Public Health Emergency of International Concern (PHEIC) following a second meeting of the Emergency Committee convened under the International Health Regulations (IHR).

To date, United States traveler-associated cases have been identified in a number of States and community-based transmission is suspected. On January 31, 2020, Secretary Azar declared a public health emergency pursuant to section 319 of the PHS Act, 42 U.S.C. 247d, for the entire United States to aid in the nation's health care community response to the COVID–19 outbreak.[1] The outbreak remains a significant public health challenge that requires a sustained, coordinated proactive response by the Government in order to contain and mitigate the spread of COVID–19.[2]

Description of This Declaration by Section

Section I. Determination of Public Health Emergency or Credible Risk of Future Public Health Emergency

Before issuing a Declaration under the PREP Act, the Secretary is required to determine that a disease or other health condition or threat to health constitutes a public health emergency or that there is a credible risk that the disease, condition, or threat may constitute such an emergency. This determination is separate and apart from the Declaration issued by the Secretary on January 31, 2020 under Section 319 of the PHS Act that a disease or disorder presents a public health emergency or that a public health emergency, including significant outbreaks of infectious diseases or bioterrorist attacks, otherwise exists, or other Declarations or determinations made under other authorities of the Secretary. Accordingly in Section I of the Declaration, the Secretary determines that the spread of SARS-CoV-2 or a virus mutating therefrom and the resulting disease, COVID–19, constitutes a public health emergency for purposes of this Declaration under the PREP Act.

Section II. Factors Considered by the Secretary

In deciding whether and under what circumstances to issue a Declaration with respect to a Covered Countermeasure, the Secretary must consider the desirability of encouraging the design, development, clinical testing or investigation, manufacture, labeling, distribution, formulation, packaging, marketing, promotion, sale, purchase, donation, dispensing, prescribing, administration, licensing, and use of the countermeasure. In Section II of the Declaration, the Secretary states that he has considered these factors.

Section III. Activities Covered by This Declaration Under the PREP Act's Liability Immunity

The Secretary must delineate the activities for which the PREP Act's liability immunity is in effect. These activities may include, under conditions as the Secretary may specify, the manufacture, testing, development, distribution, administration, or use of one or more Covered Countermeasures

[1] *https://www.phe.gov/emergency/news/healthactions/phe/Pages/2019-nCoV.aspx.*

[2] CDC COVID–19 Summary; *https://www.cdc.gov/coronavirus/2019-ncov/summary.html*, accessed 27Feb2020).

(Recommended Activities). In Section III of the Declaration, the Secretary sets out the activities for which the immunity is in effect.

Section IV. Limited Immunity

The Secretary must also state that liability protections available under the PREP Act are in effect with respect to the Recommended Activities. These liability protections provide that, ''[s]ubject to other provisions of [the PREP Act], a covered person shall be immune from suit and liability under federal and state law with respect to all claims for loss caused by, arising out of, relating to, or resulting from the administration to or use by an individual of a covered countermeasure if a Declaration has been issued with respect to such countermeasure.'' In Section IV of the Declaration, the Secretary states that liability protections are in effect with respect to the Recommended Activities.

Section V. Covered Persons

Section V of the Declaration describes Covered Persons, including Qualified Persons. The PREP Act defines Covered Persons to include, among others, the United States, and those that manufacturer, distribute, administer, prescribe or use Covered Countermeasures. This Declaration includes all persons and entities defined as Covered Persons under the PREP Act (PHS Act 317F–3(i)(2)) as well as others set out in paragraphs (3), (4), (6), (8)(A) and (8)(B).

The PREP Act's liability immunity applies to ''Covered Persons'' with respect to administration or use of a Covered Countermeasure. The term ''Covered Persons'' has a specific meaning and is defined in the PREP Act to include manufacturers, distributors, program planners, and qualified persons, and their officials, agents, and employees, and the United States. The PREP Act further defines the terms ''manufacturer,'' ''distributor,'' ''program planner,'' and ''qualified person'' as described below.

A manufacturer includes a contractor or subcontractor of a manufacturer; a supplier or licenser of any product, intellectual property, service, research tool or component or other article used in the design, development, clinical testing, investigation or manufacturing of a Covered Countermeasure; and any or all the parents, subsidiaries, affiliates, successors, and assigns of a manufacturer.

A distributor means a person or entity engaged in the distribution of drugs, biologics, or devices, including but not limited to: Manufacturers; re-packers; common carriers; contract carriers; air carriers; own-label distributors; private-label distributors; jobbers; brokers; warehouses and wholesale drug warehouses; independent wholesale drug traders; and retail pharmacies.

A program planner means a state or local government, including an Indian tribe; a person employed by the state or local government; or other person who supervises or administers a program with respect to the administration, dispensing, distribution, provision, or use of a Covered Countermeasure, including a person who establishes requirements, provides policy guidance, or supplies technical or scientific advice or assistance or provides a facility to administer or use a Covered Countermeasure in accordance with the Secretary's Declaration. Under this definition, a private sector employer or community group or other ''person'' can be a program planner when it carries out the described activities.

A qualified person means a licensed health professional or other individual authorized to prescribe, administer, or dispense Covered Countermeasures under the law of the state in which the Covered Countermeasure was prescribed, administered, or dispensed; or a person within a category of persons identified as qualified in the Secretary's Declaration. Under this definition, the Secretary can describe in the Declaration other qualified persons, such as volunteers, who are Covered Persons. Section V describes other qualified persons covered by this Declaration.

The PREP Act also defines the word ''person'' as used in the Act: A person includes an individual, partnership, corporation, association, entity, or public or private corporation, including a federal, state, or local government agency or department.

Section VI. Covered Countermeasures

As noted above, Section III of the Declaration describes the activities (referred to as ''Recommended Activities'') for which liability immunity is in effect. Section VI of the Declaration identifies the Covered Countermeasures for which the Secretary has recommended such activities. The PREP Act states that a ''Covered Countermeasure'' must be a ''qualified pandemic or epidemic product,'' or a ''security countermeasure,'' as described immediately below; or a drug, biological product or device authorized for emergency use in accordance with Sections 564, 564A, or 564B of the FD&C Act.

A qualified pandemic or epidemic product means a drug or device, as defined in the FD&C Act or a biological product, as defined in the PHS Act that is (i) manufactured, used, designed, developed, modified, licensed or procured to diagnose, mitigate, prevent, treat, or cure a pandemic or epidemic or limit the harm such a pandemic or epidemic might otherwise cause; (ii) manufactured, used, designed, developed, modified, licensed, or procured to diagnose, mitigate, prevent, treat, or cure a serious or life-threatening disease or condition caused by such a drug, biological product, or device; (iii) or a product or technology intended to enhance the use or effect of such a drug, biological product, or device.

A security countermeasure is a drug or device, as defined in the FD&C Act or a biological product, as defined in the PHS Act that (i)(a) The Secretary determines to be a priority to diagnose, mitigate, prevent, or treat harm from any biological, chemical, radiological, or nuclear agent identified as a material threat by the Secretary of Homeland Security, or (b) to diagnose, mitigate, prevent, or treat harm from a condition that may result in adverse health consequences or death and may be caused by administering a drug, biological product, or device against such an agent; and (ii) is determined by the Secretary of Health and Human Services to be a necessary countermeasure to protect public health.

To be a Covered Countermeasure, qualified pandemic or epidemic products or security countermeasures also must be approved or cleared under the FD&C Act; licensed under the PHS Act; or authorized for emergency use under Sections 564, 564A, or 564B of the FD&C Act.

A qualified pandemic or epidemic product also may be a Covered Countermeasure when it is subject to an exemption (that is, it is permitted to be used under an Investigational Drug Application or an Investigational Device Exemption) under the FD&C Act and is the object of research for possible use for diagnosis, mitigation, prevention, treatment, or cure, or to limit harm of a pandemic or epidemic or serious or life-threatening condition caused by such a drug or device.

A security countermeasure also may be a Covered Countermeasure if it may reasonably be determined to qualify for approval or licensing within 10 years after the Department's determination that procurement of the countermeasure is appropriate.

Section VI lists medical countermeasures against COVID–19 that

are Covered Countermeasures under this declaration.

Section VI also refers to the statutory definitions of Covered Countermeasures to make clear that these statutory definitions limit the scope of Covered Countermeasures. Specifically, the Declaration notes that Covered Countermeasures must be "qualified pandemic or epidemic products," or "security countermeasures," or drugs, biological products, or devices authorized for investigational or emergency use, as those terms are defined in the PREP Act, the FD&C Act, and the Public Health Service Act.

Section VII. Limitations on Distribution

The Secretary may specify that liability immunity is in effect only to Covered Countermeasures obtained through a particular means of distribution. The Declaration states that liability immunity is afforded to Covered Persons for Recommended Activities related to (a) present or future federal contracts, cooperative agreements, grants, other transactions, interagency agreements, or memoranda of understanding or other federal agreements; or (b) activities authorized in accordance with the public health and medical response of the Authority Having Jurisdiction to prescribe, administer, deliver, distribute, or dispense the Covered Countermeasures following a Declaration of an emergency.

Section VII defines the terms "Authority Having Jurisdiction" and "Declaration of an emergency." We have specified in the definition that Authorities having jurisdiction include federal, state, local, and tribal authorities and institutions or organizations acting on behalf of those governmental entities.

For governmental program planners only, liability immunity is afforded only to the extent they obtain Covered Countermeasures through voluntary means, such as (1) donation; (2) commercial sale; (3) deployment of Covered Countermeasures from federal stockpiles; or (4) deployment of donated, purchased, or otherwise voluntarily obtained Covered Countermeasures from state, local, or private stockpiles. This last limitation on distribution is intended to deter program planners that are government entities from seizing privately held stockpiles of Covered Countermeasures. It does not apply to any other Covered Persons, including other program planners who are not government entities.

Section VIII. Category of Disease, Health Condition, or Threat

The Secretary must identify in the Declaration, for each Covered Countermeasure, the categories of diseases, health conditions, or threats to health for which the Secretary recommends the administration or use of the countermeasure. In Section VIII of the Declaration, the Secretary states that the disease threat for which he recommends administration or use of the Covered Countermeasures is COVID–19 caused by SARS-CoV-2 or a virus mutating therefrom.

Section IX. Administration of Covered Countermeasures

The PREP Act does not explicitly define the term "administration" but does assign the Secretary the responsibility to provide relevant conditions in the Declaration. In Section IX of the Declaration, the Secretary defines "Administration of a Covered Countermeasure," as follows:

Administration of a Covered Countermeasure means physical provision of the countermeasures to recipients, or activities and decisions directly relating to public and private delivery, distribution, and dispensing of the countermeasures to recipients; management and operation of countermeasure programs; or management and operation of locations for purpose of distributing and dispensing countermeasures.

The definition of "administration" extends only to physical provision of a countermeasure to a recipient, such as vaccination or handing drugs to patients, and to activities related to management and operation of programs and locations for providing countermeasures to recipients, such as decisions and actions involving security and queuing, but only insofar as those activities directly relate to the countermeasure activities. Claims for which Covered Persons are provided immunity under the Act are losses caused by, arising out of, relating to, or resulting from the administration to or use by an individual of a Covered Countermeasure consistent with the terms of a Declaration issued under the Act. Under the definition, these liability claims are precluded if they allege an injury caused by a countermeasure, or if the claims are due to manufacture, delivery, distribution, dispensing, or management and operation of countermeasure programs at distribution and dispensing sites.

Thus, it is the Secretary's interpretation that, when a Declaration is in effect, the Act precludes, for example, liability claims alleging negligence by a manufacturer in creating a vaccine, or negligence by a health care provider in prescribing the wrong dose, absent willful misconduct. Likewise, the Act precludes a liability claim relating to the management and operation of a countermeasure distribution program or site, such as a slip-and-fall injury or vehicle collision by a recipient receiving a countermeasure at a retail store serving as an administration or dispensing location that alleges, for example, lax security or chaotic crowd control. However, a liability claim alleging an injury occurring at the site that was not directly related to the countermeasure activities is not covered, such as a slip and fall with no direct connection to the countermeasure's administration or use. In each case, whether immunity is applicable will depend on the particular facts and circumstances.

Section X. Population

The Secretary must identify, for each Covered Countermeasure specified in a Declaration, the population or populations of individuals for which liability immunity is in effect with respect to administration or use of the countermeasure. Section X of the Declaration identifies which individuals should use the countermeasure or to whom the countermeasure should be administered—in short, those who should be vaccinated or take a drug or other countermeasure. Section X provides that the population includes "any individual who uses or who is administered a Covered Countermeasure in accordance with the Declaration."

It should be noted that under the PREP Act, liability protection extends beyond the Population specified in the Declaration. Specifically, liability immunity is afforded (1) To manufacturers and distributors without regard to whether the countermeasure is used by or administered to this population, and (2) to program planners and qualified persons when the countermeasure is either used by or administered to this population or the program planner or qualified person reasonably could have believed the recipient was in this population. Section X of the Declaration includes these statutory conditions in the Declaration for clarity.

Section XI. Geographic Area

The Secretary must identify, for each Covered Countermeasure specified in the Declaration, the geographic area or areas for which liability immunity is in effect, including, as appropriate, whether the Declaration applies only to

individuals physically present in the area or, in addition, applies to individuals who have a described connection to the area. Section XI of the Declaration provides that liability immunity is afforded for the administration or use of a Covered Countermeasure without geographic limitation. This could include claims related to administration or use in countries outside the U.S. It is possible that claims may arise in regard to administration or use of the Covered Countermeasures outside the U.S. that may be resolved under U.S. law.

In addition, the PREP Act specifies that liability immunity is afforded (1) to manufacturers and distributors without regard to whether the countermeasure is used by or administered to individuals in the geographic areas, and (2) to program planners and qualified persons when the countermeasure is either used or administered in the geographic areas or the program planner or qualified person reasonably could have believed the countermeasure was used or administered in the areas. Section XI of the Declaration includes these statutory conditions in the Declaration for clarity.

Section XII. Effective Time Period

The Secretary must identify, for each Covered Countermeasure, the period or periods during which liability immunity is in effect, designated by dates, milestones, or other description of events, including factors specified in the PREP Act. Section XII of the Declaration extends the effective period for different means of distribution of Covered Countermeasures through October 1, 2024.

Section XIII. Additional Time Period of Coverage

The Secretary must specify a date after the ending date of the effective time period of the Declaration that is reasonable for manufacturers to arrange for disposition of the Covered Countermeasure, including accepting returns of Covered Countermeasures, and for other Covered Persons to take appropriate actions to limit administration or use of the Covered Countermeasure. In addition, the PREP Act specifies that, for Covered Countermeasures that are subject to a Declaration at the time they are obtained for the Strategic National Stockpile (SNS) under 42 U.S.C. 247d-6b(a), the effective period of the Declaration extends through the time the countermeasure is used or administered. Liability immunity under the provisions of the PREP Act and the conditions of the Declaration continue during these additional time periods. Thus, liability immunity is afforded during the "Effective Time Period," described under Section XII of the Declaration, plus the "Additional Time Period" described under Section XIII of the Declaration.

Section XIII of the Declaration provides for 12 months as the Additional Time Period of coverage after expiration of the Declaration. Section XIII also explains the extended coverage that applies to any product obtained for the SNS during the effective period of the Declaration.

Section XIV. Countermeasures Injury Compensation Program

Section 319F–4 of the PHS Act, 42 U.S.C. 247d-6e, authorizes the Countermeasures Injury Compensation Program (CICP) to provide benefits to eligible individuals who sustain a serious physical injury or die as a direct result of the administration or use of a Covered Countermeasure. Compensation under the CICP for an injury directly caused by a Covered Countermeasure is based on the requirements set forth in this Declaration, the administrative rules for the Program, and the statute. To show direct causation between a Covered Countermeasure and a serious physical injury, the statute requires "compelling, reliable, valid, medical and scientific evidence." The administrative rules for the Program further explain the necessary requirements for eligibility under the CICP. Please note that, by statute, requirements for compensation under the CICP may not align with the requirements for liability immunity provided under the PREP Act. Section XIV of the Declaration, "Countermeasures Injury Compensation Program," explains the types of injury and standard of evidence needed to be considered for compensation under the CICP.

Further, the administrative rules for the CICP specify that if countermeasures are administered or used outside the United States, only otherwise eligible individuals at United States embassies, military installations abroad (such as military bases, ships, and camps) or at North Atlantic Treaty Organization (NATO) installations (subject to the NATO Status of Forces Agreement) where American servicemen and servicewomen are stationed may be considered for CICP benefits. Other individuals outside the United States may not be eligible for CICP benefits.

Section XV. Amendments

Section XV of the Declaration confirms that the Secretary may amend any portion of this Declaration through publication in the **Federal Register.**

Declaration

Declaration for Public Readiness and Emergency Preparedness Act Coverage for medical countermeasures against COVID–19.

I. Determination of Public Health Emergency

42 U.S.C. 247d–6d(b)(1)

I have determined that the spread of SARS-CoV–2 or a virus mutating therefrom and the resulting disease COVID–19 constitutes a public health emergency.

II. Factors Considered

42 U.S.C. 247d–6d(b)(6)

I have considered the desirability of encouraging the design, development, clinical testing, or investigation, manufacture, labeling, distribution, formulation, packaging, marketing, promotion, sale, purchase, donation, dispensing, prescribing, administration, licensing, and use of the Covered Countermeasures.

III. Recommended Activities

42 U.S.C. 247d–6d(b)(1)

I recommend, under the conditions stated in this Declaration, the manufacture, testing, development, distribution, administration, and use of the Covered Countermeasures.

IV. Liability Immunity

42 U.S.C. 247d–6d(a), 247d–6d(b)(1)

Liability immunity as prescribed in the PREP Act and conditions stated in this Declaration is in effect for the Recommended Activities described in Section III.

V. Covered Persons

42 U.S.C. 247d–6d(i)(2), (3), (4), (6), (8)(A) and (B)

Covered Persons who are afforded liability immunity under this Declaration are "manufacturers," "distributors," "program planners," "qualified persons," and their officials, agents, and employees, as those terms are defined in the PREP Act, and the United States.

In addition, I have determined that the following additional persons are qualified persons: (a) Any person authorized in accordance with the public health and medical emergency response of the Authority Having Jurisdiction, as described in Section VII below, to prescribe, administer, deliver, distribute or dispense the Covered Countermeasures, and their officials, agents, employees, contractors and

volunteers, following a Declaration of an emergency; (b) any person

authorized to prescribe, administer, or dispense the Covered Countermeasures or who is otherwise authorized to perform an activity under an Emergency Use Authorization in accordance with Section 564 of the FD&C Act; and (c) any person authorized to prescribe, administer, or dispense Covered Countermeasures in accordance with Section 564A of the

FD&C Act.

VI. Covered Countermeasures

42 U.S.C. 247d–6b(c)(1)(B), 42 U.S.C. 247d–6d(i)(1) and (7)

Covered Countermeasures are any antiviral, any other drug, any biologic, any diagnostic, any other device, or any vaccine, used to treat, diagnose, cure, prevent, or mitigate COVID–19, or the transmission of SARS-CoV–2 or a virus mutating therefrom, or any device used in the administration of any such product, and all components and constituent materials of any such product.

Covered Countermeasures must be ''qualified pandemic or epidemic products,'' or ''security countermeasures,'' or drugs, biological products, or devices authorized for investigational or emergency use, as those terms are defined in the PREP Act, the FD&C Act, and the Public Health Service Act.

VII. Limitations on Distribution

42 U.S.C. 247d–6d(a)(5) and (b)(2)(E)

I have determined that liability immunity is afforded to Covered Persons only for Recommended Activities involving Covered Countermeasures that are related to:

(a) Present or future federal contracts, cooperative agreements, grants, other transactions, interagency agreements, memoranda of understanding, or other federal agreements; or

(b) Activities authorized in accordance with the public health and medical response of the Authority Having Jurisdiction to prescribe, administer, deliver, distribute or dispense the Covered Countermeasures following a Declaration of an emergency.

As used in this Declaration, the terms Authority Having Jurisdiction and Declaration of Emergency have the following meanings:

i. The Authority Having Jurisdiction means the public agency or its delegate that has legal responsibility and authority for responding to an incident, based on political or geographical (*e.g.*, city, county, tribal, state, or federal boundary lines) or functional (*e.g.*, law enforcement, public health) range or sphere of authority.

ii. A Declaration of Emergency means any Declaration by any authorized local, regional, state, or federal official of an emergency specific to events that indicate an immediate need to administer and use the Covered Countermeasures, with the exception of a federal Declaration in support of an Emergency Use Authorization under Section 564 of the FD&C Act unless such Declaration specifies otherwise;

I have also determined that, for governmental program planners only, liability immunity is afforded only to the extent such program planners obtain Covered Countermeasures through voluntary means, such as (1) donation; (2) commercial sale; (3) deployment of Covered Countermeasures from federal stockpiles; or (4) deployment of donated, purchased, or otherwise voluntarily obtained Covered Countermeasures from state, local, or private stockpiles.

VIII. Category of Disease, Health Condition, or Threat

42 U.S.C. 247d–6d(b)(2)(A)

The category of disease, health condition, or threat for which I recommend the administration or use of the Covered Countermeasures is COVID–19 caused by SARS-CoV–2 or a virus mutating therefrom.

IX. Administration of Covered Countermeasures

42 U.S.C. 247d–6d(a)(2)(B)

Administration of the Covered Countermeasure means physical provision of the countermeasures to recipients, or activities and decisions directly relating to public and private delivery, distribution and dispensing of the countermeasures to recipients, management and operation of countermeasure programs, or management and operation of locations for purpose of distributing and dispensing countermeasures.

X. Population

42 U.S.C. 247d–6d(a)(4), 247d–6d(b)(2)(C)

The populations of individuals include any individual who uses or is administered the Covered Countermeasures in accordance with this Declaration.

Liability immunity is afforded to manufacturers and distributors without regard to whether the countermeasure is used by or administered to this population; liability immunity is afforded to program planners and qualified persons when the countermeasure is used by or administered to this population, or the program planner or qualified person reasonably could have believed the recipient was in this population.

XI. Geographic Area

42 U.S.C. 247d–6d(a)(4), 247d–6d(b)(2)(D)

Liability immunity is afforded for the administration or use of a Covered Countermeasure without geographic limitation.

Liability immunity is afforded to manufacturers and distributors without regard to whether the countermeasure is used by or administered in any designated geographic area; liability immunity is afforded to program planners and qualified persons when the countermeasure is used by or administered in any designated geographic area, or the program planner or qualified person reasonably could have believed the recipient was in that geographic area.

XII. Effective Time Period

42 U.S.C. 247d–6d(b)(2)(B)

Liability immunity for Covered Countermeasures through means of distribution, as identified in Section VII(a) of this Declaration, other than in accordance with the public health and medical response of the Authority Having Jurisdiction and extends through October 1, 2024.

Liability immunity for Covered Countermeasures administered and used in accordance with the public health and medical response of the Authority Having Jurisdiction begins with a Declaration and lasts through (1) the final day the emergency Declaration is in effect, or (2) October 1, 2024, whichever occurs first.

XIII. Additional Time Period of Coverage

42 U.S.C. 247d–6d(b)(3)(B) and (C)

I have determined that an additional 12 months of liability protection is reasonable to allow for the manufacturer(s) to arrange for disposition of the Covered Countermeasure, including return of the Covered Countermeasures to the manufacturer, and for Covered Persons to take such other actions as are appropriate to limit the administration or use of the Covered Countermeasures.

Covered Countermeasures obtained for the SNS during the effective period of this Declaration are covered through the date of administration or use pursuant to a distribution or release from the SNS.

XIV. Countermeasures Injury Compensation Program

42 U.S.C 247d–6e

The PREP Act authorizes the Countermeasures Injury Compensation Program (CICP) to provide benefits to certain individuals or estates of individuals who sustain a covered serious physical injury as the direct result of the administration or use of the Covered Countermeasures, and benefits to certain survivors of individuals who die as a direct result of the administration or use of the Covered Countermeasures. The causal connection between the countermeasure and the serious physical injury must be supported by compelling, reliable, valid, medical and scientific evidence in order for the individual to be considered for compensation. The CICP is administered by the Health Resources and Services Administration, within the Department of Health and Human Services. Information about the CICP is available at the toll-free number 1–855–266–2427 or *http://www.hrsa.gov/cicp/.*

XV. Amendments

42 U.S.C. 247d–6d(b)(4)

Amendments to this Declaration will be published in the **Federal Register**, as warranted.

Authority: 42 U.S.C. 247d–6d.

Dated: March 10, 2020.

Alex M. Azar II,

Secretary of Health and Human Services.

[FR Doc. 2020–05484 Filed 3–12–20; 4:15 pm]

BILLING CODE P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute of Diabetes and Digestive and Kidney Diseases; Notice of Closed Meeting

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended, notice is hereby given of the following meeting.

The meeting will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., as amended. The grant applications and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the grant applications, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: National Institute of Diabetes and Digestive and Kidney Diseases Special Emphasis Panel; PAR–18–423: NIDDK Multi-Center Clinical Study Implementation Planning Cooperative Agreements (U34) in Digestive Diseases.

Date: May 22, 2020.

Time: 11:00 a.m. to 1:00 p.m.

Agenda: To review and evaluate grant applications.

Place: National Institutes of Health, Two Democracy Plaza, 6707 Democracy Boulevard, Bethesda, MD 20892 (Telephone Conference Call).

Contact Person: Dianne Camp, Ph.D., Scientific Review Officer, Review Branch, Division of Extramural Activities, NIDDK, National Institutes of Health, Room 7013, 6707 Democracy Boulevard, Bethesda, MD 20892–2542, (301) 594–7682, *campd@extra.niddk.nih.gov.*

(Catalogue of Federal Domestic Assistance Program Nos. 93.847, Diabetes, Endocrinology and Metabolic Research; 93.848, Digestive Diseases and Nutrition Research; 93.849, Kidney Diseases, Urology and Hematology Research, National Institutes of Health, HHS)

Dated: March 10, 2020.

Miguelina Perez,

Program Analyst, Office of Federal Advisory Committee Policy.

[FR Doc. 2020–05361 Filed 3–16–20; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Center for Scientific Review; Amended Notice of Meeting

Notice is hereby given of a change in the meeting of the Center for Scientific Review Special Emphasis Panel, Small Business: Cardiovascular Sciences, March 19, 2020 08:00 a.m. to March 20, 2020, 01:00 p.m., Embassy Suites Alexandria Old Town, 1900 Diagonal Road, Alexandria, VA 22314 which was published in the **Federal Register** on February 20, 2020, 85 FR 9791.

The meeting location is being held at the National Institutes of Health, 6701 Rockledge Drive, Bethesda, MD 20892, at 09:00 a.m. The meeting date remains the same. The meeting is closed to the public.

Dated: March 11, 2020.

Miguelina Perez,

Program Analyst, Office of Federal Advisory Committee Policy.

[FR Doc. 2020–05417 Filed 3–16–20; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Center for Scientific Review; Amended Notice of Meeting

Notice is hereby given of a change in the meeting of the Center for Scientific Review Special Emphasis Panel, PAR 19–059: Global Noncommunicable Diseases and Injury Across the Lifespan (R21), March 23, 2020, 8:00 a.m. to 5:00 p.m., at the Hotel Palomar, 2121 P Street NW, Washington, DC 20037, which was published in the **Federal Register** on February 25, 2020, 85 FR 10708.

The meeting will be held at the National Institutes of Health, 6701 Rockledge Drive, Bethesda, MD 20892. The format of the meeting has been changed to a Video Assisted Meeting. The meeting date and time remain the same. The meeting is closed to the public.

Dated: March 11, 2020.

Ronald J. Livingston, Jr.,

Program Analyst, Office of Federal Advisory Committee Policy.

[FR Doc. 2020–05419 Filed 3–16–20; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute of Diabetes and Digestive and Kidney Diseases; Notice of Closed Meeting

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended, notice is hereby given of the following meeting.

The meeting will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., as amended. The grant applications and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the grant applications, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: National Institute of Diabetes and Digestive and Kidney Diseases Special Emphasis Panel; Consortium for the Study of Chronic Pancreatitis, Diabetes, and Pancreatic Cancer Clinical Centers Special Emphasis Panel.

Date: April 2, 2020.

Time: 10:00 a.m. to 6:00 p.m.

Agenda: To review and evaluate grant applications.

EXECUTIVE ORDERS

Executive Order on Prioritizing and Allocating Health and Medical Resources to Respond to the Spread of Covid-19

HEALTHCARE

Issued on: **March 18, 2020**

By the authority vested in me as President by the Constitution and the laws of the United States of America, including the Defense Production Act of 1950, as amended (50 U.S.C. 4501 *et seq*.) (the "Act"), and section 301 of title 3, United States Code, it is hereby ordered as follows:

Section 1. Policy and Findings. On March 13, 2020, I declared a national emergency recognizing the threat that the novel (new) coronavirus known as SARS-CoV-2 poses to our national security. In recognizing the public health risk, I noted that on March 11, 2020, the World Health Organization announced that the outbreak of COVID-19 (the disease caused by SARS-CoV-2) can be characterized as a pandemic. I also noted that while the Federal Government, along with State and local governments, have taken preventive and proactive

measures to slow the spread of the virus and to treat those affected, the spread of COVID-19 within our Nation's communities threatens to strain our Nation's healthcare system. To ensure that our healthcare system is able to surge capacity and capability to respond to the spread of COVID-19, it is critical that all health and medical resources needed to respond to the spread of COVID-19 are properly distributed to the Nation's healthcare system and others that need them most at this time.

Accordingly, I find that health and medical resources needed to respond to the spread of COVID-19, including personal protective equipment and ventilators, meet the criteria specified in section 101(b) of the Act (50 U.S.C. 4511(b)). Under the delegation of authority provided in this order, the Secretary of Health and Human Services may identify additional specific health and medical resources that meet the criteria of section 101(b).

Sec. 2. Priorities and Allocation of Medical Resources.

(a) Notwithstanding Executive Order 13603 of March 16, 2012 (National Defense Resource Preparedness), the authority of the President conferred by section 101 of the Act to require performance of contracts or orders (other than contracts of employment) to promote the national defense over performance of any other contracts or orders, to allocate materials, services, and facilities as deemed necessary or appropriate to promote the national defense, and to implement the Act in subchapter III of chapter 55 of title 50, United States Code, is delegated to the Secretary of Health and Human Services with respect to all health and medical resources needed to respond to the spread of COVID-19 within the United States.

(b) The Secretary of Health and Human Services may use the authority under section 101 of the Act to determine, in consultation with the Secretary of Commerce and the heads of other executive departments and agencies as appropriate, the proper nationwide priorities and allocation of all health and medical resources, including controlling the distribution of such materials (including applicable services) in the civilian market, for responding to the spread of COVID-19 within the United States.

(c) The Secretary of Health and Human Services shall issue such orders and adopt and revise appropriate rules and regulations as may be necessary to implement this order.

Sec. 3. General Provisions. (a) Nothing in this order shall be construed to impair or otherwise affect:

(i) the authority granted by law to an executive department or agency, or the head thereof; or

(ii) the functions of the Director of the Office of Management and Budget relating to budgetary, administrative, or legislative proposals.

(b) This order shall be implemented consistent with applicable law and subject to the availability of appropriations.

(c) This order is not intended to, and does not, create any right or benefit, substantive or procedural, enforceable at law or in equity by any party against the United States, its departments, agencies, or entities, its officers, employees,

or agents, or any other person.

DONALD J. TRUMP

THE WHITE HOUSE,

March 18, 2020.

Coronavirus Preparedness and Response Supplemental Appropriations Act, 2020

H.R. 6074, CORONAVIRUS PREPAREDNESS AND RESPONSE SUPPLEMENTAL APPROPRIATIONS ACT, 2020

Title-By-Title Summary

This $8.3 billion package will fully fund a robust response to coronavirus, including vaccine development, support for state and local governments, and assistance for affected small businesses.

DIVISION A – Coronavirus Preparedness and Response Supplemental Appropriations Act, 2020

Prepared by the Democratic staff of the House Appropriations Committee

Title I – Agriculture, Rural Development, Food and Drug Administration, and Related Agencies

Food and Drug Administration – $61 million to facilitate the development and review, both pre-market and post-market, of medical countermeasures, devices, therapies, and vaccines to combat the coronavirus. This funding will help FDA maintain our national drug and device product inventory through extensive outreach to medical product manufacturers to identify and mitigate potential supply chain interruptions. Funds will also assist FDA's enforcement work against counterfeit and misbranded products and its review of emergency use authorizations for medical products, such as diagnostics. Additionally, these resources will enable FDA to build on its efforts to strengthen the U.S. medical product manufacturing sector by supporting efforts to foster more investment and innovation in advanced manufacturing methods for drugs, devices, vaccines, and other therapies.

Title II – Financial Services and General Government

Small Business Disaster Loans – Allows $1 billion in loan subsidies to be made available to help small businesses, small agricultural cooperatives, small aquaculture producers, and non-profit organizations which have been impacted by financial losses as a result of the coronavirus outbreak. This funding could enable the Small Business Administration to provide an estimated $7 billion in loans to these entities. In addition, provides $20 million to administer these loans.

Title III – Labor, Health and Human Services, Education, and Related Agencies

Centers for Disease Control and Prevention – $2.2 billion to support federal, state, and local public health agencies to prevent, prepare for, and respond to the coronavirus, including:

- $950 million, of which $475 million must be allocated within 30 days, to support States, locals, territories, and tribes to conduct public health activities such as:
  - surveillance for coronavirus;
  - laboratory testing to detect positive cases;
  - contact tracing to identify additional positive cases;
  - infection control at the local level to prevent additional cases;
  - migration in areas with person-to-person transmission to prevent additional cases; and
  - other public health preparedness and response activities

- $300 million to replenish the Infectious Diseases Rapid Response Reserve Fund, which supports immediate response activities during outbreaks.

- At least $300 million for global disease detection and emergency response.

In addition –

- The supplemental supports CDC's repatriation and quarantine efforts, laboratory testing, emergency operations, epidemiological investigations, public information, and surveillance and data analysis.

Furthermore, the supplemental includes –

- A general provision to reimburse State or local costs incurred for coronavirus preparedness and response activities between January 20 and the date of enactment of this emergency supplemental.
- A proviso to allow funds to be used for construction or renovation of facilities to improve preparedness and response capabilities at the State and local level.

Vaccines, Therapeutics, and Diagnostics – More than $3 billion for research and development of vaccines, therapeutics, and diagnostics to prevent or treat the effects of coronavirus, including:

- More than $2 billion for the Biomedical Advanced Research and Development Authority (BARDA) to support advanced research and development of vaccines, therapeutics, and diagnostics, prioritizing platform-based technologies with U.S.-based manufacturing capabilities.
- $826 million for the National Institutes of Health to support basic research and development of vaccines, therapeutics, and diagnostics.
- $300 million in contingency funding for procurement of vaccines, therapeutics, and diagnostics.

In addition –

- Requires that vaccines, therapeutics, and diagnostics developed using taxpayer funds must be available for purchase by the Federal government at a fair and reasonable price.
- Allows the Secretary of Health and Human Services to ensure that vaccines, therapeutics, and diagnostics developed using taxpayer funds be affordable in the commercial market.

Healthcare Preparedness, Pharmaceuticals and Medical Supplies, Community Health Centers – Nearly $1 billion for procurement of pharmaceuticals and medical supplies, to support healthcare preparedness and Community Health Centers, and to improve medical surge capacity:

- Approximately $500 million for procurement of pharmaceuticals, masks, personal protective equipment, and other medical supplies, which can be distributed to state and local health agencies in areas with a shortage of medical supplies.
- $100 million for health services through Community Health Centers, which will support smaller health clinics across the country in under-served urban and rural areas.
- Continues support for healthcare preparedness, including the National Ebola and Special Pathogens Training and Education Center (NETEC), regional, State and local special pathogens treatment centers, and hospital preparedness cooperative agreements.
- In addition, the bill allows funding for medical surge capacity, which will increase the supply of biocontainment beds at additional health facilities.

Additional Items

- Requirement to reimburse $136 million to programs across the Department of Health and Human Services that were temporarily transferred to support emergency preparedness and response activities at the CDC and the Assistant Secretary for Preparedness and Response.
- $10 million for worker-based training through the National Institute of Environmental Health Sciences to prevent and reduce exposure of hospital employees, emergency first responders, and other workers who are at risk of exposure to coronavirus through their work duties.
- $2 million for the HHS Office of Inspector General to conduct oversight of activities related to coronavirus preparedness and response.
- Authority for HHS to hire public health experts, as expeditiously as necessary, to perform critical work relating to coronavirus.

Title IV – State, Foreign Operations, and Related Programs

State Operations – $264 million for consular operations, emergency evacuations of State Department staff and dependents, and other emergency preparedness needs at embassies around the world. Increases transfer threshold for emergency evacuations from $10 million to $100 million.

Global Health Response – $435 million to support health systems overseas to prevent, prepare and respond to the coronavirus, of which $200 million is for the Emergency Reserve Fund.

Humanitarian Assistance – $300 million to respond to humanitarian needs arising in countries coping with a coronavirus disease outbreak.

Economic and Security Stabilization – $250 million to protect against the effects of an outbreak including economic, security, and stabilization requirements.

Oversight – $1 million for the USAID Inspector General to perform oversight of coronavirus response activities.

In addition –

- Allows for increased flexibility to transfer funds to respond to the coronavirus.
- Requires a comprehensive strategy to respond to the coronavirus outbreak and regular reporting on the use of funding.

Title V – Bill-Wide

Technical budgetary provisions.

In addition –

- Ensures that the President cannot use funds appropriated in this bill for any other purpose, except for repayment of transfers within the Department of Health and Human Services.
- Requires enhanced Government Accountability Office oversight of funds appropriated in this bill.
- Defines coronavirus.

DIVISION B – Telehealth Services During Certain Emergency Periods

Prepared by the Committee on Energy and Commerce

Emergency Telehealth Waiver: Allows the Secretary of Health and Human Services (HHS) to waive certain Medicare telehealth restrictions during the coronavirus public health emergency. These waivers would allow Medicare providers to furnish telehealth services to Medicare beneficiaries regardless of whether the beneficiary is in a rural community. This provision would also allow beneficiaries to receive care from physicians and other practitioners in their homes. This provision is estimated to cost $500 million.

Supplemental Request from Office of Management and Budget

EXECUTIVE OFFICE OF THE PRESIDENT
OFFICE OF MANAGEMENT AND BUDGET
WASHINGTON, D.C. 20503

March 17, 2020

The Honorable Michael R. Pence
President of the Senate
United States Senate
Washington, DC 20510

Dear Mr. President:

The Administration continues to place its full weight and resources behind the response to COVID-19. From the declaration of a public health emergency, to signing a major supplemental spending bill, to limiting air travel from impacted countries, to dozens of other major actions undertaken by agencies, the Administration is driving a whole-of-Government response that puts the health of the American people first.

To date, the President has signed into law the Coronavirus Preparedness and Response Supplemental Appropriations Act, 2020 (Public Law 115-123), which provided $8.3 billion for combatting the spread of the coronavirus at the local, State, national, and international levels and to prepare for the impacts of the coronavirus on the Nation.

The Administration appreciates the Congress' expeditious action on its last supplemental request. With the pandemic growing, resource needs have also grown. The unprecedented mobilization the Administration has achieved has forced agencies to incur unanticipated costs. These costs must be met with a legislative response to ensure full operational capacity.

The aim of this request is to maintain that capacity and ensure that resource needs created by the pandemic response are met. It is not intended as a broad-based solution to the major economic dislocation wrought by the virus, nor is it the primary means by which the Federal Government plans to address the hardships of families, individuals, and communities who have been touched by the disease. We are currently in active dialogue with the Congress on additional proposals that speak to these broader, vital issues.

At this time, the Administration is requesting additional fiscal year (FY) 2020 funding in the amount of $45.8 billion and the necessary authorities to address ongoing preparedness and response efforts. The details of this funding are included as an attachment to this letter. As the need for this funding arises from unforeseen and unanticipated events, the Administration believes it is appropriate that the amounts proposed be provided and designated as emergency requirements pursuant to section 251(b)(2)(A)(i) of the Balanced Budget and Emergency Deficit Control Act of 1985 (BBEDCA).

In addition to the emergency supplemental resources requested in this letter, the Administration also seeks to amend its FY 2021 Budget request for the Centers for Disease Control and Prevention (CDC) and the National Institutes of Health's (NIH) National Institute of Allergy and Infectious Diseases (NIAID). This FY 2021 Budget amendment increases funding for CDC to ensure that the Agency has the resources beginning October 1, 2020, to continue its critical public health mission. This amendment requests a total FY 2021 funding level of $8,329,102,000 for CDC, which is $1,328,196,000 above the FY 2021 Budget request. The additional funding will support priority CDC activities such as Immunization and Respiratory Diseases, Emerging and Zoonotic Infectious Diseases, Global Health, Public Health Preparedness and Response, and the Infectious Diseases Rapid Response Reserve Fund, among other activities. The additional funding is also for the proposed America's Health Block Grant to allow States and localities to address their most pressing non-infectious disease issues.

The Budget amendment would also increase funding for NIAID to ensure it has the resources beginning October 1, 2020, to continue critical basic and applied research on coronaviruses and other infectious diseases. NIAID is NIH's leading institute on infectious disease research and is at the forefront of the Federal Government's pursuit of a vaccine for the novel coronavirus. This FY 2021 Budget amendment would increase the NIAID total funding level within the NIH to $5,885,470,000, which is $439,584,000 above the FY 2021 Budget request.

Further, as a matter of comity, this FY 2020 supplemental request includes, without change, three requests from the Judiciary totaling $7.5 million.

Thank you for your consideration of these funding needs. I urge the Congress to take swift action to provide the additional funding requested to support the United States response to COVID-19. I stand ready to work with you to achieve this goal.

Sincerely,

Russell T. Vought
Acting Director

Enclosures

Agency:	DEPARTMENT OF DEFENSE—MILITARY PROGRAMS
Bureau:	OPERATION AND MAINTENANCE
Account:	Emergency Response Fund
Subcommittee:	Defense
Estimated Need:	$8,300,000,000

This request would provide $8.3 billion in additional FY 2020 funding for the Department of Defense (DOD) to mitigate the risk of COVID-19 to United States servicemembers, their dependents, and DOD civilians; minimize the impacts of the virus on strategic mission readiness; and support national response efforts. The request includes resources to facilitate changes in servicemember personnel policy; expedite access to rapid COVID-19 diagnostics; ensure access to medical care, including additional medical countermeasures; address the impacts of the pandemic on logistics and supply chains, including pharmaceuticals and personal protective equipment; and bolster the overall national response.

In addition, this request would provide transfer authority from the Emergency Response Fund to other currently available DOD accounts.

Agency:	DEPARTMENT OF HEALTH AND HUMAN SERVICES
Bureau:	DEPARTMENTAL MANAGEMENT
Account:	Public Health and Social Services Emergency Fund
Subcommittee:	Labor, Health and Human Services, Education, and Related Agencies
Estimated Need:	$5,277,000,000

This request would provide $5,277 billion in additional FY 2020 funding to the Department of Health and Human Services, Assistant Secretary for Preparedness and Response, Public Health and Social Services Emergency Fund account for the following: $75 million for the U.S. Public Health Service Commissioned Corps to support training and equipment, the Ready Reserve, the Public Health and Emergency Response Strike Team, and information technology requirements; $2 million would support the Office of National Security staffing, specifically the need for additional contracted intelligence analysts and specialists that would support an expanded intelligence analytical team for one year to allow for expanded hours and/or address a degraded workforce; and $5.2 billion to support the development and manufacturing of vaccines, therapeutics, and diagnostics. It also would support procurement of supplies for the Strategic National Stockpile, emergency medical management and field operations, pandemic forecasting and situational awareness and activities related to emergency workforce modernization and telehealth infrastructure, in response to coronavirus.

Operational Task Force Updates – 04-17-20	
Data Analysis	Accomplishments 1. Completed development of the Minimal Viable Product (MVP) version of the Resource Allocation Dashboard (RAD) which will be used to inform supply and demand decision-making. Completed April 16, 2020. 2. Defined summary statistics and model specifications for visualization on Johns Hopkins Infectious Disease Dynamics Model user interface and use in visualizing projections out one to two weeks. Completed April 15, 2020. Currently Working 1. Validating short-term forecasting trajectory to help determine resourcing (PPE and vent) requirements. ETA April 24, 2020. 2. Developing Minimal Viable Product (MVP) Infectious Disease Dynamics (IDD) model interactive web interface for rapid recall and retrieval of model data for visualization and data extraction. Estimated MVP prototype completion April 17, 2020. 3. Adjusting IDD model to improved calibrate against observed data. Phase 1 estimated completion April 17, 2020.
Community Mitigation	Accomplishments 1) Tiger Team: Finalizing reopening guidance, in collaboration with the WH, for the following settings: childcare facilities, schools and day camps, communities of faith, and employers with vulnerable workers, mass transit operators/riders and restaurants and bars. 2) Guidance: CMTF Lead briefed the FEMA RAs. Questions focused on vulnerable populations, risks of multiple waves as mitigation measures are lifted, awareness of CDC and other federal teams being deployed to regions without informing FEMA partners, and how CDC determines where to deploy teams and experts. 3) SLTT Engagement: a) Discussed re-opening criteria and guidance, CDC support, and technical assistance needs with Louisiana, Oklahoma, California, and Texas. b) Held a call with NY Department of Health to provide technical assistance and parameters for modeling changes to current community mitigation activities. c) Held a call with the NBA on guidance regarding disinfecting procedures, products, and related best practices for their facilities. 4) At Risk Individuals: Updated the Guidance for Homeless Service Providers to include messaging about using cloth face coverings, situations where PPE should be used by homeless shelter staff, and social distancing in sleeping arrangements. Currently Working 1) Tiger Team: Community Mitigation Strategy, including when and how to adjust mitigation strategies using specific indicators and thresholds. Received feedback from the WH COVID TF, and the NRCC TF is adjudicating feedback. 2) Guidance: a) The Minority Health Outreach Plan is under development with interagency partners. b) CDC continues to support correctional facilities that are experiencing outbreaks and is working to scale technical assistance since the number of requests may outpace available resources. TF is also working closely with CISA partners on this. 3) SLTT: State school superintendents and chiefs are asking the Department of Education for guidance on reopening schools. 4) At Risk Individuals: ASPR/ARI Team participated in discussion on increased food demand driven by unemployment and self-isolation requirements.

Health Care Resilience	Accomplishments in last 24 Hours 1. *Healthcare Workforce Virtual Toolkit*: first version of toolkit in final clearance for posting to the Assistant Secretary for Preparedness and Response (ASPR) Technical Resources, Assistance Center, and Information Exchange (TRACIE) website (*aligns with TF Goal 2: Optimization of Healthcare Workforce*) 2. *National PPE Preservation Strategy:* cleared through NJIC; beginning stakeholder engagement strategy as of 4/17/20 (*aligns with TF Goal 2: Optimization of Healthcare Workforce - Protection*) 3. Project Extension for Community Healthcare Outcomes (ECHO®) peer to peer sessions on *COVID-19: Emergency Department Patient Care and Clinical Operations* held on 4/16; 874 total participants, predominantly from the U.S., with 16 international participants in attendance (*aligns with TF Goal 1: Optimization of Healthcare Delivery*) Currently Working 1. *Medical operations coordination cell (MOCC)*: MOCC implementation plan and toolkit in development (completion exp. 4/20/20) and discussing with regions on 4/23/20 during 10-1 session 2. *Healthcare Delivery outside of hospitals*: continuing to work existing and emerging issues in healthcare settings outside of hospitals, including nursing homes and dialysis centers: a. *Press release on data reporting*: CDC and the Centers for Medicare and Medicaid (CMS) are working on a press release to highlight a new National Healthcare Safety Network (NHSN) module for nursing homes to report data on COVID-19. The press release will include information on COVID-19 cases, as well as on staffing, PPE, and testing supplies. 3. *Nursing Homes*: The CDC DC field team is helping the DC health department to address COVID-19 issues in two nursing homes.
Laboratory Diagnostics	Accomplishments 1. Dr. Beckham briefed the House Committee on Transportation and Infrastructure with Administrator Gaynor on April 16. 2. Established a process for Indian Health Service to report Abbott ID Now testing data to the HHS Protect Now system. This provides the federal interagency visibility into testing being done by tribal partners and in remote and rural areas. 3. The IRR is sending 30K Abbot ID now tests to 57 public health labs and 15K tests to Indian Health Services; these tests should begin arriving on April 20. Currently working: 1. Testing at Scale TF: Continuing to work across the federal interagency to identify and secure resources to enable the nation expand testing 2. Meeting with Association of Public Health Laboratories (APHL) to discuss Abbott ID Now and other equipment platforms in public health labs. 3. Continuing to work with Palantir to optimize hospital testing data in the new online system, targeting to have the system be the single source for testing data by April 20. 4. Developed an "Introduction to Serology" overview deck and Dr. Beckham will present this briefing at today's 12:30 VTC 5. Dr. Beckham is briefing the House Committee on Oversight and Reform on serological testing today.
Community Based Testing Sites (CBTS)	Accomplishments 1. Since 3/23/20, there have been 105,713 individuals screened and 96,850 individuals tested at CBTS locations 2. Since 3/23/20, 98,394 tests processed and received by the call center with 18,758 positive, 820 indeterminate, 78,815 negative 3. All PHS officers have access to CovidResponder and will be reporting sitreps daily in CovidResponder, final transition from SurveyMonkey will be made over the weekend. Currently Working 1. Implementing reporting via CovidResponder at all federally-supported (1.0) sites; developing CovidResponder data flow chart to cover PII/PHI concerns from Privacy Office at private partnership (2.0) sites. 2. Monitoring the expansion and implementation of the CBTS 2.0 plan and finalizing messaging strategy and materials for CBTS 2.0.

	3. Finalizing and implement proposed transition process after extensions. 4. Conducting legal review of CBTS cost share requirements 5. Creating updated CBTS 2.0 fact sheets
Supply Chain	Accomplishments 1) 16 Apr 20 Airbridge Activity: 5 Flights: (3)(b)(3):42 (1)(b)(3):42 and (1)(b)(3):42 55=flights complete; 45=flights scheduled. (100 total) a) The 51st Airbridge flight departed Bangkok 13 Apr 20 at 1001 (L) and arrived in(b)(3):42 16 Apr 20 at 0500 (L). The cargo is 48K face shields. b) The 52nd Airbridge flight departed Shanghai 15 Apr 20 at 1400 (L) and arrived in (b)(3):42 16 Apr 20 at 0249 (L). The anticipated cargo is gloves. c) The 53rd Airbridge flight departed Shanghai 16 Apr 20 at 0650 (L) and arrived in (b)(3):4 16 Apr 20 at 0915 (L). The anticipated cargo is masks and gowns. d) The 54th Airbridge flight departed Cambodia 14 Apr 20 at 1344 (L) and arrived in (b)(3):42 16 Apr 20 at 2045 (L). The anticipated cargo is gowns. e) The 55th Airbridge flight departed Shanghai 15 Apr 20 at 1400 (L) and arrived in(b)(3):42 16 Apr 20 at 0120 (L). The cargo is 9.8M gloves and 150K N95 masks. 2) (PRESERVATION) The 7th and 8th Battelle Critical Care Decontamination System (CCDS) units arrived to Secaucus, NJ on 15 Apr 20 and to (b)(3):42 on 16 Apr 20. The 9th system completed production 16 Apr 20 and will arrive in (b)(3):42 on 20 Apr 20. These are the first 9 units of a scheduled 60. 3) (ALLOCATION) The shipment of 10M DoD supplied masks was completed. The final 1M arrived at the (b)(3):42 U.S.C. (b)(3):4 16 Apr 20. 4) (ALLOCATION) 6,000 FEMA procured test kits (600,000 tests) arrived in Washington, DC (Dulles Airport) 16 Apr 20 at 1347 (L). The kits are now in(b)(3):42 for inspection. Once cleared, kits will ship to (b)(3):42 for cold storage and distribution. DPA Activity: 1) NSTR Currently Working 1) 17 Apr 20 Airbridge Activity: 4 Flights: (2)(b)(3):42, (2)(b)(3):42 a) The 56th Airbridge flight departed Kuala Lumpur 17 Apr 20 at 1530 (L) and is scheduled to arrive in(b)(3):42 17 Apr 20 at 0120 (L). The cargo will be determined 18 Apr 20. b) The 57th Airbridge flight departed Shanghai 17 Apr 20 and is scheduled to arrive in(b)(3): 17 Apr 20 at 1058 (L). The cargo will be determined 18 Apr 20. c) The 58th Airbridge flight departed Shanghai 18 Apr 20 at 0005 (L) and is scheduled to arrive in(b)(3):42 17 Apr 20 at 2030 (L). The cargo will be determined 18 Apr 20. d) The 69th Airbridge flight departed Shanghai 17 Apr 20 at 0805 (L) and is scheduled to arrive in (b)(3): 17 Apr 20 at 2330 (L). The cargo will be determined 18 Apr 20. 2) (ALLOCATION) The 3rd HHS Tyvek suit airlift of 266K Tyvek suits is scheduled to arrive in Dallas, TX on 17 Apr 20. The cargo will be in transit to the (b)(3):42 f(b)(3):42 U.S.C. § on 18 Apr 20.
Medical Countermeasure (MCM)	Accomplishments 1) 2276 (+46) market research submissions and 216 (+1) CoronaWatch meetings held 2) ACTT1 clinical trial to test remdesivir for treatment of COVID-19: 881 (+122) new patients at 69 (+2) sites (target = 700) 3) Phase 1 safety trial for mRNA vaccine: 49 (+10) healthy volunteers enrolled (target = 105); target increased by 60 to include older adults 4) Emergency Use Authorizations granted by FDA: 33 (+1) molecular diagnostic tests, 15 (+3) laboratory-developed tests, 4 (+1) antibody tests, and 2 repurposed treatments (chloroquine, hydroxychloroquine) 5) Requests for chloroquine/hydroxychloroquine from the SNS a) 4 clinical trial requests received, 2 (+1) fulfilled b) 24 (+1) EUA requests received, 24 (+2) shipped

	Currently working 1) Continuing to enroll patients in clinical trials to evaluate vaccines and therapeutics for COVID-19 2) Accelerating vaccine manufacturing efforts to ensure rapid delivery of vaccines 3) Continuing to identify lead antibody treatment candidates for further development and manufacturing
Continuity	Accomplishments 1) Over past 24 hours, 1 Wireless Emergency Alert (WEA) message related to COVID-19 sent by local authorities. a) 1 of 1 was a stay at home/curfew reminder. Currently Working 1. In coordination with NSC, addressing follow-up questions from 4/16 Continuity Coordinators call 2. Developing reconstitution guidance for Federal and non-Federal stakeholders; product expected to be available NLT 22 April 2) Developing an exercise starter kit for both Federal and non-Federal stakeholders to aid adaptation of reconstitution plans in returning the workforce to primary facilities; product expected to be available NLT 1 May.

SARS-CoV-2 Medical Countermeasures Task Force

Christopher Houchens, PhD
Director, Division of Chemical, Biological, Radiological, and Nuclear Medical Countermeasures
BARDA/ASPR/HHS

SARS-CoV-2 Medical Countermeasures Task Force

Align MCM development across interagency partners to avoid duplication of effort, identify opportunities for synergy, and fill potential gaps

SARS-CoV-2 MCM Task Force Working Groups

- Therapeutics
- Vaccines
- Diagnostics
- Clinical Trials

Sub-Working Groups

- Therapeutics Prioritization
- Sample Sharing
- NIAID RCT

Partnering to Improve Preparedness

VACCINES
- Proven platforms
- Large scale manufacturability
- Speed
- Multiple approaches

DIAGNOSTICS

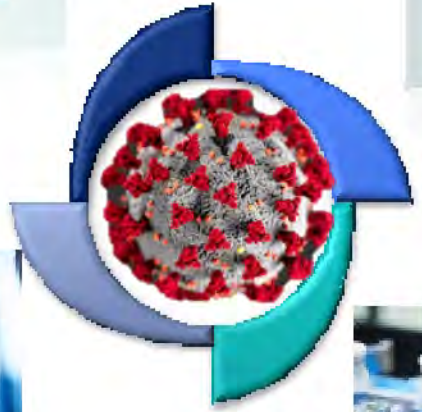
Faster and easier to use
More accurate

⬇

Earlier Identification

⬇

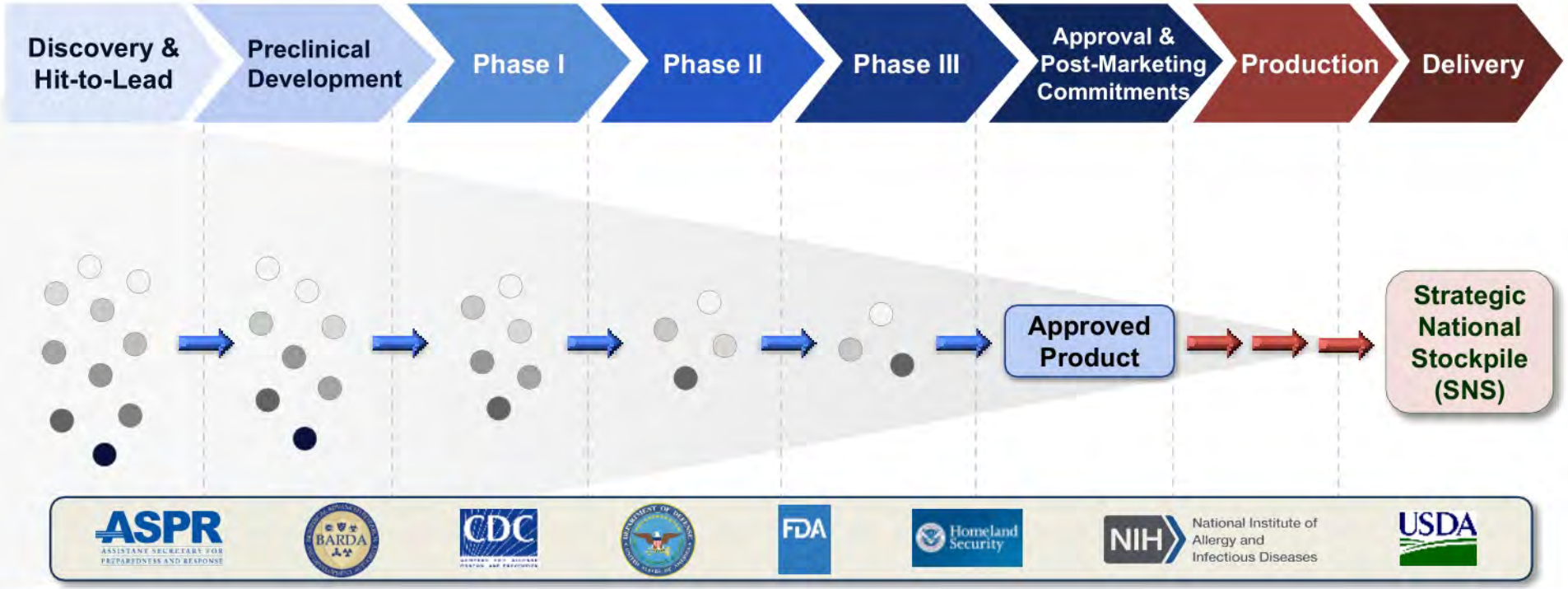
Earlier Treatment



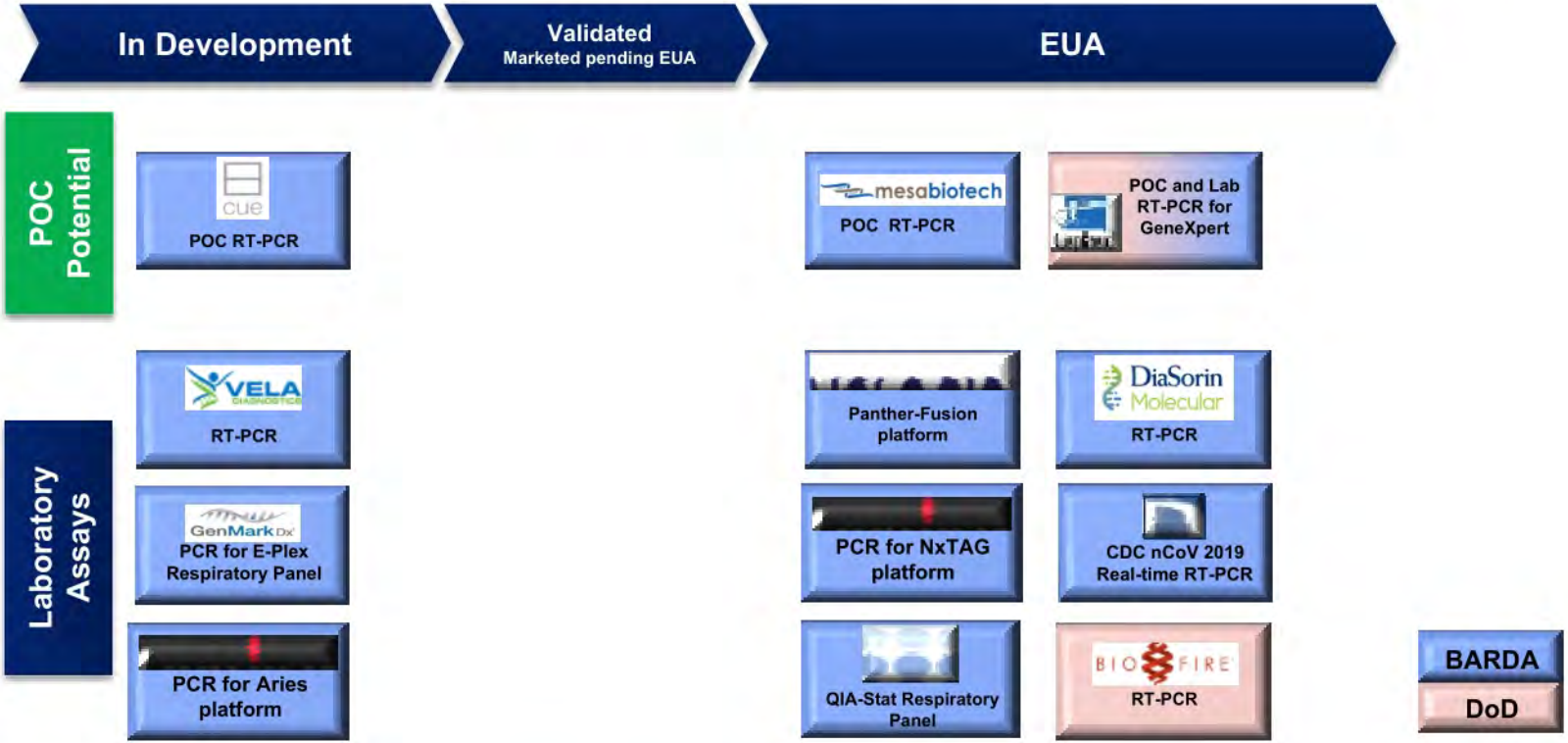
THERAPEUTICS
- Platform-based monoclonal antibodies
- Repurposed therapeutics
- Host targeted therapeutics

DOMESTIC MANUFACTURING
- Expand production
- Increase fill/ finish capacity

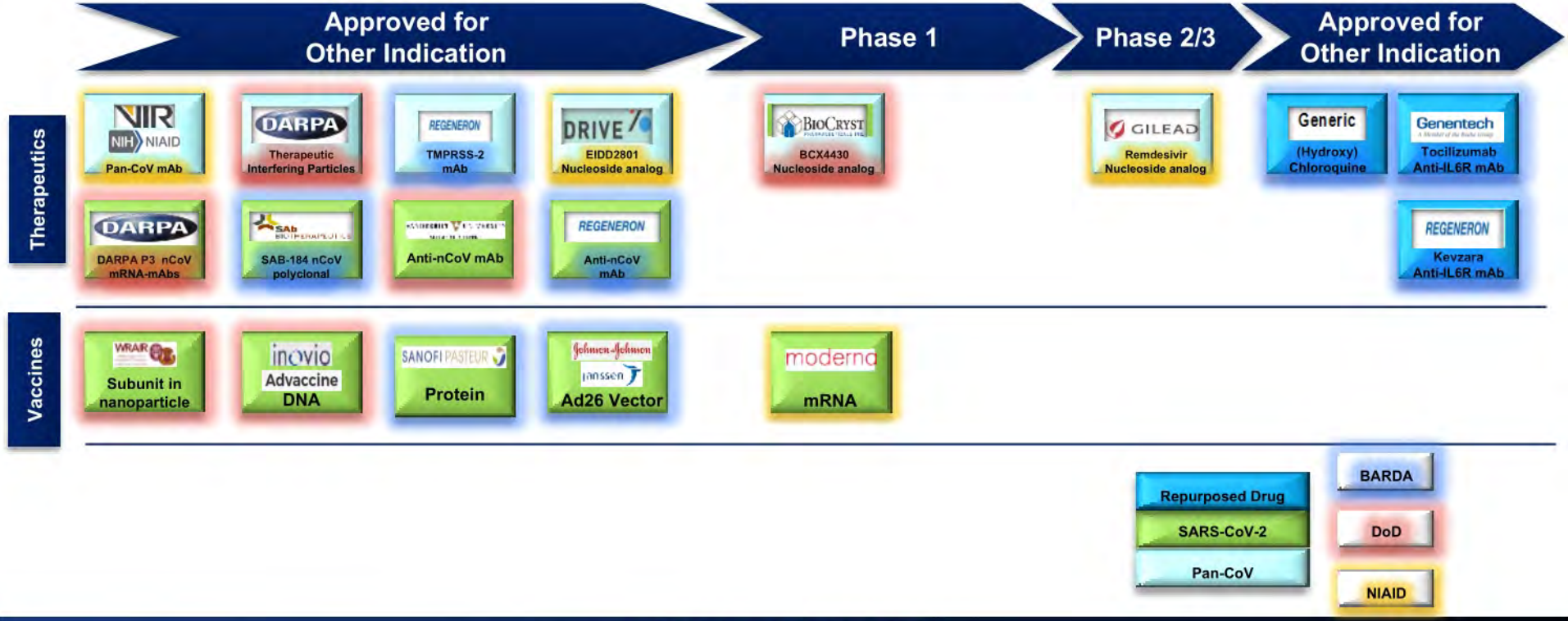
SARS-CoV-2 Interagency Partnerships: Early Development to Large-scale Production of MCMs



USG-Sponsored SARS-CoV-2 Molecular Diagnostic Tests



USG-Supported SARS-CoV-2 Therapeutics and Vaccines



MCM Development / Scientific Priorities

- BARDA BAA and EZ-BAA open for COVID-19 vaccines, therapeutics, and diagnostics
- 720 MCM concept papers, resulting in 75 *TechWatch* meetings
- **Therapeutics**
  - NIAID global Randomized Clinical Trial for remdesivir
    - ✓ 8 US and 2 non-US sites activated, additional sites pending
    - ✓ 11 patients (10 US, 2 non-US) enrolled
  - Assays to screen compound libraries for anti-SARS-CoV-2 activity are being validated
- **Vaccine**
  - Phase 1 trial for *Moderna mRNA-1273*, healthy volunteer screening began 3/5/2020
    - ✓ First vaccination planned for week of 3/16/2020
- **Diagnostics**
  - BARDA issued 3 EZ-BAA awards for SARS-CoV-2 rapid diagnostic tests

From: S Barer (b)(6)

To: Bright, Rick (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=53034752f35a4317aa74f46348442d39-Bright, Ric <Rick.Bright@hhs.gov>

Subject: Fwd: Chloroquine - senate action.?

Date: 2020/03/19 10:13:05

Priority: Normal

Type: Note

Dr. Sol J. Barer
Chairman of the Board of Directors
TEVA Pharmaceutical industries Ltd.
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sol.barer@tevapharm.com
https://protect2.fireeye.com/url?k=c76de157-9b39f82b-c76dd068-0cc47adc5fa2-e5656208536e0889&u=http://www.tevapharm.com/

Begin forwarded message:

From: "Levin, Jeremy" <jlevin@ovidrx.com>
Date: March 19, 2020 at 10:11:20 AM EDT
To: Sol Barer <sjbarer@gmail.com>
Cc: "Kåre (Kaare) Schultz" <Kare.Schultz@teva.co.il>
Subject: Re: Chloroquine

Sol
On the medical side its a group with Mike Osterholm
https://en.wikipedia.org/wiki/Michael_Osterholm
On the Government side it Seema
On the Senate side its Grassley and Schumer with a some input from McConnell
On the House its Pellosi
J

On Mar 19, 2020, at 10:02 AM, S Barer <(b)(6)> wrote:

Thanks Jeremy. We are working on this with the government as we speak - indeed they recognize Teva's role. Good to know your contacts. I will let Kare respond from his perspective- but appreciate the note and the offer and will be in contact!
Sol

Dr. Sol J. Barer
Chairman of the Board of Directors

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sol.barer@tevapharm.com
https://protect2.fireeye.com/url?k=e55de210-b909fb6c-e55dd32f-0cc47adc5fa2-56a9fa4905c47d39&u=http://www.tevapharm.com/

On Mar 19, 2020, at 9:59 AM, Levin, Jeremy <jlevin@ovidrx.com>wrote:

Dear Kåre and Sol

I trust you are both weathering this unpleasant period.

I suspect you know all about this matter but would like to make sure you saw the note below. I have reviewed all the medical background and am working with a panel physicians and world health experts. All would like to get their hands on Chloroquine in the USA.

I don't recall if this was in th Teva portfolio, but I would be delighted to make the introduction to the panel who are all world leaders and deeply embedded into the system in Washington.

Do let me know

J

AN OLD DRUG FOR THE NEW VIRUS

Howard Kaplan, MD
Howard Kaplan, MD
Mar 11 · 6 min read

By: Dr. Andrea Savarino

Under the prevailing circumstances of uncertainty and limited options, We believe an old, cheap, oral, off-patented drug — ***chloroquine*** — should be considered for certain populations at high risk of exposure to the COVID-19 virus. ***In the meantime, production of chloroquine must be scaled up immediately: drug supply could quickly become the gating item of life and death.***

The history of Chloroquine (and its cousin hydroxychloroquine) dates back to 17th century Peru, where a related compound, quinine, was extracted from the bark of Cinchona trees and used to treat chills and fever. Chloroquine itself was synthesized in 1934 by Hans Andersag at the Bayer laboratories. During World War II, U.S. government-sponsored clinical trials demonstrated the antimalarial effects of the drug.

Chloroquine is now being studied in multiple clinical trials in China as a treatment for COVID-19, the disease caused by the SARS-CoV-2 coronavirus. China, Korea, Belgium, Poland, France and Italy have added it to treatment guidelines for patients infected with COVID-19. We believe there is sufficient evidence regarding the safety and efficacy of chloroquine to recommend making the drug immediately available to specific high-risk patient populations. More is known about chloroquine than nearly all new drug candidates which, by definition, lack human experience of both safety and efficacy. For this reason, chloroquine may be the one and only immediately available "stopgap" therapy, while potentially better drugs move through the development process. For the time being, chloroquine only needs to possess a superior risk/benefit profile relative to the *status quo* of no therapy. Chloroquine is available as a generic drug and is uniquely inexpensive at approximately $13 per day.

We strongly believe that a compelling risk/benefit profile exists today for specific "high-risk" COVID-19 populations: 1) Health-care providers (HCPs) at high-risk for COVID-19 exposure, and 2) Housebound COVID-19 patients and their family members 3) Mild cases of COVID-19. None of these groups receives any therapy today. Should Chloroquine show a positive signal in these populations, consideration should then be given to mass distribution with the intention of bending and breaking the COVID-19 mortality curve.

Our recommendation has a close analogy and precedent with AZT, an old generic drug approved in 1987 as the first therapy for HIV. In the 1990s, many hospitals adopted AZT prophylaxis protocols for health care providers at high risk of HIV infection prior to the emergence of conclusive evidence from controlled clinical trials. The rationale was similar (superior risk/benefit versus doing nothing), as was the unique stopgap role of AZT treatment, while potentially better drugs moved through the development process. AZT played a vital role in the history of HIV.

Why might chloroquine be effective for COVID-19? In a 2006 paper from *The Lancet Infectious Diseases*, one of us (Dr. Savarino) discussed findings that chloroquine alters the sugar structure of ACE2, which the SARS Coronaviruses use to gain entry to cells. This altered structure inhibits the ability of SARS-CoV-2 to enter and infect cells. In 2020, Dr. Manli Wang discovered that chloroquine is effective in an *in-vitro* experiment at concentrations achievable by chloroquine doses routinely taken by Lupus patients.

All drugs have side effects. Unique to chloroquine, the risks here are predominantly known *potential* side effects: eye damage, heart complications, and impairment of the body's ability to fight an infection. A short course of chloroquine therapy is very unlikely to cause any of these complications, as they are almost always seen after years of treatment. Realistic short term side effects include mild dizziness and GI upset.

We must urgently consider the risk /benefit of maintaining the status quo. Healthcare systems around the globe are becoming overwhelmed, leaving patients to fend for themselves. testing for COVID-19 will likely continue to be inadequate in the US in the near term Alternative drugs may become supply-limited or reserved for severe patients. Remdesivir is a promising drug for COVID-19, but it is given intravenously and thus likely limited to severe hospitalized patients. Novel therapies and vaccines in development are likely at least one year away from an expedited FDA approval, even in a best-case scenario. Developing countries critical to fully eradicating COVID-19 will require an inexpensive drug like chloroquine.

We propose the following immediate concrete actions to help curb this pandemic. ***Generic manufacturers significantly increase production of***

chloroquine and hydroxychloroquine. A quick Google search reveals a significant spike in searches for chloroquine which has been followed by a similar spike in prescriptions for the drug. Its availability is currently limited. Health care providers raise awareness of the favorable risk/benefit for the discussed patient populations. We all collaborate to generate clinical data on chloroquine in these populations as rapidly as possible.

Although randomized, double blind clinical trials are considered the gold standard of evidence, logistical challenges would likely preclude timely execution of these trials, and lives may be unnecessarily lost by further delay. We propose an unconventional, alternative idea that would put chloroquine in the hands of at-risk individuals and suspected patients quickly. Patients and HCPs would receive chloroquine on a voluntary basis. They would self-report drug use, symptoms, side effects, and hospital visits to an online data depository. Outcomes and risk/benefit could be assessed in real time, comparing the group which elects to take chloroquine versus the group that declines. This study would be observational in nature and far from perfect. Nevertheless, if chloroquine proves highly effective with minimal side effects, such a study is likely to reveal this signal, ignite broad use of chloroquine, and save many lives in the process.

Our bottom line: If we were on the Princess Diamond cruise ship today and were fortunate enough to have a bottle of chloroquine, we would unequivocally elect to take the drug prophylactically. All high-risk individuals can and should be offered the same option immediately.

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Sender:	S Barer (b)(6)
Recipient:	Bright, Rick (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=53034752f35a4317aa74f46348442d39-Bright, Ric <Rick.Bright@hhs.gov>
Sent Date:	2020/03/19 10:12:44
Delivered Date:	2020/03/19 10:13:05

SARS-CoV-2 Medical Countermeasures Task Force

Christopher Houchens, PhD
Director, Division of Chemical, Biological, Radiological, and Nuclear Medical Countermeasures
BARDA/ASPR/HHS

SARS-CoV-2 Medical Countermeasures Task Force

Align MCM development across interagency partners to avoid duplication of effort, identify opportunities for synergy, and fill potential gaps

SARS-CoV-2 MCM Task Force Working Groups

- Therapeutics
- Vaccines
- Diagnostics
- Clinical Trials

Sub-Working Groups

- Therapeutics Prioritization
- Sample Sharing

Partnering to Improve Preparedness

VACCINES
- Proven platforms
- Large scale manufacturability
- Speed
- Multiple approaches

DIAGNOSTICS
Faster and easier to use
More accurate

⬇

Earlier Identification

⬇

Earlier Treatment

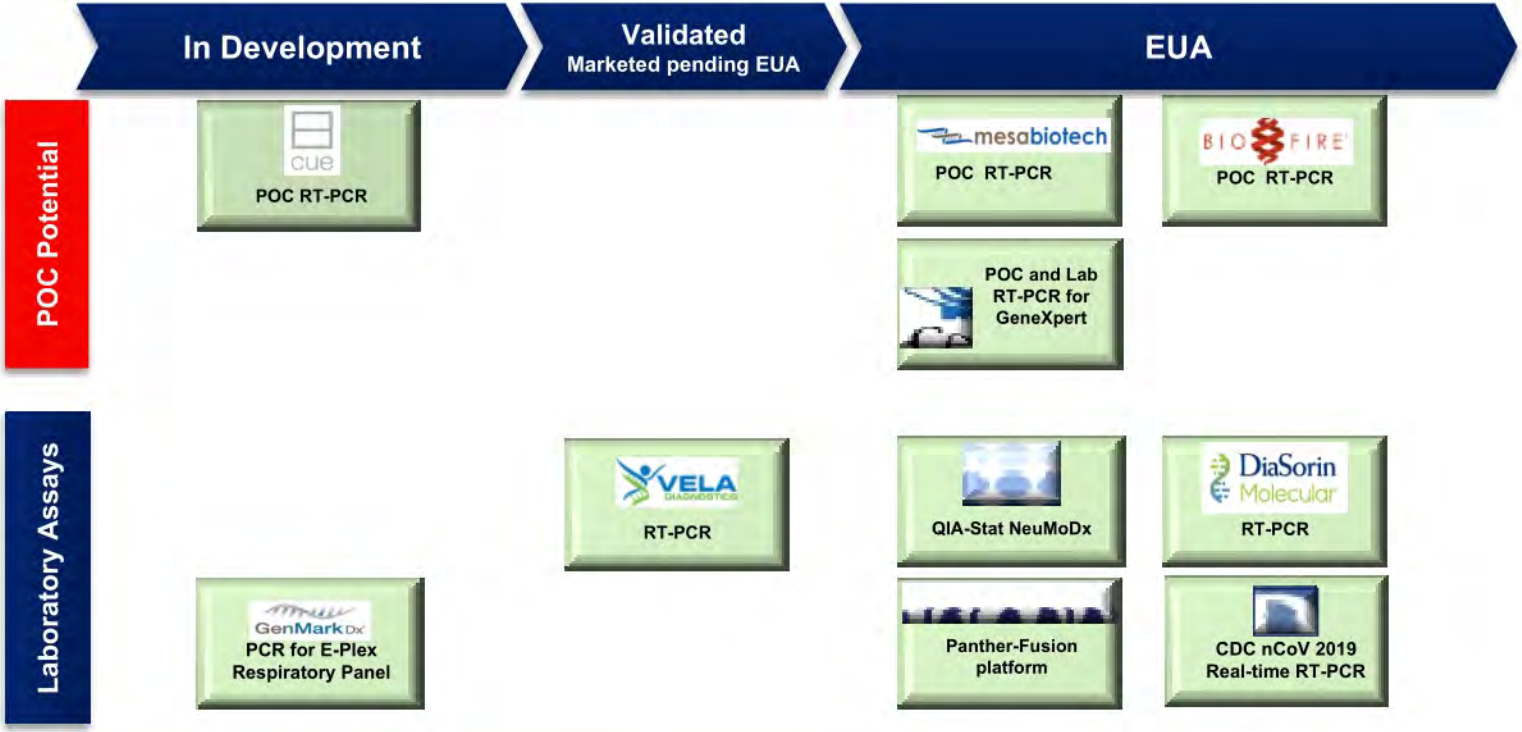
THERAPEUTICS
- Platform-based monoclonal antibodies
- Repurposed therapeutics
- Host targeted therapeutics

BIOMEDICAL ADVANCED RESEARCH AND DEVELOPMENT AUTHORITY
BARDA

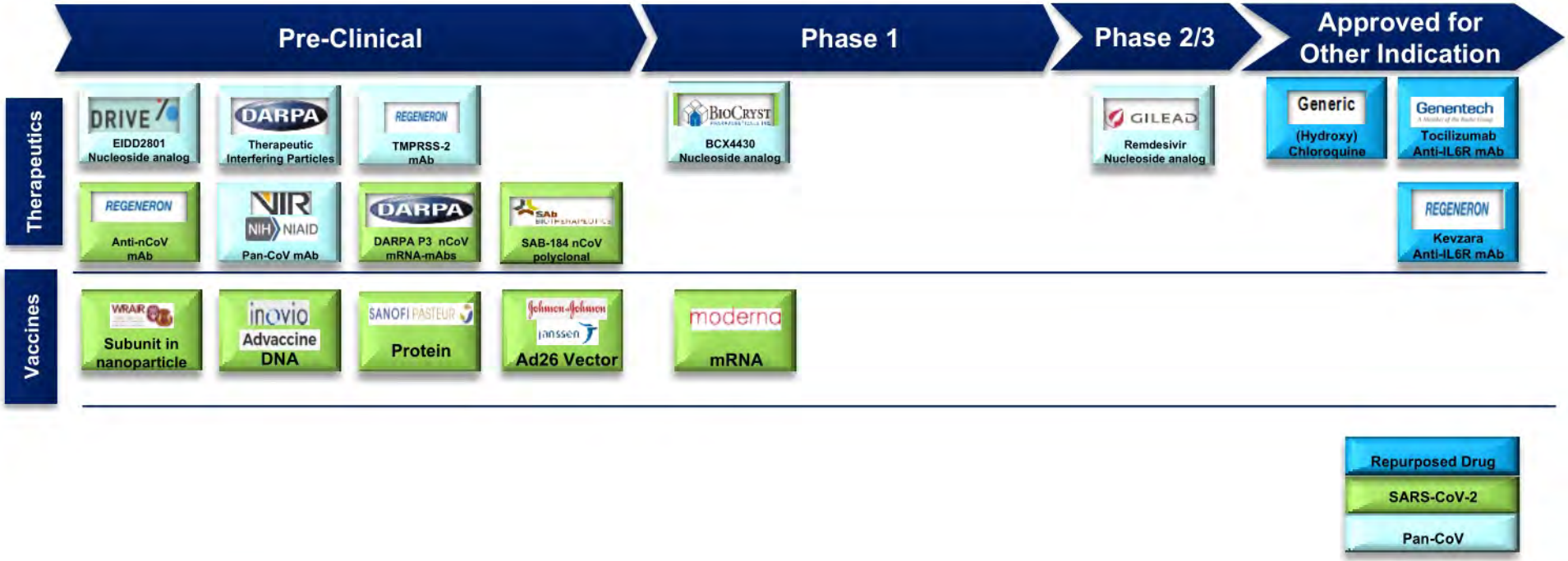
DOMESTIC MANUFACTURING
- Expand production
- Increase fill/ finish capacity

SARS-CoV-2 Interagency Partnerships: Early Development to Large-scale Production of MCMs

USG-Sponsored SARS-CoV-2 Molecular Diagnostic Tests



USG-Supported SARS-CoV-2 Therapeutics and Vaccines



COVID-19 MEDICAL COUNTERMEASURE UPDATE

XXX XX, 2020

UNCLASSIFIED

ASPR Mission

Save Lives and Protect Americans from 21st Century Health Security Threats

The BARDA Model

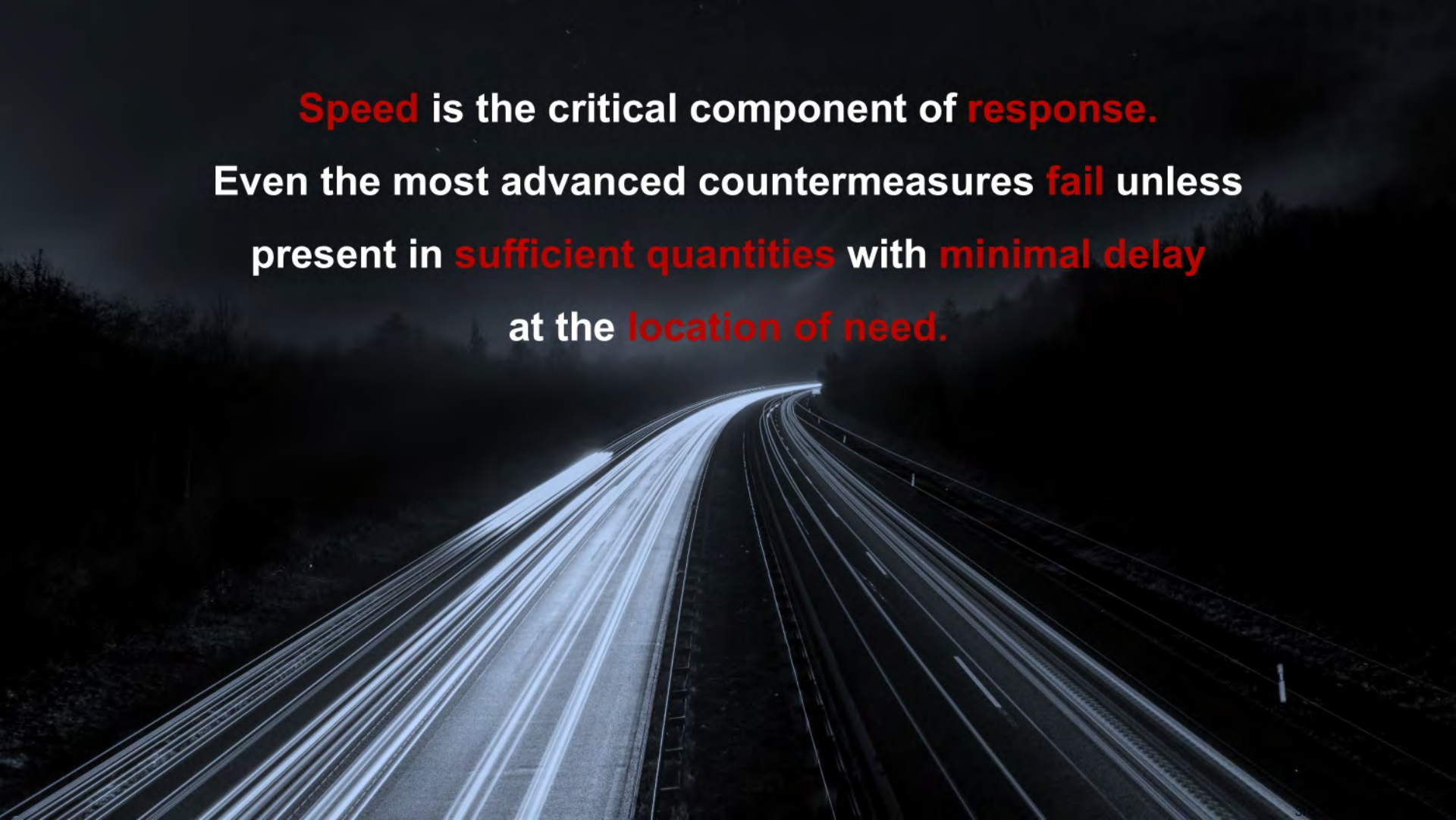
BARDA develops and makes available medical countermeasures **(MCMs)** by forming unique public-private partnerships to drive innovation off the bench to the patient to save lives.

Our Industry Partners

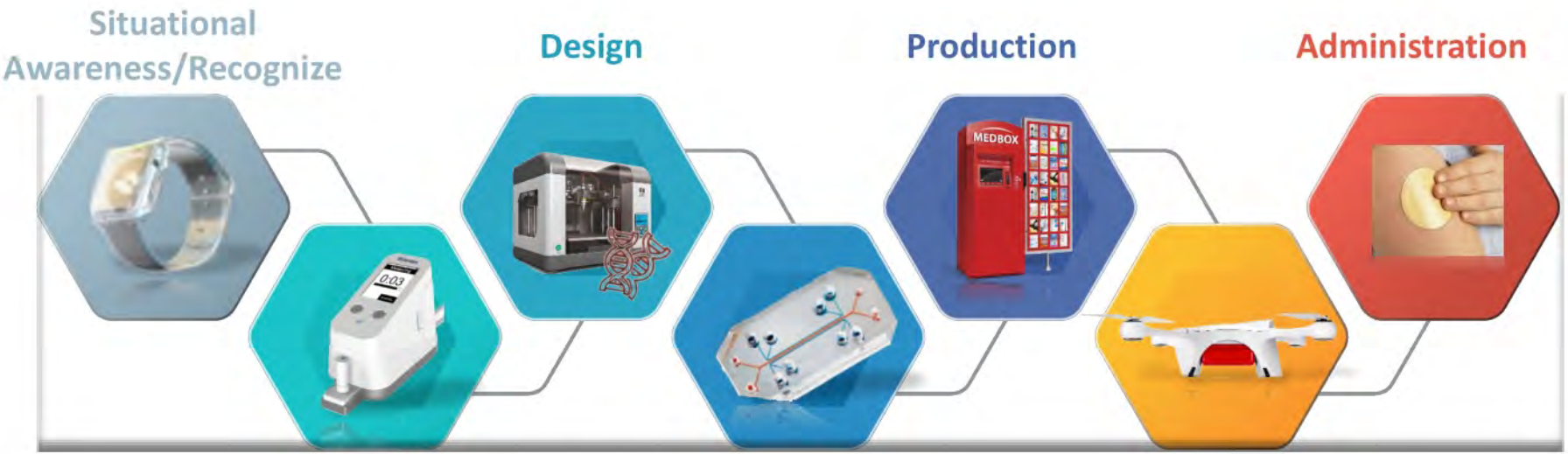
Our Government Partners

National Institute
of Allergy and
Infectious Diseases

54 FDA Approvals, Licensures, and Clearances


Speed is the critical component of response.
Even the most advanced countermeasures fail unless
present in sufficient quantities with minimal delay
at the location of need.

Addressing End to End Solutions



16 Years

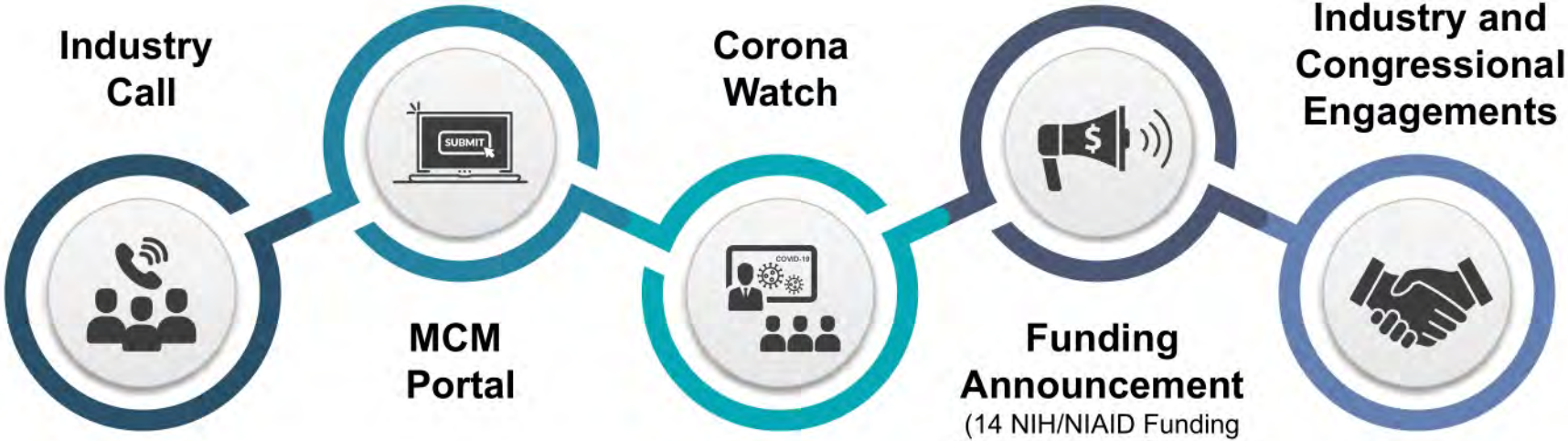
3rd Coronavirus Outbreak

No Licensed products

2019-nCoV Medical Countermeasures Task Force

Align and prioritize MCM development across Interagency partners to avoid duplication of effort, identify opportunities for synergy, and fill potential gaps

Agency-Wide Engagement with Developers



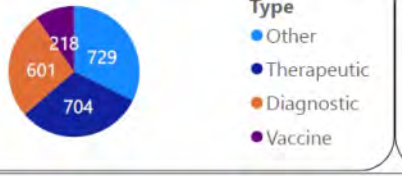
COVID-19 Market Research Portal Submissions

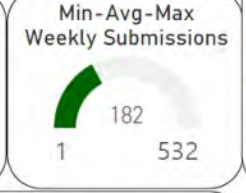
U//FOUO - FOR OFFICIAL USE ONLY - DO NOT DISTRIBUTE

BARDA COVID-19 Submissions Report - **Overview**

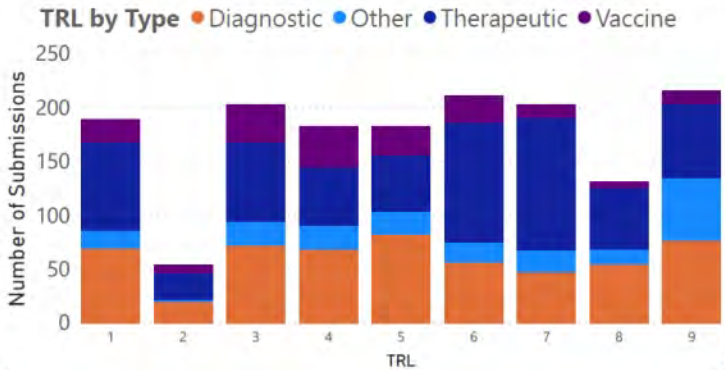
2020-04-08 12:13:37
Last Refreshed

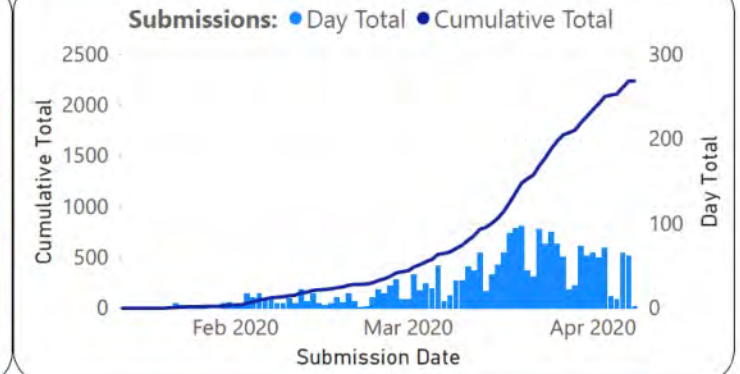
Total Submissions	Market Research Submissions	BAA Submissions	EZ-BAA Submissions
2252	2015	66	171





Market Research Contacts	Total	Dx	Tx	Vx	Other
TechWatch Held	190	70	50	36	34
TechWatch Scheduled	8	6	1	1	
All Contacts	**2015**	**464**	**683**	**201**	**667**





COVID-19 MEDICAL COUNTERMEASURE DEVELOPMENT STRATEGY

ACCELERATE DEVELOPMENT

- Platform technologies
- Repurpose licensed products
- Parallel, not sequential, activities

MITIGAGE RISK

- Multiple technologies
- Multiple targets
- Redundancy

DOMESTIC MANUFACTURING

- Scale Up & Scale Out
- Raw materials and supply chains
- Leverage existing facilities

Therapeutics Development

FDA-approved therapeutics licensed for other indications
- Ready for immediate clinical testing

e.g., inhibitors of viral activation, host pathway modulators

e.g., 2019-CoV specific monoclonal antibodies, small molecule antivirals, and immunoglobulins

Leverage existing infrastructure for rapid MCM generation and production through partnerships (contracts and OTA) including other USG agencies

Repurposed Therapeutics

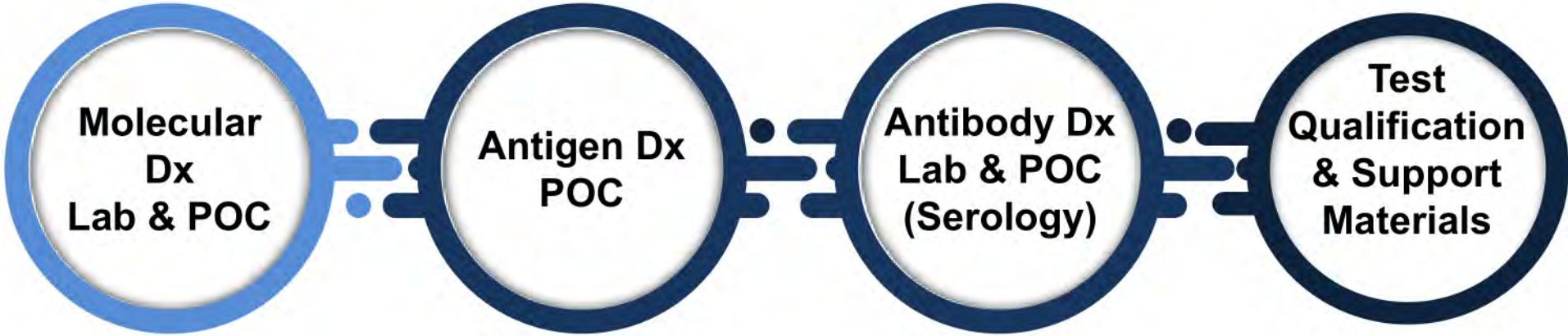
Thousands of compounds currently being screened-low cost/high impact
Many candidates identified and undergoing clinical evaluation

Allows rapid advancement to clinical trials (i.e. IL-6 monoclonal antibody trial started 2-weeks after identification)

Utilize existing facilities for production;
Expand capacity through partnerships with large pharmaceutical partners

BARDA seeking to leverage existing infrastructure for rapid clinical trial initiation

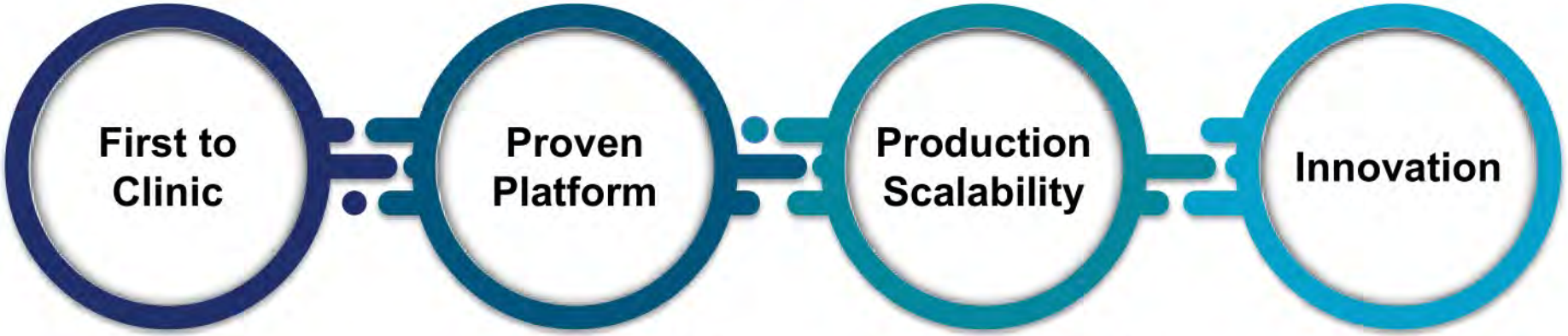
Diagnostics Development: Four-Pronged Approach



Leverage existing Laboratory Infrastructure & Equipment
Leverage Existing & Complete In-Development POC Equipment

04/02/20

Vaccine Development



e.g., mRNA based vaccines that allow rapid early development

e.g., viral vectors with demonstrated safety and efficacy

e.g., Existing or readily amenable to large scale manufacturing, including experienced workforce

e.g., novel platforms, delivery approaches, or new thinking to transform the field

Leverage existing infrastructure for rapid MCM generation and production through partnerships (contracts and OTA) including other USG agencies

Vaccine Approach

Accelerate Development

Rapid Vaccine Platform Approaches
- Nucleic Acid
- Vectors
- Recombinant protein

Repurpose Licensed Products
- Viral Vector
- Recombinant Protein

Parallel Activities
- Overlapping clinical trials
- Scale up in parallel with clinical development

Mitigate Risk

Multiple Platforms
- Address potential yield risks
- Address potential dose risk

Multiple Presentations (recombinant, vector, etc.)
- Disease enhancement mitigation
- Alternative routes of delivery

Redundancy
- Take multiple products through large scale clinical trials
- Multiple manufacturing facilities for each product

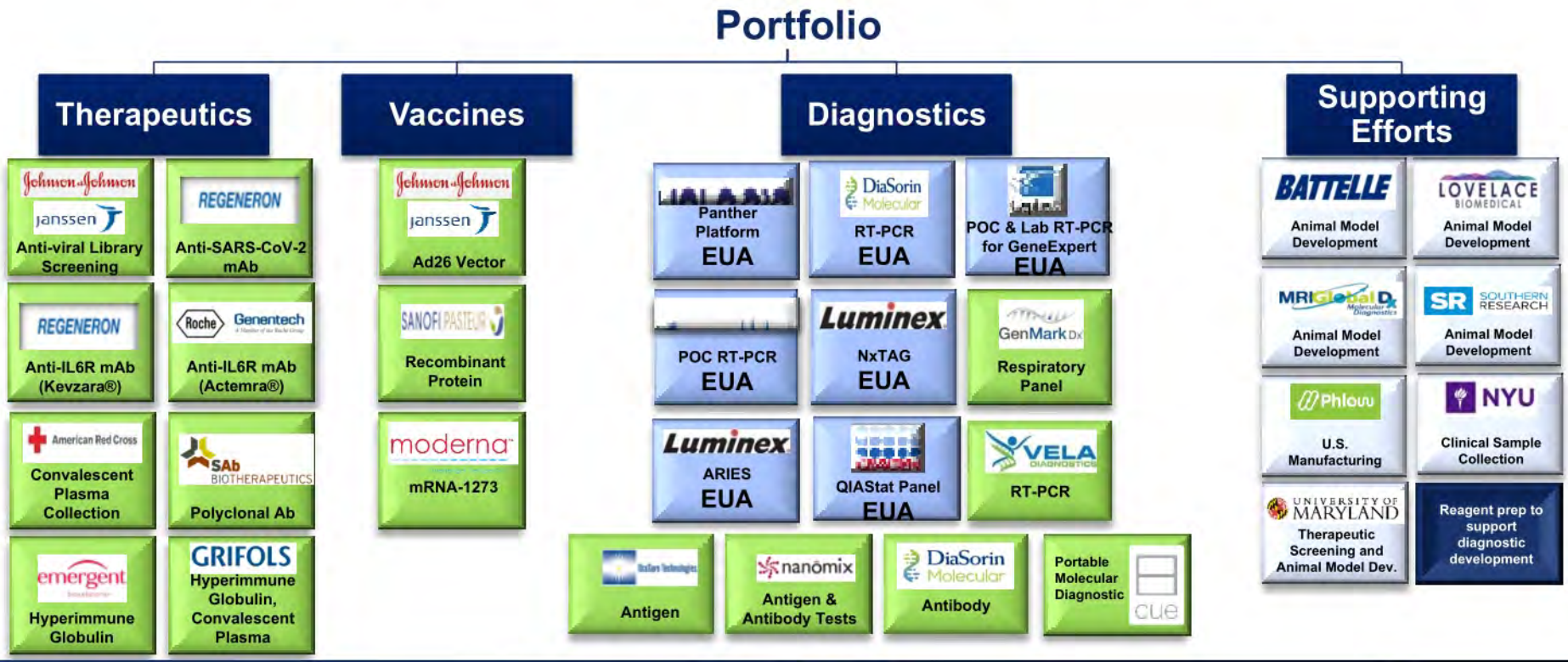
Domestic Manufacturing

Scale Up & Scale Out
- Validate large scale process (i.e. larger tanks)
- Technology transfer to more facilities
- Increase fill/finish capacity

Raw Materials Supply Chains
- Remove bottlenecks
- Establish stockpiles

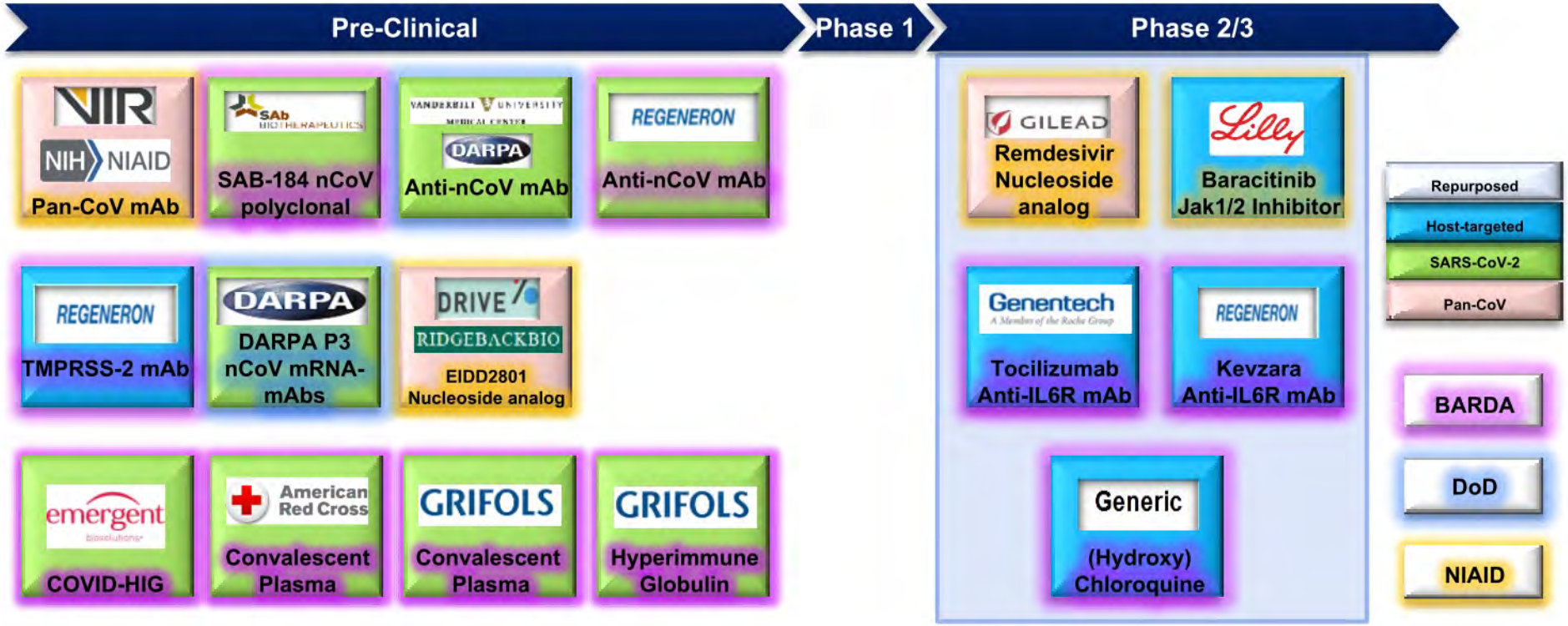
Leverage Existing Facilities
- Facilities of large pharma partners
- CMOs

BARDA Medical Countermeasures Response

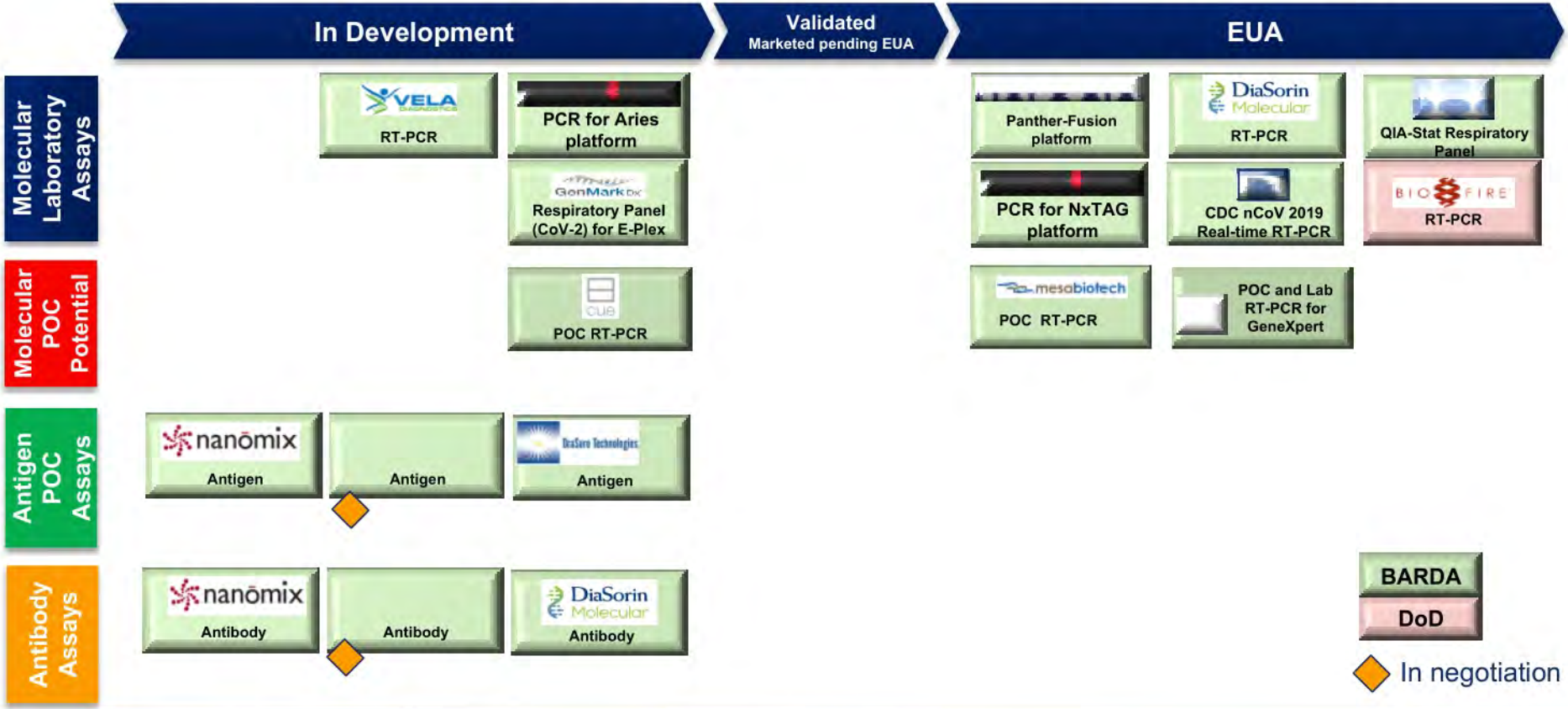


Background

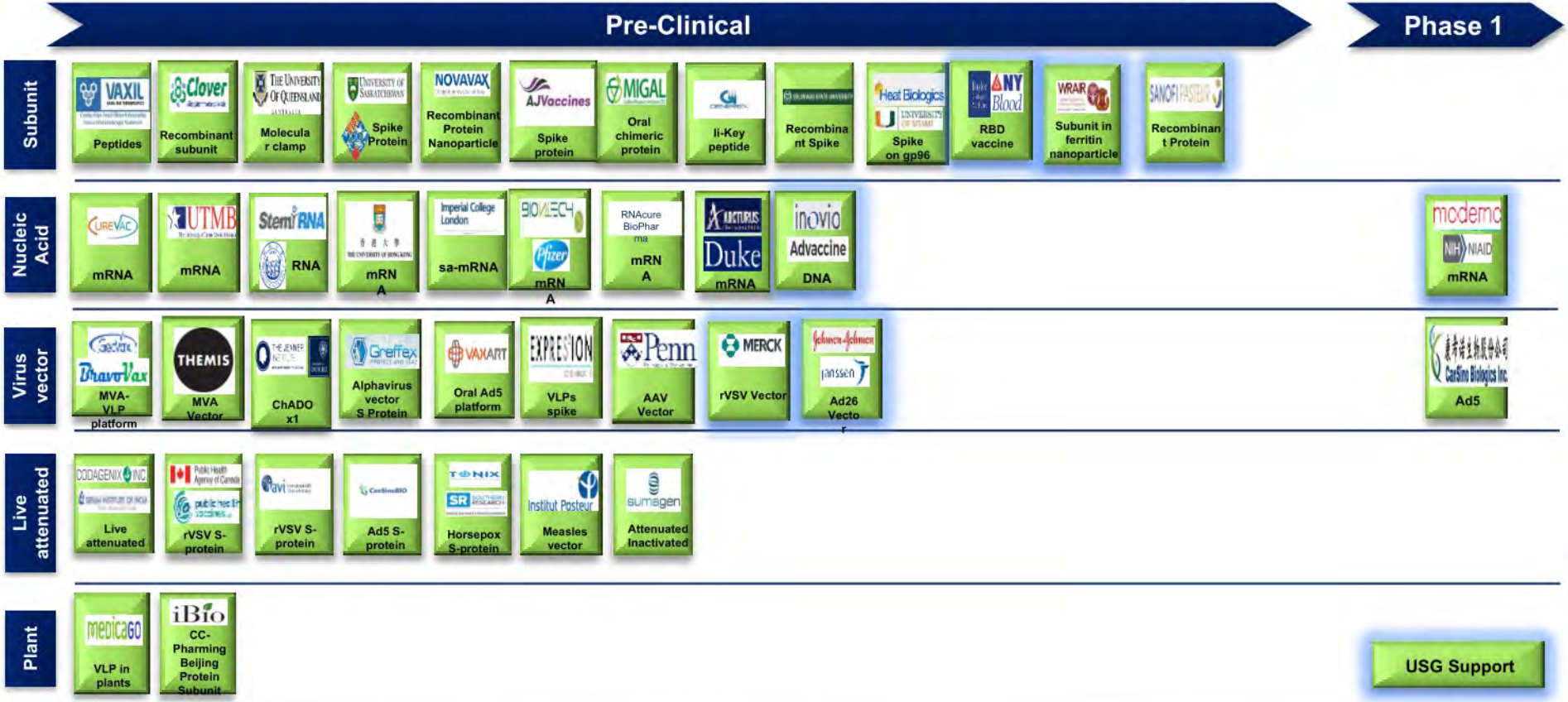
USG-Supported SARS-CoV-2 Therapeutics



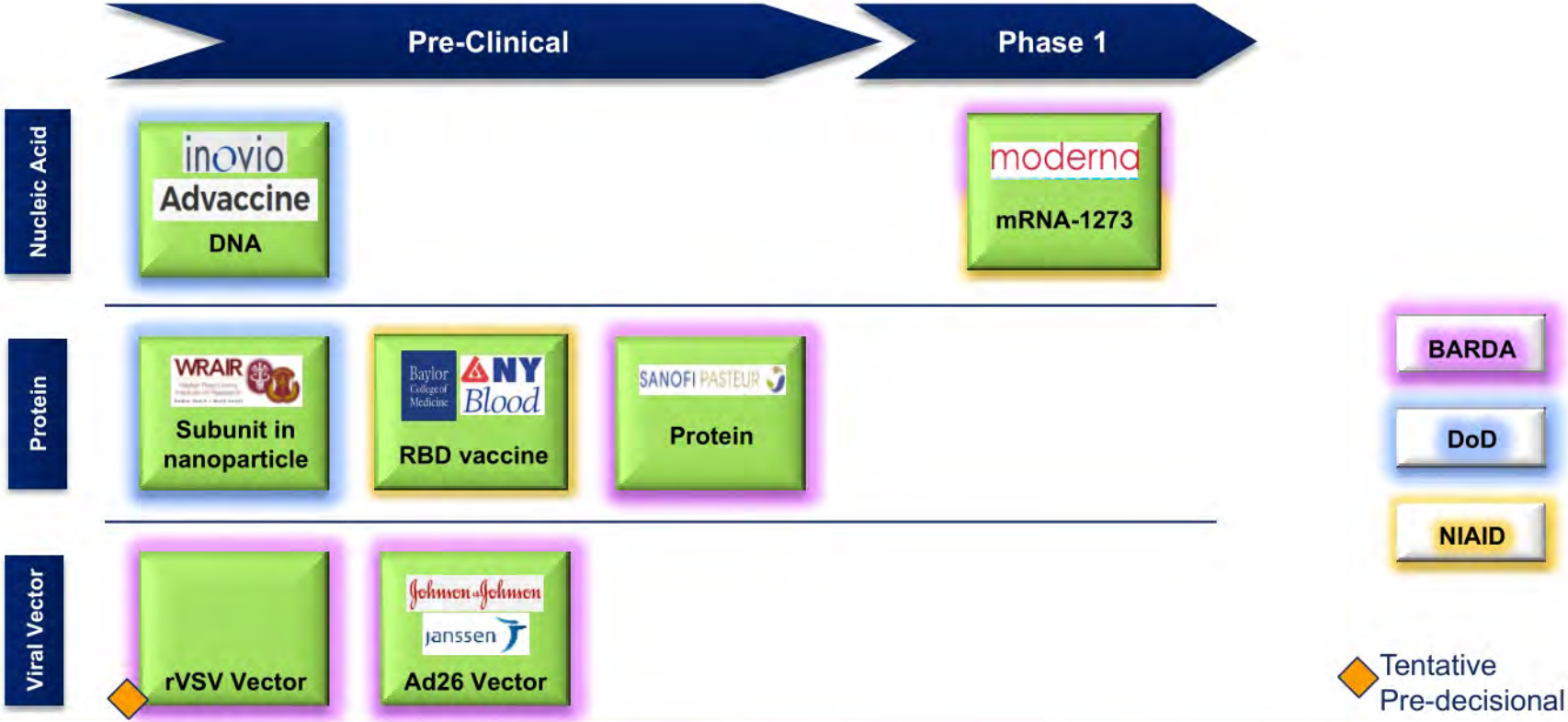
USG-Sponsored SARS-CoV-2 Diagnostic Tests



SARS-CoV-2 Vaccine Landscape



USG-Supported SARS-CoV-2 Vaccines



HHS accepts donations of medicine to Strategic National Stockpile as possible treatments for COVID-19 patients

FDA issues emergency use authorization of both drugs

The U.S. Department of Health and Human Services (HHS) today accepted 30 million doses of hydroxychloroquine sulfate donated by Sandoz, the Novartis generics and biosimilars division, and three million doses of chloroquine phosphate donated by Bayer Pharmaceuticals for use in clinical trials and for possible treatment of patients hospitalized with COVID-19. The companies ramped up production to provide the medication.

(b)(5)

Hydroxychloroquine sulfate and chloroquine phosphate are oral prescription drugs approved to treat malaria among other diseases. Although there are no currently approved treatments for COVID-19, both drugs have shown activity in laboratory studies against coronaviruses, including SARS-CoV-2 (the virus that causes COVID-19). Anecdotal reports or case series suggest that these drugs may offer some benefit in the treatment of COVID-19 patients.

"President Trump is taking every possible step to protect Americans from the coronavirus and provide them with hope," said HHS Secretary Alex Azar. "Scientists in America and around the world have identified a number of potential therapeutics for COVID-19, including chloroquine and hydroxychloroquine. The President's bold leadership and the hard work of FDA and HHS's Assistant Secretary for Preparedness and Response have succeeded in securing this large donation of potential treatments. We'll continue working around the clock to get American patients access to therapeutics that may help them battle COVID-19, while building more evidence around which options have proven effectiveness."

(b)(5)

HHS' Office of the Assistant Secretary for Preparedness and Response (ASPR) worked with the Department of State, the Department of Homeland Security, and the companies to receive the donated shipments.

At ~~BARDA's~~ HHS's request, the FDA reviewed the donated products and then issued an Emergency Use Authorization (EUA) to allow the hydroxychloroquine sulfate and chloroquine phosphate products to be donated to the Strategic National Stockpile and distributed to states for doctors to provide patients hospitalized with COVID-19 when a clinical trial is not available for feasible.

Commented [JR(3]: BARDA did not request-HHS requested this.

The EUA includes a fact sheet that provides important information for health care providers and patients about using chloroquine phosphate and hydroxychloroquine sulfate in treating COVID-19.

The National Institutes of Allergy and Infectious Diseases, part of the National Institutes of Health, and the Biomedical Advanced Research and Development Authority (BARDA), part of ASPR, will collaborate with a network of hospitals on clinical trials of both drugs.

Commented [KE(4]: BARDA, NIAID, please confirm whether this is the case.

In addition, the Strategic National Stockpile, managed by ASPR, will work with Federal Emergency Management Agency (FEMA) to ship donated doses to states. The SNS does not regularly stock either drug.

The FDA also is working with manufacturers of chloroquine and hydroxychloroquine to increase production to ensure these drugs also remain available for patients dependent on them for treatment of malaria, lupus and rheumatoid arthritis. Some states and retail pharmacies also have taken action to preserve the supply of these and other drugs.

HHS continues to work across the U.S. government, including with the Department of Defense, to review potential products from public and private sectors to identify promising candidates that could detect, protect against, or treat COVID-19 for development and use.

The FDA has the regulatory emergency use authority to facilitate access to unapproved medical countermeasures (MCMs) or unapproved uses of approved MCMs needed to prepare for and respond to chemical, biological, radiological and nuclear threats.

A product may be considered for an EUA if the FDA determines that, among other criteria, the known and potential benefits of the product, when used to diagnose, prevent, or treat the identified disease or condition, outweigh the known and potential risks of the product, and there are no adequate, approved, available alternatives. Emergency access to a medical product under an EUA is separate from use of a medical product under an investigational drug application.

In addition to accepting and distributing the donated chloroquine, HHS is funding clinical trials of two drugs, Kevzara and remdesivir, and is supporting the development of multiple potential therapeutic treatments, vaccines, and diagnostic tests for COVID-19. In addition, the FDA has issued emergency use authorization for multiple diagnostics and personal protective equipment for the COVID-19 response. HHS continues to seek partners for COVID-19 medical countermeasures, and offers multiple ways to submit proposals for potential products or technologies.

Commented [HC(5]: And the NIH Moderna mRNA vaccine study

Sandoz and Bayer are the latest companies stepping up to strengthen the U.S. response to COVID-19. Companies interested in donating goods or services should contact fema-nrcc-iagsupv@fema.dhs.gov or visit https://www.fema.gov/coronavirus/how-to-help.

About HHS, ASPR, and FDA

HHS works to enhance and protect the health and well-being of all Americans, providing for effective health and human services and fostering advances in medicine, public health, and social services. The mission of ASPR is to save lives and protect Americans from 21st century health security threats, and within ASPR, the Strategic National Stockpile represents the nation's largest stockpile of life-saving pharmaceuticals and medical supplies for use in supplementing state and local supplies in a public health emergency. The FDA protects the public health by assuring the safety, effectiveness, and security of human and veterinary drugs, vaccines and other biological products for human use, and medical devices. The agency also is responsible for the safety and security of our nation's food supply, cosmetics, dietary supplements, products that give off electronic radiation, and for regulating tobacco products.

###

Edits: MFelberbaum, OMA, 3/25/20

cleared by: R. Roberts, J. Farley, D. Ashley, J. Corrigan, P. Cavazzoni. 3/26/20

Edits: MFelberbaum, OMA, 3/25/20

COVID-19 BARDA Overview

Date: April 11, 2020

1. Diagnostics
    - 32 Diagnostics with EUA
    - Cue Health submitted EUA 04/09/2020 for their POC diagnostic
    - Partnered with Hologic, DiaSorin, Qiagen, MesaBioTech, GenMark, Cepheid, Luminex (NxTag and Aries), Vela, OraSure, Nanomix, Cue, Hemics to develop SARS-CoV-2 diagnostics
        - Molecular, Antibody, and Antigen based tests

2. Therapeutics
    - Shipments of Chloroquine/Hydroxychloroquine have left SNS for use under EUA
    - SAb, Grifols, and Emergent developing polyclonal Ab, convalescent plasma, and hyper-immune globulin therapeutics
    - Genentech Tocilizumab (α-IL-6R) clinical trial for COVID-19 targeting start early April
        i. 25 patients enrolled 04/12/2020 (12 Patients in U.S)
        ii. 28 sites activated (8 U.S., 6 Spain, 6 France , 3 Denmark, 1 Netherlands)
    - Regeneron adaptive phase 2/3 study of Sarilumab (α-IL-6R antibody) for COVID-19
        i. 51 sites activated in U.S.
        ii. 1128 total dosed as of 04/09/2020
            1. Phase 2– 463
            2. Phase 3– 665
                a. Second DMC meeting scheduled 04/10/2020
    - Regeneron has identified mAbs that neutralize SARs-CoV-2 virus in vitro
        i. Lead candidates expected by end of April
    - Janssen currently screening compounds with clinical data for antiviral activity

3. Vaccines
    - Sanofi Pasteur and Merck vaccine programs given ASPR approval to more forward
    - Janssen 1 lead candidate in two different forms identified; clinical trials expected early fall 2020
        i. Preliminary non-clinical in mice showing immunogenicity at 3 weeks

1) **BARDA Diagnostics**
    a) **Current Diagnostic EUAs**
        i) 32 Diagnostics with (EUA):
            I. https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations#covid19ivd
    b) **Cepheid**
        i) **Completed saline stability studies as an alternative medium and early-assay-termination studies**
    c) **Cue**
        i) **Pre-EUA application reviewed by BARDA**
            I. **Submitted EUA to FDA 04/09/2020**
    d) **[PROCUREMENT SENSITIVE] EZ-BAA submissions**
        i) **Hologic**
            I. **Targeting to submit EUA amendment 04/13/2020 to include lower respiratory tract specimen**
        ii) **DiaSorin Molecular**
            I. **No Update**
        iii) **MesaBioTech Point of care (hand-held device)**
            I. **No update**
        iv) **Qiagen**
            I. **No update**
        v) **Genmark**
            I. **No Updates**
        vi) **Luminex Corp**
            I. **Luminex NxTAG-No Update**
            II. **Luminex Aries- No Update**
        vii) **Vela Diagnostics**
            I. **No updates**
        viii) **Nanomix-No updates**
        ix) **OraSure-No updates**
        x) **Hememics (Antigen/Antibody)-No update**
        xi) **Pending EZ-BAA contract actions**
            I. **DiaSorin (Antibody) targeting sign-off by COB 04/10/2020**
                (a) **Accepted modified budget and SOW**
            II. **Inbios (Antigen/Antibody): Stage 2 negotiations in process**
2) **BARDA Therapeutics**
    a) **Regeneron**
        i) **2019-nCoV specific mAb on track to have leads by end of April and production in August**
            1. **Lead candidates expected by end of April**
            2. **Scaling up manufacturing of potential labs**

ii. Regeneron adaptive phase 2/3 study of Sarilumab (α-IL-6R antibody) for COVID-19
iii. 1128 total dosed as of 04/09/2020
1. Phase 2– 463
2. Phase 3– 665
a. Second DMC meeting scheduled 04/10/2020
iv. Request supplemental funding as of 04/10/2020

b) Genentech IL-6R antibody (Tocilizumab) clinical trial in COVID-19 patients
i) 25 patients enrolled 04/12/2020 (12 Patients in U.S)
ii) 28 sites activated (8 U.S., 6 Spain, 6 France , 3 Denmark, 1 Netherlands)

c) Antiviral screening
i) JOC on 4/17 strategy regarding hits from screening

d) SAb Biotherapeutics – Polyclonal antibody product
i) Targeting manufacturing to start on 05/26/2020, final fill 06/01/2020

e) Grifols (Convalescent Plasma and HIG)
i) No updates

f) Emergent
i) Received pre-IND briefing booklet 04/09/2020
ii) Kick off meeting 04/16/2020

g) American Red Cross
i) Need distribution protocol in place
ii) BARDA requested a weekly report of units collected, transfused, and geographic location of treatment.

3) BARDA Vaccines
a) Entered negotiations with company developing oral COVID-19 vaccine
b) Janssen Ad26 vaccine
i) Down selected to two forms of the same candidate
I. Soluble and transmembrane
ii) Targeting to start clinical trial early September
c) Sanofi Pasteur
i) Awarded for development through Phase 1 clinical study on 04/10/2020
d) Moderna
i) Project award on hold pending ASPR review
e) Merck given ASPR approval to move forward with award
f) Pfizer-No Update

4) BARDA Rapidly Deployable Technology
a) Cytovale –Pilot study to evaluate potential progression to sepsis in patients with suspected respiratory infections/COVID-19
b) In negotiations with Vital Connect

5) Sample Sharing Working Group
i) Purchase order awarded to ICON for the delivery of convalescent serum samples

ii) Cantor Bioconnect to delivery convalescent serum samples to BEI Resources 04/13/2020

6) **BARDA Clinical**
   a) NIAID ACTT Trial
      i) Will be a 4 arm study investigating standard of care, remdesivir, baracitinib, combination of remdesivir, and baracitinib
   b) **Chloroquine/Hydroxychloroquine EUA**
      i) **One million doses of chloroquine donated by Bayer arrived to the SNS**
   c) **Working with RQA on RFI for CROs providing clinical trial support**
7) **BARDA Non-clinical**
   a) **Expecting two natural history studies to start**
      i) **One week of 04/20/2020 (Ferret) and one 05/04/2020 (NHP)**
   b) **Strategy to cost share and manage laboratory bandwidth with BARDA and NIAID cross over being considered/worked out with contracting and labs**
   c) **BARDA non-clinical will be invited to join NIAID task order calls and vice versa**
8) **BARDA RQA**
   a) **Standing weekly meetings scheduled with CDER and CBER**
9) **BARDA Manufacturing**
   a) **Targeting award to Phlow 04/10/2020**
   b) **SSA brief for TAMUS/IDRI/iBio White paper held on 4/9/2020**
      i) **Decision on invitation for full proposal postponed until after further discussion.**
   c) **EZ BAA AOI #4.4: Requesting full proposals from the following:**
      i) **UT-Austin: 3D Printed Drug Delivery System**
      ii) **Snapdragon Chemistry: Continuous Manufacturing of ribonculeotide triphosphate for mRNA**
      iii) **Colorado State University: Viral inactivation process development and analytical development**
      iv) **MyTide: Peptide antiviral screening**
   d) **Proposals from Vaxess and MedsForAll under review.**

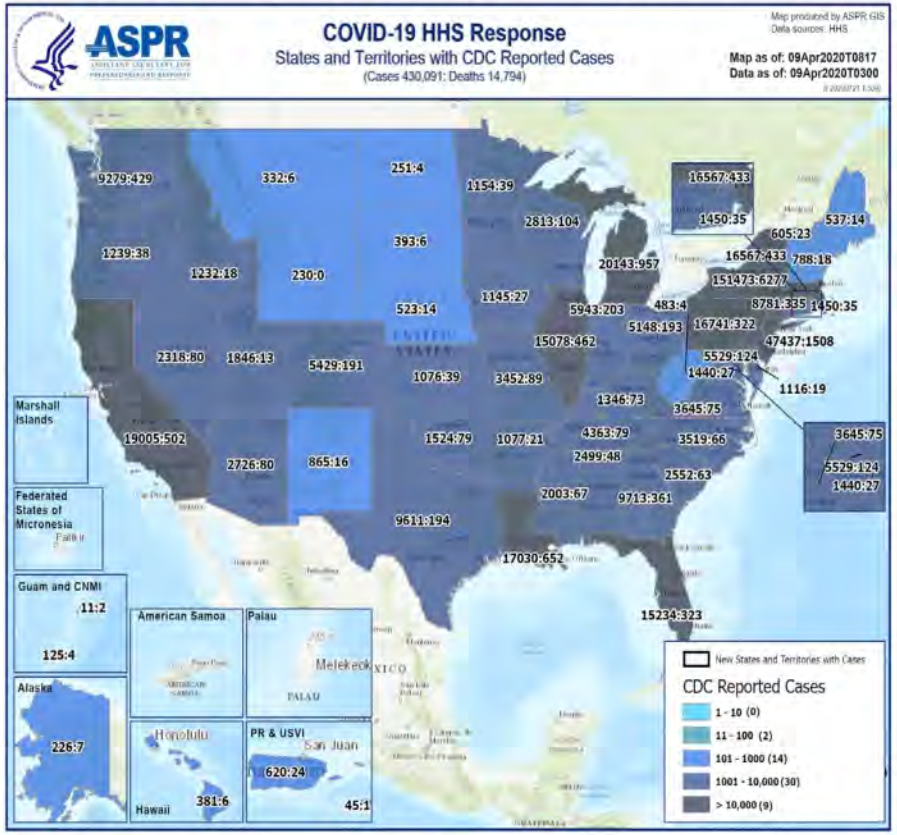
Senior Leadership Brief COVID-19
April 10, 2020 12:00 p.m. ET

For the most up to date COVID-19 data: https://geohealth.hhs.gov/arcgis/home/

Current Situation: FEMA, HHS, and our federal partners are working with state, local, tribal and territorial governments to execute a whole-of-America response to the COVID-19 pandemic. The federal government is coordinating the deployment of PPE and ventilators from multiple sources including the SNS, donations, and vendor procurements. These shipments are being sent nationwide with prioritization given to areas in greatest need. **CDC Update:** CDC confirmed and presumptive U.S. cases of COVID-19: 464,079 (+33,988) across 50 states and D.C., Guam, PR, CNMI, and USVI; Deaths: 17,390 (+2,596); Combined CDC and WHO reported global cases: 1,436,198 (+82,837); global deaths: 84,420 (+5,185); Countries and areas with cases: 211 *(HHS Update, April 9, 2020, 7:30 a.m. ET)* **Testing:** 2,180,783 (+112,716) cumulative as of April 10 (includes samples tested by State/Local Public Health Laboratories, Commercial Laboratories, Hospital Laboratories, CDC, and VA)

Operational Task Forces

Medical Counter-Measure (MCM) Development	• Phase 1 safety trial for mRNA vaccine: 34 (+4) healthy volunteers enrolled (target: 45) *(MCM TF Update, April 10, 2020, 9:01 a.m. ET)* • Clinical trial to test remdesivir for treatment: 604 (+44) new patients (target: 700) at 64 (+3) sites *(MCM TF Update, April 10, 2020, 9:01 a.m. ET)* • USDA is identifying animals susceptible to infection with SARS-CoV-2 to determine if mosquitoes and midges (type of small fly) could be vectors that could transmit the virus *(MCM TF Update, April 10, 2020, 9:01 a.m. ET)*
Health Care Resilience (HCR)	• Centers for Medicare and Medicaid Services (CMS) temporarily suspending rules reducing supervision/certification requirements to hire practitioners faster *(HCR TF Update, April 9, 2020, 10:08 a.m. ET)* • Hosting two webinars on April 10 on ventilation best practices and EMS patient care *(HCR TF Update, April 9, 2020, 10:08 a.m. ET)*
Lab Diagnostics	• Provided public health lab equipment data to help prioritization allocations of extraction kits *(Lab Diagnostics TF, April 10, 2020, 11:15 a.m. ET)* • Clarifying actions needed on outstanding requests for reagents, swabs, and other diagnostics and developing Regional talking points *(Lab Diagnostics TF, April 10, 2020, 11:15 a.m. ET)*
Community Based Testing Sites (CBTS)	• 81,076 (+3,732) cumulative tested since March 23 at CBTS locations *(CBTS TF Update, April 10, 2020, 10:26 a.m. ET)* • Issued transition/extension letters to CBTS 1.0 locations; 17 locations extending to May 30 *(CBTS TF Update, April 10,, 2020, 10:26 a.m. ET)*
Supply Chain Stabilization	• Second distribution of 10.1M Hydroxychloroquine tablets shipped April 9: 1M to Veterans Affairs; 1M to DoD; 100K to (b)(3) and 8M to (b)(3):42 U.S.C. § 247d-6b(d) (b)(3):42 (b)(3):42 U.S.C. § 247d-6b(d) • 26 Airbridge flights complete; Airbridge flight #24 landed in (b)(3) April 8; cargo: 7,770,000 gloves; #25 landed in (b)(3) April 9; cargo: 21, 555,000 gloves; #26 landed in (b)(3) April 9; cargo: 25,350,000 gloves; 54 remaining flights scheduled *(SC TF Update, April 10, 2020, 10:38 a.m. ET)*
Community Mitigation Measures	• Draft Framework for Reopening America plan in CDC clearance process *(CMM TF Update, April 10, 2020, 10:34 a.m. ET)* • Developing SLTT dashboard with Data & Analytics team to evaluate mitigation risk categories when determining timing and adjustment strategies for easing community mitigation measures *(CMM TF Update, April 10, 2020, 10:34 a.m. ET)*
Continuity of Operations and Essential Services	• 4 Wireless Emergency Alert (WEA) messages sent by local authorities; 4 were reminders of protective measures; 1 also announced closure of public areas *(COOP TF Update, April 10, 2020, 7:58 a.m. ET)*
Data and Analysis	• State data for 50 states and 6 territories integrated into the HHS GeoHealth Common Operating Picture (COP) to support decision making *(DA TF Update, April 10, 2020, 10:00 a.m. ET)*



Key Updates/Actions

All 50 states, the District of Columbia, 5 territories, and 27 (+2) tribal nations are working directly with FEMA under the nationwide emergency declaration for COVID-19 *(Tribal Update, April 9, 2020, 7:18 p.m. ET)*

FEMA HQ: National Watch Center Steady State; NRCC Level I (6:00 a.m. ET to 12:00 a.m. ET); Level 1: Region I, IX; Level 2: Regions II, III, IV, V, VI, VII, VIII, X; COVID-19 Major Declarations: 54 (+2) (AK, ID) *(FEMA Update, April 10, 2020, 7:03 a.m. ET)*

HHS: SOC at Level I (24/7) co-located with FEMA; CDC EOC activated, ACF OHSEPR at Level I *(FEMA National SITREP, March 21, 2020, 6:00 a.m. ET and HHS Update, March 20, 2020, 2:14 p.m. ET)*

Department of Homeland Security: 2,852 (+48) FEMA employees deployed to support COVID-19 Response; IMAT-A teams deployed to 26 states, territories, and DC; LNOs deployed to 37 states and territories *(FEMA Update, April 10, 2020, 9:25 a.m. ET)*

Health and Medical Lifeline

Public Health

Federal Assistance

- USACE has 22 mission assignments (MAs) for design and builds of Alternate Care Sites (ACS) in NY, CA, WA, IL, NJ, MI, PA, CO, NM, FL, OR, TN, ID, IA, KA, VA, NV, MD, MO, AK, DC, Navajo Nation; 2 MAs under EM Dec (AZ, WI); and 7 MAs for planning and assessment (ME, UT, MT, ND, HA, GU, CNMI); 2,143 (+65) USACE personnel supporting *(ESF-3 Update, April 10, 2020, 8:39 a.m. ET)*

Medical Equipment/Personal Protective Equipment

- DLA awarded contract for 60 N95 decontamination system units; Five systems deployed (NY, WA, MA, IL); 55 additional units to deploy across the U.S. by early May *(SC TF Update, April 10, 2020, 10:38 a.m. ET)*
- TX: 36 Infantry Division teaming with Prestige Ameritech's Headquarters in Fort Worth, TX to produce of 2 million medical protective masks a week *(NGB Update, April 10, 2020, 7:52 a.m. ET)*

Medical Care

Hospital Capacity

- NYC: Javits Center (JNYMS) 255 (+100)/703 (-297) beds filled; 0/42 (-42) beds with ventilators filled; 16 (+9)/48 ICU beds filled; 344 (+137) patients seen *(DoD Update, April 9, 2020, 9:00 a.m. ET)*
- NYC: 4 Urban Augmentation Medical Task Forces (UAMTF) deploying to support JNYMS *(DoD Update, April 9, 2020, 9:00 a.m. ET)*
- NYC: USNS Comfort 64 (+4)/500 beds filled; 8 (-8)/80 ICU beds filled; 18 (+2)/68 (+16) beds with ventilator filled; 87 (+11) patients seen *(DoD Update, April 9, 2020, 9:00 a.m. ET)*
- NYC: USNS Comfort to provide back-up support to Federal Medical Stations and to decompress land hospitals in NJ *(DoD Update, April 9, 2020, 9:00 a.m. ET)*
- CA: USNS Mercy currently with 18 (+5)/1000 beds filled; 6/80 ICU beds filled; 1 (+1)/80 (+10) beds with ventilator filled; 40 (+8) patients seen *(DoD Update, April 9, 2020, 9:00 a.m. ET)*
- LA: Ernest N. Morial Convention Center in New Orleans; 5 (+2)/265 (+61) beds filled; 6 (+3) patients seen *(DoD Update, April 9, 2020, 9:00 a.m. ET)*
- Seven UAMTFs order to deploy to augment ACSs in NJ, CT, MI, and MA *(DoD Update, April 9, 2020, 9:00 a.m. ET)*

Other Domestic Lifelines

Safety & Security

- At least 42 states, D.C., 4 territories, and 36 (+5) tribes issued shelter-in-place orders *(FEMA Tribal Update, April 9, 2020, 7:18 p.m. ET)*
- CDC indefinitely extended the U.S. government's March 14 no-sail order for cruise ships *(CISA Update, April 10, 2020, 5:30 a.m. ET)*
- CBP interdicted 95 unapproved COVID-19 test kits; seized 2 counterfeit face masks shipments and 10 FDA prohibited chloroquine tablets shipments since January 31 *(ESF-8 Update, April 10, 2020, 8:57 a.m. ET)*

Food, Water, & Shelter

- Food Supply Chain Task Force meeting with USDA, FDA, and Eisenhower School staff on April 10 to discuss Food/Ag supply chain issues and PPE requirements *(FSC TF Update, April 10, 2020, 9:55 a.m. ET)*

FEMA

Senior Leadership Brief COVID-19

April 10, 2020 12:00 p.m. ET

For the most up to date COVID-19 data: https://geohealth.hhs.gov/arcgis/home/

(b)(3):42 U.S.C. § 247d-6b(d)

Data last updated
4/9/2020 21:02:00

FEMA

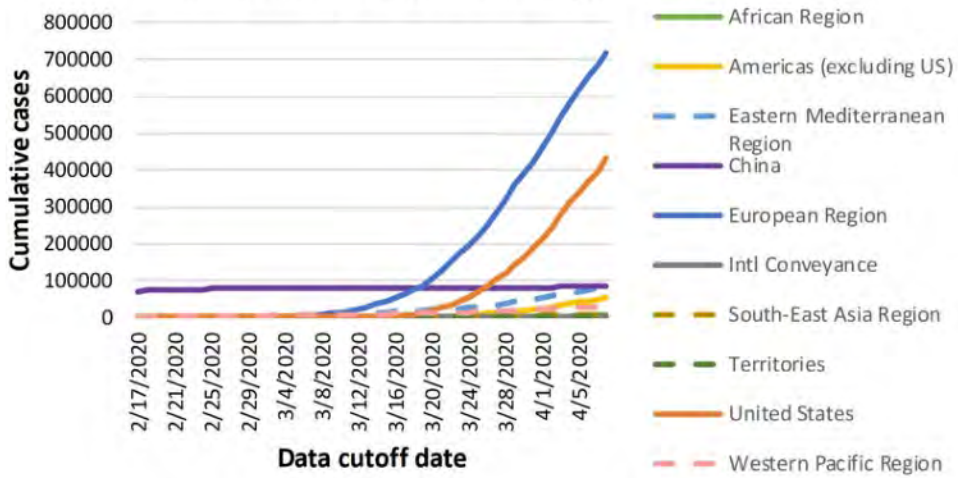
Senior Leadership Brief COVID-19

April 10, 2020 12:00 p.m. ET

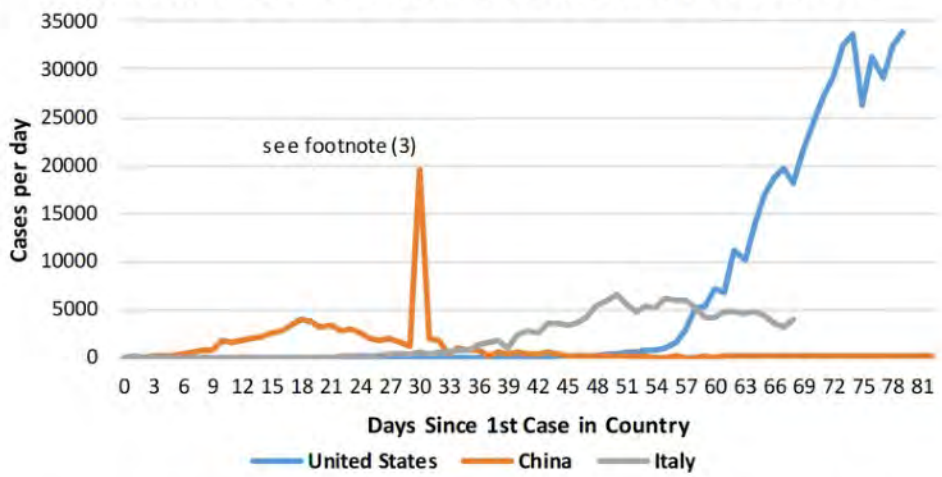
For the most up to date COVID-19 data: https://geohealth.hhs.gov/arcgis/home/

COVID-19 Cases (CDC SITREP data as of April 10, 2020)

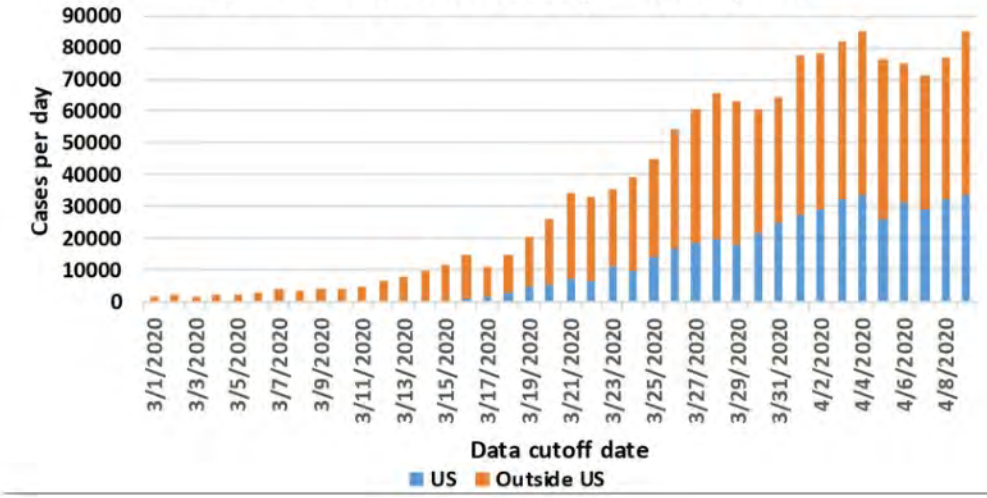
Cumulative COVID-19 cases (n = 1,505,247)



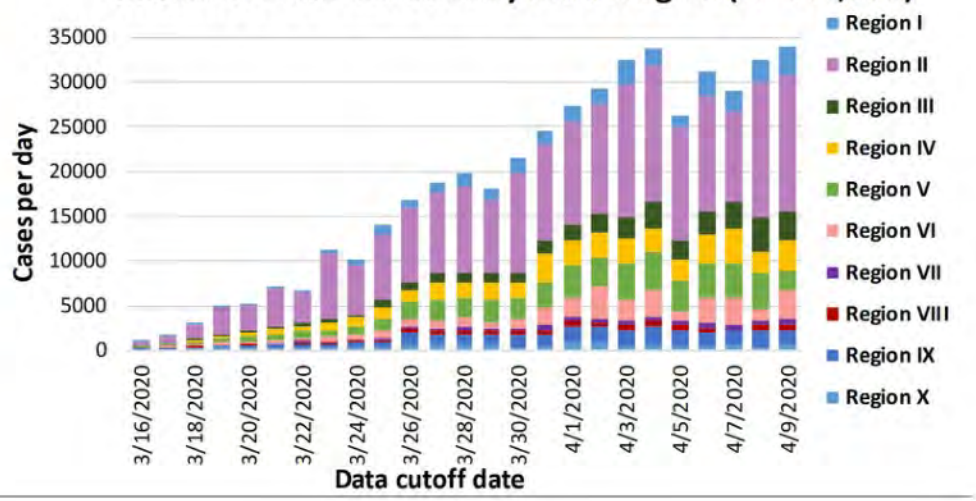
Incident Case Trends: China, Italy, and United States



Incident COVID-19 cases (n = 1,505,247)



Incident COVID-19 cases by FEMA region (n =464,079)



FEMA

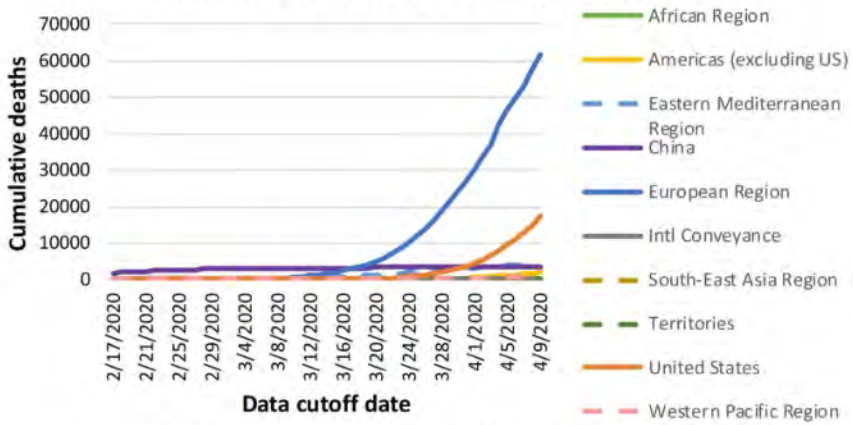
Senior Leadership Brief COVID-19

April 10, 2020 12:00 p.m. ET

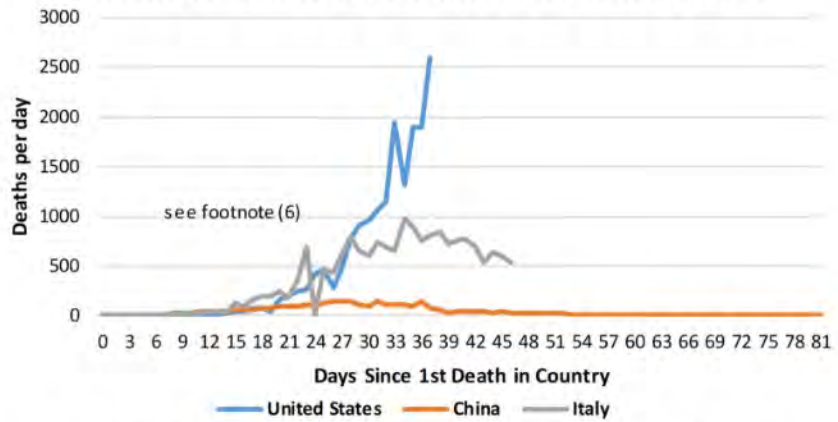
For the most up to date COVID-19 data: https://geohealth.hhs.gov/arcgis/home/

COVID-19 Deaths (CDC SITREP data as of April 10, 2020)

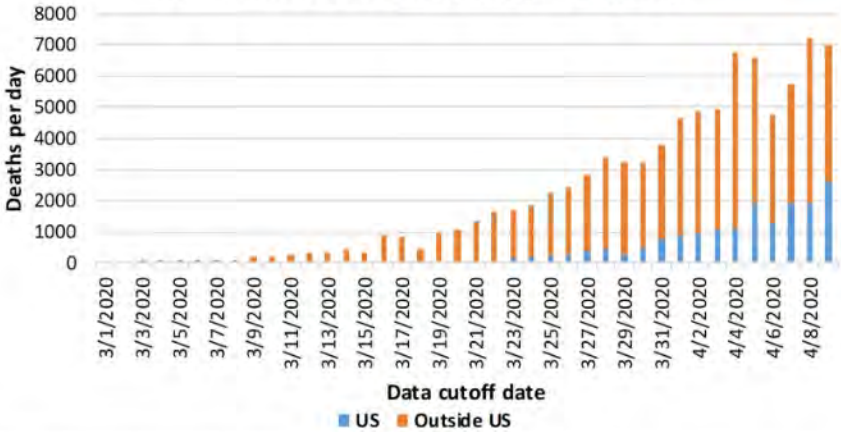
Cumulative COVID-19 deaths (n = 90,172)



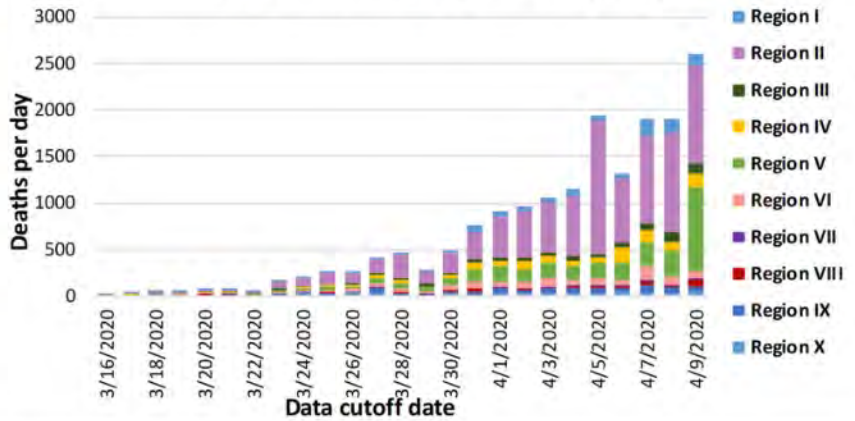
Incident Death Trends: China, Italy, and United States



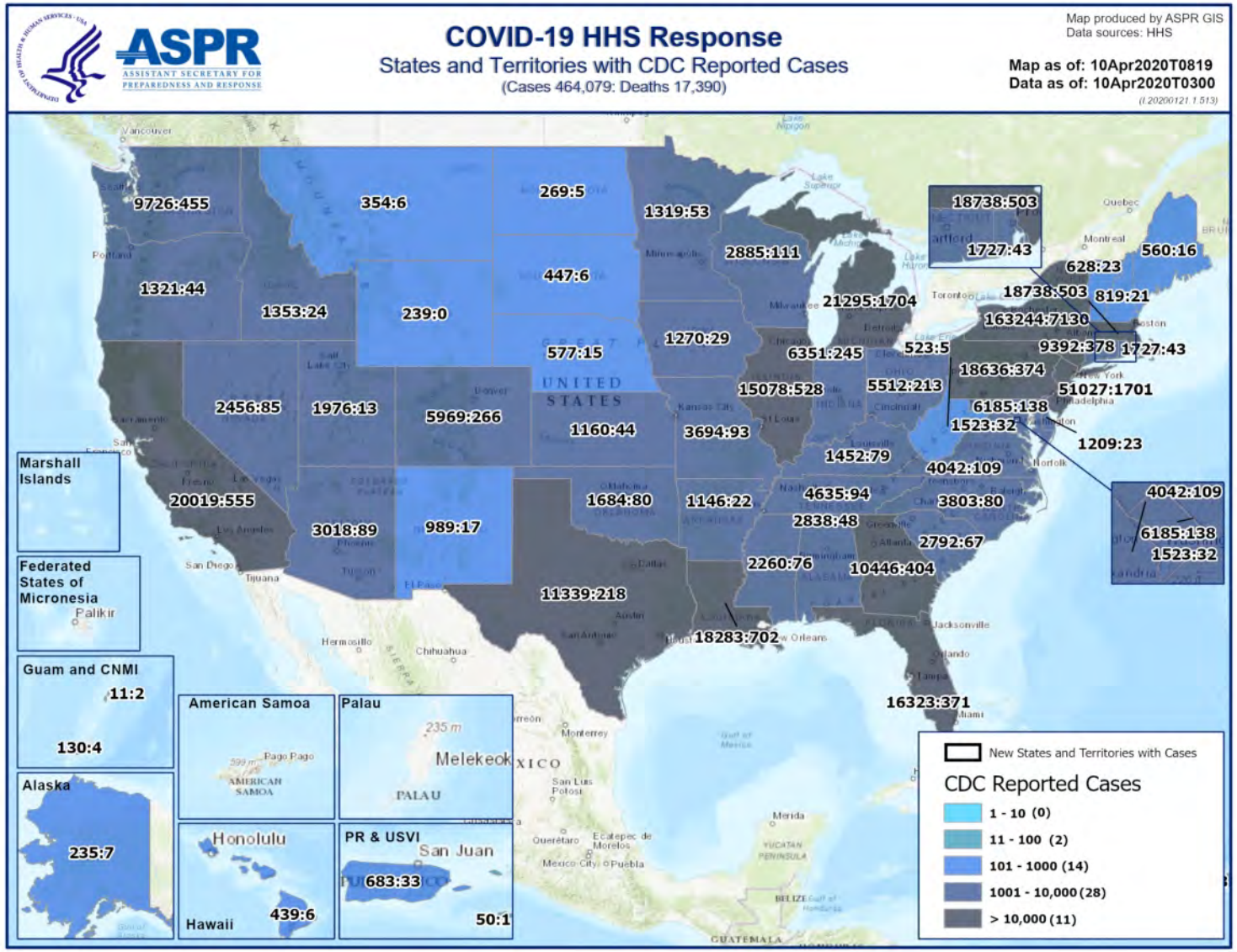
Incident COVID-19 deaths (n = 90,172)



Incident COVID-19 deaths by FEMA region (n =17,390)



Analyst notes: (1) International Conveyance captures the cruise ship "Diamond Princess," which arrived in Japan on February 3rd. (2) Cumulative chart displays data since 17FEB2020. China's first death was reported on 19JAN2020 and the first death outside China on 02FEB2020. (3) Region I: CT, ME, MA, NH, RI, VT; Region II: NJ, NY, PR, VI; Region III: DE, DC, MD, PA, VA, WV; Region IV: AL, FL, GA, KY, MS, NC, SC, TN; Region V: IL, IN, MI, MN, OH, WI; Region VI: AR, LA, NM, OK, TX; Region VII: IA, KS, MO, NE; Region VIII: CO, MT, ND, SD, UT, WY; Region IX: AS, AZ, CA, GU, HI, MH, FM, NV, MP, PW; Region X: AK, ID, OR, WA. (4) Titles show cumulative deaths through most recent date. (5) As of 03MAR2020, the deaths data were reported from WHO SITREPS. Previously the data were obtained from the CDC updates and SITREPS. (6) The 18MAR2020 WHO SITREP did not have death updates for Italy. (7) FEMA region chart displays data since 16MAR2020. Total deaths before 16MAR2020 was 68. (8) Incident COVID-19 deaths graph displays data since 01Mar2020. Total US deaths prior to 01Mar is 0. Total deaths outside the US prior to 01Mar is 2922.


ASPR
ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE
COVID-19 HHS Response
States and Territories with CDC Reported Cases
(Cases 464,079: Deaths 17,390)
Map produced by ASPR GIS
Data sources: HHS
Map as of: 10Apr2020T0819
Data as of: 10Apr2020T0300
(I.20200121.1.513)
9726:455
354:6
269:5
1319:53
2885:111
18738:503
1727:43
560:16
628:23
819:21
1321:44
1353:24
239:0
447:6
21295:1704
18738:503
163244:7130
1270:29
577:15
6351:245
523:5
9392:378
1727:43
18636:374
15078:528
5512:213
51027:1701
2456:85
1976:13
5969:266
1160:44
3694:93
6185:138
1523:32
1209:23
1452:79
4042:109
Marshall Islands
20019:555
1684:80
1146:22
4635:94
3803:80
4042:109
3018:89
989:17
2838:48
6185:138
1523:32
2792:67
Federated States of Micronesia
Palikir
2260:76
10446:404
11339:218
18283:702
Guam and CNMI
11:2
130:4
American Samoa
Pago Pago
AMERICAN SAMOA
Palau
Melekeok
PALAU
16323:371
Alaska
235:7
Honolulu
Hawaii
439:6
PR & USVI
San Juan
683:33
50:1
New States and Territories with Cases
CDC Reported Cases
1 - 10 (0)
11 - 100 (2)
101 - 1000 (14)
1001 - 10,000 (28)
> 10,000 (11)

ASPR
ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

UNCLASSIFIED// FOR OFFICIAL USE ONLY

USG COVID-19 Response

USG Medical Resources, Force Laydown and County Hotspots

Map produced by ASPR GIS
Data sources: CDC, DoD, HHS, FEMA, USACE

Map as of: 08Apr2020T2212

USG Total

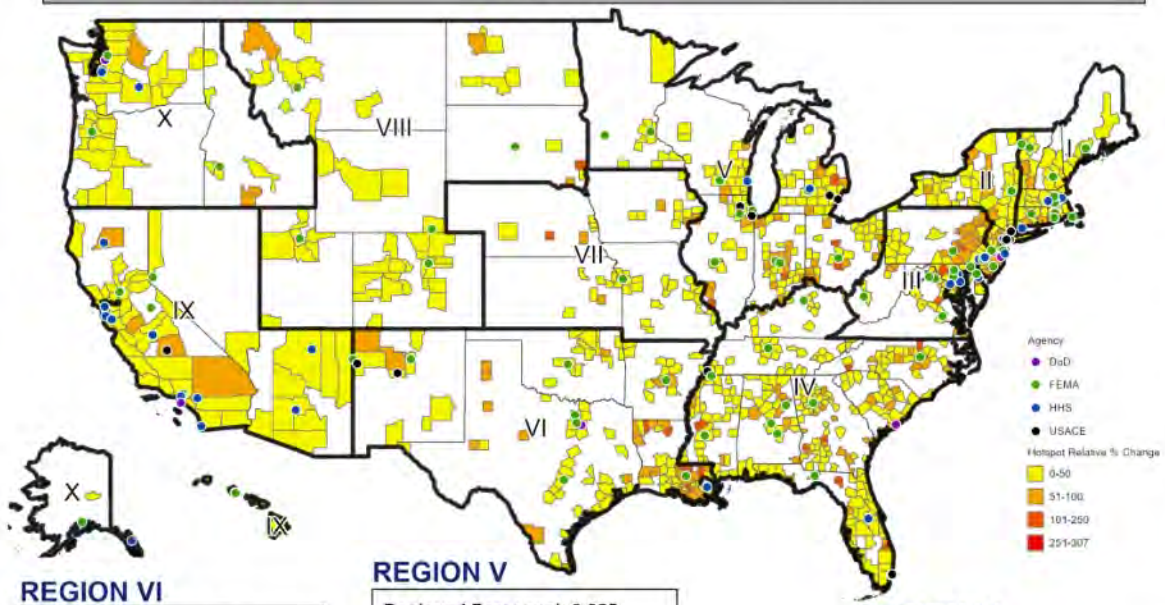
Deployed Personnel: 19,870
- CDC: 99
- HHS: 438
- DoD: 16,651
- FEMA: 2,781

Equipment / Supplies
- FMS 250 (32)
- FMS 50 (9)
- ASPR Rx (8)
- DoD Field Hospital (2)

ACS (51)
- Total Beds: 24,350
  - ASPR Beds: 8,200
  - DoD Beds: 534
  - USACE: 15,616

Ventilators (9,340)

USNS Medical Ship (2)



REGION X

Deployed Personnel: 1,417
- HHS: 136
- DoD: 1,132
- FEMA: 149

Equipment / Supplies
- FMS 250 (2)
- FMS 50 (2)
- ASPR Rx (4)
- DoD Field Hospital (1)

ACS (3)
- Total Beds: 850
  - ASPR Beds: 600
  - DoD Beds: 250

Ventilators (560)

REGION IX

Deployed Personnel: 2,755
- HHS: 37
- DoD: 2,534
- FEMA: 184

Equipment / Supplies
- FMS 250 (8)
- FMS 50 (5)

ACS (13)
- Total Beds: 2,496
  - ASPR Beds: 2,250
  - USACE Beds: 246

Ventilators (200)

USNS Mercy: 1,000 Beds

REGION VIII

Deployed Personnel: 387
- HHS: 9
- DoD: 265
- FEMA: 113

ACS (1)
- Total Beds: 2,000
  - USACE Beds: 2,000

Ventilators (100)

REGION VII

Deployed Personnel: 98
- FEMA: 98

REGION VI

Deployed Personnel: 597
- HHS: 4
- DoD: 448
- FEMA: 145

Equipment / Supplies
- FMS 250 (3)
- FMS 50 (1)
- ASPR Rx (1)

ACS (5)
- Total Beds: 1,050
  - ASPR Beds: 800
  - USACE Beds: 250

Ventilators (370)

REGION V

Deployed Personnel: 3,925
- HHS: 69
- DoD: 3,708
- FEMA: 148

Equipment / Supplies
- FMS 250 (4)

ACS (8)
- Total Beds: 7,061
  - ASPR Beds: 750
  - USACE Beds: 6,311

Ventilators (1,350)

REGION IV

Deployed Personnel: 1,652
- HHS: 29
- DoD: 1,453
- FEMA: 170

Equipment / Supplies
- FMS 250 (1)

ACS (4)
- Total Beds: 1,947
  - ASPR Beds: 250
  - USACE Beds: 1,697

Ventilators (350)

REGION I

Deployed Personnel: 2,067
- HHS: 2
- DoD: 1,877
- FEMA: 188

Equipment / Supplies
- FMS 250 (3)

ACS (1)
- ASPR Beds: 750

Ventilators (250)

REGION II

Deployed Personnel: 4,365
- HHS: 141
- DoD: 3,970
- FEMA: 254

Equipment / Supplies
- FMS 250 (8)
- ASPR Rx (3)
- DoD Field Hospital (1)

ACS (10)
- Total Beds: 8,396
  - ASPR Beds: 2,000
  - DoD Beds: 284
  - USACE Beds: 5,112

Ventilators (5,890)
- DoD Ventilators (300)

DoD Mortuary Affairs Team (1)

USNS Comfort: 1,000 Beds

REGION III

Deployed Personnel: 2,607
- HHS: 11
- DoD: 1,264
- FEMA: 1,332

Equipment / Supplies
- FMS 250 (3)
- FMS 50 (1)

ACS (4)
- Total Beds: 800
  - ASPR Beds: 800

Ventilators (270)

SNS Hydroxychloroquine/Chloroquine Requests

Requestor/State	Clinical Trial Material	Hydroxychloroquine/ Chloroquine	# of Pills*	Date
Department of Veteran's Affairs		Hydroxycholoroquine	1,008,000	Received 04/09/20
Henry Ford Hsopital,2799 West Grand Blvd, A-Basement Pharmacy, Detroit, MI		Hydroxycholoroquine	100,800	Received 04/09/20
NRDC McKesson Warehouse 8313 Polk Lane, Olive Branch, MS 38654		Hydroxycholoroquine	4,003,200	Received 04/09/20
AmerisourceBergen, 6305 La Salle Drive, Lockbourne, OH 43137		Hydroxycholoroquine	1,003,200	Received 04/09/20
AmerisourceBergen, 6001 Global Distribution Way, Louisville, KY 40228		Hydroxycholoroquine	4,003,200	Received 04/09/20
Federal Bureau of Prisons, 1000 Air Base Rd, Pollock, LA 71467		Hydroxycholoroquine	120,000	Shipped 04/08/20
Cardinal Health Wheeling, WA 26003		Hydroxycholoroquine	345,600	Shipped 04/09/20
Cardinal Health Lakeland, Fl 33805		Hydroxycholoroquine	196,800	Delivered 04/10/20
Cardinal Health St. Charles, Mo 63301		Hydroxycholoroquine	196,800	Delivered 04/10/20
Cardinal Health Staford, TX 77477		Hydroxycholoroquine	196,800	Shipped 04/09/20
Cardinal Health Groveport, OH 43125		Hydroxycholoroquine	3,048,000	Shipped 04/09/20

*Calculations of pills and bottles/blister packs are made by RQA based on data provided by SNS for cases of product. These amounts are based on assumptions and may not be exact.

HQ: 22,790 Bottles* Remain: (100 pills/bottle)
CHQ: 3,952 Blister Packs* Remain: (250 pills/pack)

FOUO

SNS Hydroxychloroquine/Chloroquine Requests

Requestor/State	Clinical Trial Material	Hydroxychloroquine/ Chloroquine	# of Pills*	Date
Cardinal Health		Hydroxychloroquine	3,081,600	Received on 04/07/2020
Amerisource		Hydroxychloroquine	3,216,000	Received on 04/07/2020
McKesson		Hydroxychloroquine	3,024,000	Received on 04/07/2020
Seminole Tribe of Florida		Hydroxychloroquine	9600	Received on 04/07/2020
North Carolina Division of Public Health		Hydroxychloroquine	998,400	Received 04/05/2020(993,600) Shipped 04/06/2020(4800)
Nevada Public Health & Human Services		Hydroxychloroquine	14,400	Received 04/06/2020
Mississippi Dept of Public Health		Hydroxychloroquine	24,000	Received 04/05/2020(14,400) Shipped 04/06/2020(9600)
California Dept of Public Health		Hydroxychloroquine	3,297,400	Received 04/06/2020
Henry Ford Hospital, Detriot MI	Yes	Hydroxychloroquine	81,600	Received 4/05/2020
US Virgin Islands		Hydroxychloroquine	19,200	Received 04/03/2020
California, LA County Public Health		Hydroxychloroquine	28,800	Received 04/03/2020
New York, NYS Dept of Corrections and Community Supervision Central Pharmacy		Hydroxychloroquine	139,200	Received 04/03/2020

*Calculations of pills and bottles/blister packs are made by RQA based on data provided by SNS for cases of product. These amounts are based on assumptions and may not be exact.

HQ: 22,790 Bottles * Remain: (100 pills/bottle)
CHQ: 3,952 Blister Packs* Remain: (250 pills/pack)

FOUO

AGENDA

COVID-19

Joint HHS / FEMA Interagency VTC

4-15-2020 at 12:30 p.m. ET

Call-in Number: 1-800-320-4330; Muted PIN: (b)(6)#

Closed captioning available.

(Complete connection instructions provided below.)

BLUF:

1. **Situation Update:** Centers for Disease Control and Prevention
   a. US Domestic: 602,510, cases/ 25,520 new (4.6%), 24,462 deaths/ 2,507 new (9.1%)
      i. New York State: 195,081 cases
      ii. New York City: 7,095 deaths
   b. Globally: 1,914,916 cases/ 71,572 new, (3.73%) 123,010 deaths

2. **Lines of Effort:**
   a. **Medical Countermeasures (BARDA)**
      i. ACTT Clinical trial to test remdesivir for treatment of COVID-19: 759 (+55) new patients at 67 (+2) sites, including 9 patients at 5 military treatment facilities, in last 24 hrs (target = 700)
      ii. ORCHID Clinical trial (NHLBI) to test hydroxychloroquine in COVID-19 patients: 20 (+10) patients enrolled (target = 510)
   b. **Medical Diagnostics**
      i. 2.9 Million tests completed,
      ii. Working with Palantir to have all daily testing data pushed to Geo Health platform, providing the federal interagency a common operating picture
      iii. One-pager on Abbott ID Now is being finalized and will be cleared by HHS April 15th
   c. **Data Analytics**
      i. **Doubling times continue to improve (slowing) overall with the exceptions of some large cities and rural counties**
      ii. Completed PPE burn analysis for all 50 states leveraging inputs from John Hopkins Infectious Dynamics Disease model to support White House COVID-19 Task Force; delivered to Executive Office of the President and USAID on April 14th
      iii. Completed modeling support to FEMA Region IX with Kinsey model to support engagements with Region IX states; delivered to FEMA

3. **HHS/FEMA Regional Priorities/Concerns**
   a. **Region VIII** is recovering from severe weather over the weekend with 32 fatalities
   b. **Region II** stated DoD clarified that it will only provide medical care in existing hospitals and only ancillary care in ACFs
      i. DoD North Comm responded to this saying this is **not true** and will follow up
   c. **Region X** reported total cases increased only 1.7%
   d. **Region VI** reported that doubling rate doubles every day among Navajo Nation. FEMA is engaging with them
   e. HQ stated that it will follow up with **Region VII** about an email stating there no PPEs in Nebraska
      i. If this is true, HQ wants to work with private and public hospitals to amend this

AGENDA

Objective

- To discuss COVID-19 and related Federal response operations

Opening Comments HHS / FEMA

Situation Update Centers for Disease Control and Prevention

- US Domestic: 602,510, cases/ 25,520 new (4.6%), 24,462 deaths/ 2,507 new (9.1%)
  - New York State: 195,081 cases,
  - New York City: 7,095 deaths
- Globally: 1,914,916 cases/ 71,572 new, (3.73%) 123,010 deaths

Lines of Effort

- Community Based Testing
  - 94,598 (+5,411) tests processed and received by the call center since March 23rd, with 18,226 positive (19.3%), 767 indeterminate, 75,604 negative
  - Conducted analysis on locations for CBTS private partner sites; continue to refine future CBTS sites with private partners
- Healthcare Systems Resilience
  - Medical operations coordination cells (MOCCs) strategy received UCG approval;
    - MOCCs embed into existing emergency operation centers (EOCs) to coordinate patient transfers and improve the distribution of patients across a geography;
    - implementation plan in development
- Supply Chain
  - 7.4M of 10M DoD supplied N95 masks arrived to end point destinations;
    - 2.6M masks in transit, expected delivery April 15th
    - 1M to (b)(3):42 U.S.C. § 247d-6b(d)
    - 1.6M
  - 266K Tyvek suits arrived at (b)(3):42 U.S.C. § 247d-6b(d)
    - this cargo will be distributed to greater New York area
- Medical Countermeasures (BARDA)
  - ACTT Clinical trial to test remdesivir for treatment of COVID-19: 759 (+55) new patients at 67 (+2) sites, including 9 patients at 5 military treatment facilities, in last 24 hrs (target = 700)
  - ORCHID Clinical trial (NHLBI) to test hydroxychloroquine in COVID-19 patients: 20 (+10) patients enrolled (target = 510)
- Medical Diagnostics
  - 2.9 Million tests completed,
  - Working with Palantir to have all daily testing data pushed to Geo Health platform, providing the federal interagency a common operating picture
  - One-pager on use of Abbott ID Now is being finalized and expected to be cleared by HHS April 15th
- Data Analytics
  - Doubling times continue to improve (slowing) overall with the exceptions of some large cities and rural counties
  - Completed PPE burn analysis for all 50 states leveraging inputs from John Hopkins Infectious Dynamics Disease model to support White House COVID-19 Task Force; delivered to Executive Office of the President and USAID on April 14th
  - Completed modeling support to FEMA Region IX with Kinsey model to support engagements with Region IX states; delivered to FEMA
- Community Mitigation
  - Updated Guidance for Childcare Programs that Remain open
  - provides additional screening options for children upon arrival to ensure children with symptoms are not admitted and additional options when PPE is in short supply
- Communications

- Working on video to show delivery of Patel units
- Seeing positive return on how deliveries are affecting recipients

HHS/FEMA Regional Priorities/Concerns

- Region II
  - Stated that DoD clarified that it will only provide medical care in existing hospitals and only ancillary care in ACFs
    - **DoD North Comm responded to this saying this is not true and will follow up with Region II**
  - New York State will open COVID-19 walk in sites for testing around NYC
  - PR non-essential businesses are closed through May 3rd
  - VI mobilizing supplies to support ACF
  - 787 in Javits Center and 138 cases aboard the Comfort (more complicated cases)
  - Establishing first ACF in PR
- Region X
  - Total cases increased only 1.7%
  - Oregon has USAID building out ACF
  - Developed a PPE exchange dashboard with private sector
  - Working out details to acquire high speed testing
- Region IX
- Region IV
  - Severe weather over Easter Sunday
  - 32 confirmed fatalities across the region
  - Received request for major declaration from Mississippi
  - PPE 1.95 M masks have arrived in Florida
  - Working with DoD to evaluate support staff for Tennessee mission assignment
  - Working on surge for Florida long term care facilities
  - Cruise lines must submit implementation plans prior to docking in Florida
- Region V
- Region III
- Region I
- Region VI
  - Moving team members from Dallas to Baton Rouge
  - Texas is increasing test capacity (500 tests per site per day is the target)
  - New Mexico working with tribal nations
    - Doubling rate doubles every day among Navajo Nation
  - Request information/clarity for details about supply chain and elective surgery
- Region VIII
  - South Dakota is a new hot spot among plants and meat processing sites
  - 2 ACF are in the process of being built
  - Region 8 states are interested in expanding lab testing
- Region VII
  - Inquiring about email stating no PPEs in Nebraska
    - If this is true, HQ wants to work with private and public hospitals to amend this
    - Region VII will follow up with HQ

Interagency Support

- Emergency Support Functions (by exception)
  - ESF 3 (ACS): no new contracts in last 24 hours
  - Received two additional task orders for New Jersey and Nevada
- Department of Veterans Affairs
  - 169 civilians admitted to VA hospitals
  - Working with Region II on 90 VA personnel to support New Jersey beds
- Department of Defense, Office of the Secretary of Defense
  - DoD will follow up on comment about DoD providing care in New York
  - U.S. Northern Command

        - Pushing DoD capabilities in New York City hospitals
        - More DoD personnel arriving throughout the regions during the remainder of the week
    - US IndoPACom
        - Guam: C2 personnel flow
            - 80 active duty postured for support on Guam
            - CNMI 6 nurses will arrive by April 20th
    - National Guard Bureau
        - 31,000 currently serving COVID-19
        - Priorities are supporting CBT sites and allocating medical supplies and food
        - Providing PPE to residential care homes
        - Providing law enforcement on Guam
    - Defense Logistics Agency
        - Human remain pouches are continuing to be delivered in Frederick, Maryland
        - Patel unit on route to New Jersey

WH National Security Council (NSC)

-

Closing Comments

- FEMA / HHS
    - Thank DoD for Secretary's visit today
    - Appreciate all support from DoD

From:	Houchens, Christopher (OS/ASPR/BARDA) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7AC94A574BD04528B7C91BBD61893975-HOUCHENS, C <Christopher.Houchens@hhs.gov>
To:	Bright, Rick (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=53034752f35a4317aa74f46348442d39-Bright, Ric <Rick.Bright@hhs.gov>
CC:	Ventura, Christy (OS/ASPR/BARDA) (CTR) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=9bb949caca464329823ca3cf77654a06-Ventura, Ch <Christy.Ventura@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0851e89240324306b78740a4a60745e2-Johnson, Ro <Robert.Johnson@hhs.gov>; Oshansky, Christine (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d7bd764440b44b06af644cdcd22e42d6-Oshansky, C <Christine.Oshansky@hhs.gov>; Boucher, David (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=41293945651d475fa0413062a819aac5-Boucher, Da <David.Boucher@hhs.gov>
Subject:	RE: TPs
Date:	2020/03/25 21:27:42
Priority:	Normal
Type:	Note

Rick,

Thanks Chris. These are great but eerily similar to todays. There was not a lot that was reported today from those that reported (only three reported). I have emphasized to the TF that criticality of reporting out daily but I can only report what is provided to me. I will emphasize this again tomorrow at my daily MCM TF leadership meeting and it would be very helpful if you are able to do the same if you can attend.

Except the moderna number has gone down. Something switched with numbers. This shows the challenge that we have had getting the data from WGs (which give one number) and agencies (which give another). This is why I am hoping that a more streamlined, top-down reporting approach that I described earlier to you will improve the process.

What's status of the NIH RCt for chloroquine? Hydroxychloroquine? The NIAID HCQ/CQ study is being run by ACTG. They met earlier this week to discuss the protocol. Hilary said today that there is nothing that can be reported at this time.

Status of Genentech Il-6 study? The IL-6R Ab study has not yet started.

Status of remdesivir manufacturing? I will ask Mike A. I do not know.

Is the blood collecting today the same as yesterday? This is different. Today's was about convalescent serum, this is about isolating antibody producing cells from infected patients.

From: Bright, Rick (OS/ASPR/BARDA) <Rick.Bright@hhs.gov>
Sent: Wednesday, March 25, 2020 8:59 PM
To: Houchens, Christopher (OS/ASPR/BARDA) <Christopher.Houchens@hhs.gov>
Cc: Ventura, Christy (OS/ASPR/BARDA) (CTR) <Christy.Ventura@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) <Robert.Johnson@hhs.gov>; Oshansky, Christine (OS/ASPR/BARDA) <Christine.Oshansky@hhs.gov>; Boucher, David (OS/ASPR/BARDA) <David.Boucher@hhs.gov>
Subject: Re: TPs

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What's status of the NIH RCt for chloroquine? Hydroxychloroquine?

Status of Genentech Il-6 study?

Status of remdesivir manufacturing?

Is the blood collecting today the same as yesterday?

Sent from my iPhone

On Mar 25, 2020, at 8:25 PM, Houchens, Christopher (OS/ASPR/BARDA) <Christopher.Houchens@hhs.gov>wrote:

Rick – Please see attached and below. Trying a new format here. TPs are below and on page 1. More details of all other activities are on following pages. Chris

Agencies reporting: BARDA, NIAID, DoD
Agencies not reporting: FDA, CDC, DHS, USDA

- NIAID multi-center, multi-country, multi-arm adaptive RCT with remdesivir
- 28 sites (24 US, 4 global)
- 113/440 enrolled (101 US, 12 global)

- Moderna mRNA-1273 vaccine: 19/45 healthy volunteers vaccinated as of 03/25/2020
- 15 subjects in cohort 1 (25mcg) completed
- 4 sentinel subjects in cohort 2 (100mcg) vaccinated
- 4 sentinel subjects in cohort 3 (250mcg) will be vaccinated following completion of cohort 2

- Blood samples are being collected from infected patients in Washington, DC and Hawaii. These blood samples are being provided to scientists and may contain antibody producing cells that can be used to make new therapies. (Note: This study is being supported by NIAID VRC)

Christopher Houchens, PhD
Director (Acting) Division of CBRN Countermeasures
Biomedical Advanced Research and Development Authority (BARDA)
Office of Assistant Secretary for Preparedness and Response (ASPR)
Department of Health and Human Services (DHHS)
Office: 202-205-3633
BB: (b)(6)
Christopher.houchens@hhs.gov

<MCM Task Force Update_03262020_v3.docx>

Sender:	Houchens, Christopher (OS/ASPR/BARDA) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7AC94A574BD04528B7C91BBD61893975-HOUCHENS, C <Christopher.Houchens@hhs.gov>
Recipient:	Bright, Rick (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=53034752f35a4317aa74f46348442d39-Bright, Ric <Rick.Bright@hhs.gov>; Ventura, Christy (OS/ASPR/BARDA) (CTR) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=9bb949caca464329823ca3cf77654a06-Ventura, Ch <Christy.Ventura@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0851e89240324306b78740a4a60745e2-Johnson, Ro <Robert.Johnson@hhs.gov>; Oshansky, Christine (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d7bd764440b44b06af644cdcd22e42d6-Oshansky, C <Christine.Oshansky@hhs.gov>; Boucher, David (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=41293945651d475fa0413062a819aac5-Boucher, Da <David.Boucher@hhs.gov>
Sent Date:	2020/03/25 21:27:41
Delivered Date:	2020/03/25 21:27:42

Clinical Trial Considerations for the Supply Chain Working Group

March 1, 2020

Background:

Although there are currently no FDA approved vaccines or therapeutics for the prevention or treatment of COVID-19, clinical trials are presently poised to start or underway in the United States for two candidate countermeasures:

- mRNA-1273 vaccine candidate – Moderna, Inc. and National Institute of Allergy and Infectious Diseases (NIAID) Vaccine Research Center (VRC)
- Remdesivir (GS-5734) therapeutic candidate (nucleotide analogue), Gilead Sciences

Other candidates and repurposed approved drugs are under assessment in China, and/or are in the pipeline for preclinical testing in the United States. Should preclinical data and/or clinical data from China show promise, those countermeasures would be considered for clinical trial evaluation in the United States. A full overview of medical countermeasure (MCM) development strategy has been drafted by the MCM task force. The information below provides an overview of candidates currently/nearing trials and their supply chain prospects.

Criteria for candidate identification:

The MCM task force is tracking a range of vaccine and therapeutics candidates, along with approved drugs that could be repurposed. With the exception of mRNA-1273 and remdesivir, none of these have impending or launched clinical trials in the United States. Therefore, the following criteria will be used to determine which candidates should be included in assessments for the Supply Chain working group: 1. availability of clinical grade material, and 2. funding/planning underway for a clinical trial in the United States. The former is particularly important for working group consideration: until clinical grade material has been produced, one knows neither the type nor quantity of raw material to be used in the final product. Therefore, one cannot project supply chain requirements and cost of goods sold. At present, no other candidates meet these criteria. The MCM task force will reconsider candidates for inclusion in coming months.

mRNA-1273 Vaccine Candidate – Moderna, Inc. and National Institute of Allergy and Infectious Diseases Vaccine Research Center

NIAID, in partnership with the biotechnology company Moderna, Inc., is utilizing a messenger RNA (mRNA) platform to develop a candidate vaccine for SARS-CoV-2. The mRNA technology uses the body's cells to express a SARS-CoV-2 protein, generating a broad immune response including high levels of neutralizing antibodies. The specific candidate, called mRNA-1273, encodes the SARS-CoV-2 spike protein, which has been genetically modified to stabilize it in its most immunogenic form. Prior studies for other coronaviruses have shown that the stabilized form of the spike protein generates a more robust immune response and produces higher manufacturing yields.

mRNA platform: The mRNA platform takes viral nucleic acid (RNA) and introduces it into the body's cells in a proprietary lipid coating called a lipid nanoparticle (LNP), which allows the mRNA to enter the cell without being destroyed. Therefore, manufacturing requires both LNP and nucleotide raw materials.

mRNA-1273 candidate: The specific vaccine candidate, called mRNA-1273, includes mRNA encoding a stabilized SARS-CoV-2 spike protein, the protein found on the virus surface. Prior studies for other coronaviruses have shown that the stabilized spike protein generates more robust immune responses while producing higher manufacturing yields.

Progress to date: Preclinical studies in mice have shown that the candidate can generate an immune response. Follow on studies assessing protection in mice and non-human primates (NHPs) are planned. Phase 1 material was shipped to the clinical trial site on February 22, 2020. The protocol is under review by the FDA and could launch in March 2020. Scientists plan to enroll 45 health volunteers, administering two doses 28 days apart. Three dose levels will be assessed and response will be measured after the first and second doses. These findings will have important implications for final dose selection.

A Phase 2 trial would be planned thereafter. Even with very rapid development pathways, it may take 1.5 to 2 years for a vaccine to be available for the general public.

Manufacturing:

Moderna is currently producing its mRNA candidate in its (b)(4) production platform, using a process that can yield (b)(4) This could support immediate clinical development needs. The company is currently evaluating approaches, timelines, and cost for altering and scaling up manufacturing to produce significantly more doses faster.

ASPR is in discussions with the company to determine manufacturing capacity at their current facilities and how assistance can be provided to increase capacity using additional contract manufacturing organizations.

Remdesivir (GS-5734) therapeutic candidate, Gilead Sciences

Remdesivir is a broad spectrum antiviral, specifically a nucleotide analogue, with activity against many RNA viruses. For example, it has demonstrated in vitro and in vivo activity against SARS, Ebola and Marburg. It has been assessed in several human trials, including Phase 1 safety studies and two Ebola studies. In addition, it has been evaluated in mouse and non-human primate models for MERS, demonstrating protection against severe disease.

It is an intravenous medication, and a treatment course comprises 10 daily doses each infused over 30-60 minutes time. Transient/reversible renal and hepatotoxicity have been observed in trials, though typically at doses above those proposed for SARS-CoV-2.

Remdesivir and SARS-CoV-2: Early results from DoD scientists have demonstrated in vitro activity against SARS-CoV-2. NIAID scientists are initiating NHP studies in March 2020. Based on data for related diseases, both the World Health Organization and the MCM task force placed remdesivir atop the list of candidates for priority evaluation in trials.

Several groups have initiated clinical trials testing remdesivir efficacy in treating COVID-19:

1. Dr. Cao Bin launched two randomized controlled trials, Remdesivir 1 in mild-to-moderate patients, and Remdesvir 2 in severe patients. The latter is over fifty percent enrolled, with an interim assessment planned in the near future.

2. Gilead Sciences has launched two randomized controlled trials evaluating different dose schedules in moderate and severe patients. The trials will launch in several sites in Asia in mid-March 2020, and in 1-2 sites in the U.S. thereafter.
3. NIAID launched a randomized, double blinded, placebo controlled clinical trial to evaluate the safety and efficacy of remdesivir in hospitalized adults diagnosed with COVID-19 on February 21, 2020. The trial is currently active in two sites: University of Nebraska Medical Center in Omaha and Providence Sacred Heart in Spokane. It will expand to up to 50 sites in total, with roughly 30 in the United States.

Manufacturing: Gilead currently has ~5,000 treatment courses (TCs) fill finished, with an additional ~70,000 TCs from drug substance (95kg) that has been reported to have been shipped to filling facilities in WA and CA. HHS was also informed that the company retained 40kg of material in Canada and anticipates sending this to China where it will be fill finished. The TC numbers assume a regimen of 10 daily infusions, and it is possible that trials will demonstrate efficacy with a shorter treatment duration, thereby extending supply. However, assuming the duration remains unchanged, the company reports it will fill-finish the 70,000 TCs over the Spring, having an additional 23,000 TCs available by the end of March 2020, and the balance by the end of May 2020. The company has reported it is manufacturing yet more drug substance at a 28kg and 60kg scale and looking at options to increase manufacturing for both drug substance and drug product.

As stated above, additional candidates will be presented for consideration of the supply chain working group based on 1. availability of clinical grade material, and 2. presence of funding/planning underway for a clinical trial in the United States. At this time, mRNA-1273 and remdesivir are the only candidates that meet these criteria.

COVID-19 BARDA Overview

Date: April 08, 2020

1. Diagnostics
    - Partnered with Hologic, DiaSorin, Qiagen, MesaBioTech, GenMark, Cepheid, Luminex (NxTag and Aries), Vela, OraSure and Nanomix to develop SARS-CoV-2 diagnostics
    - 29 Diagnostics with EUA

2. Therapeutics
    - Shipments of Chloroquine/Hydroxychloroquine have left SNS for use under EUA
    - Griffols IAA to DoD signed 04/07/2020 for convalescent plasma and hyperimmune globulin
    - Emergent developing a plasma-derived Polyclonal Antibody-based COVID-19 Rx
    - Genentech Tocilizumab (α-IL-6R) clinical trial for COVID-19 targeting start early April
        i. 9 patients enrolled 04/06/2020
    - Regeneron adaptive phase 2/3 study of Sarilumab (α-IL-6R antibody) for COVID-19
        1. 51 sites activated (15 in NY, 5 in NJ, 4 in FL, 3 in MA, 2 in CA, GA, IL, PA, TX, WA, 1 each in CO, CT, DC, LA, MI, MN, OK, UT, VA)
        2. 916 total dosed as of 04/06/2020
            a. Phase II – 463
            b. Phase III - 453

    b. 5Regeneron has identified mAbs that neutralize SARs-CoV-2 virus in vitro
        i. Screening candidate mAbs for neutralizing activity and scaling up manufacturing
    - Janssen high throughput screening assay has been validated as of 04/07/2020

3. Vaccines
    - Sanofi Pasteur is pursuing a vaccine construct that is thought to be more stable.
        i. Award in process for development through Phase 1
    - Janssen preliminary non-clinical data in immunogenicity in mice
        i. 1 lead candidate in two different forms identified
        ii. Clinical trials expected early fall 2020

1) BARDA Diagnostics
    a) 14 White Papers submitted, reviews in progress.
    b) Current Diagnostic EUAs
        i) 29 Diagnostics with (EUA):
            I. https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations#covid19ivd
    c) Cepheid
        i) No Update
    d) Cue
        i) Targeting EUA submission week of 04/13/2020
    e) [PROCUREMENT SENSITIVE] EZ-BAA submissions
            I. Hologic shipped 192,000 tests as of 04/06/2020
        ii) DiaSorin Molecular
            I. 88K tests shipped to US labs as of 04/06/2020
        iii) MesaBioTech Point of care (hand-held device)
            I. Targeting to ship 7500 tests week of 04/06/2020
        iv) Qiagen
            I. No update
        v) Genmark
            I. No Updates
        vi) Luminex Corp
            I. Luminex NxTAG-Shipped ~84K tests as of 04/07/2020
            II. Luminex Aries- Targeting shipments week of 04/24/2020
        vii) Vela Diagnostics
            I. LOD study completed, verification and validation in progress
        viii) Nanomix kick off meeting in process of being scheduled
        ix) OraSure kick off meeting 04/08/2020
        x) Pending EZ-BAA contract actions
            I. DiaSorin (Antibody) waiting for signature from company
            II. Hememics and Inbios (Antigen/Antibody): Stage 2 negotiations in process
2) BARDA Therapeutics
    a) Regeneron
        i) 2019-nCoV specific mAb on track to have leads by end of April and production in August
            1. Screening leads for neutralizing activity and scaling up manufacturing
        iii. Regeneron adaptive phase 2/3 study of Sarilumab (α-IL-6R antibody) for COVID-19
            1. 51 sites activated (15 in NY, 5 in NJ, 4 in FL, 3 in MA, 2 in CA, GA, IL, PA, TX, WA, 1 each in CO, CT, DC, LA, MI, MN, OK, UT, VA)
            2. 916 total dosed as of 04/06/2020
                a. Phase II – 463

b. **Phase III - 453**

3. **DMC met 04/04/2020 study given safe to proceed**

b) Genentech IL-6R antibody (Tocilizumab) clinical trial in COVID-19 patients

i) 9 patients enrolled 04/06/2020

c) Antiviral screening

i) Discussions on steps to test hits (itraconazole) in non-clinicals models

d) SAb Biotherapeutics – Polyclonal antibody product

i) Clinical trial planned for late June/July

e) Grifols (Covalescent Plasma and HIG)

i) IAA with DoD signed 04/07/2020

f) Emergent

i) Possible submission of pre-IND submission to FDA week of 04/06/2020

3) BARDA Vaccines

a) Janssen Ad26 vaccine

i) Down selected to two forms of the same candidate

I. Soluble and transmembrane

ii) Targeting to start clinical trial early September

b) Sanofi Pasteur

i) Award for development through Phase 1 clinical study on hold pending ASPR review

c) Moderna

i) Project award on hold pending ASPR review

4) Merck SOW in review

5) Pfizer

a) No update

6) BARDA Rapidly Deployable Technology

a) Modifications to ENACT and Sepsis contracts targeting week of 04/06/2020

7) Sample Sharing Working Group

i) Launched campaign to rapidly secure convalescent serum in support of serological testing program.

ii) Will pursue 5 partnerships: Stanford, UMD, UCSD, Cantor Bioconnect, ICON

8) BARDA Clinical

a) NIAID ACTT Trial

i) Will be a 4 arm study investigating standard of care, remdesivir, baracitinib, combination of remdesivir, and baracitinib

b) Chloroquine/Hydroxychloroquine EUA

i) One million doses of chloroquine donated by Bayer arrived to the SNS

9) BARDA Non-clinical

a) Non-clinical kick off meetings scheduled

i) Kick of meetings for MRI Global and Lovelace scheduled 04/08/2020

ii) Strategy to cost share and manage laboratory bandwidth with BARDA and NIAID cross over being considered/worked out with contracting and labs

iii) BARDA non-clinical will be invited to join NIAID task order calls and vice versa

10) BARDA RQA

a) Standing weekly meetings scheduled with CDER and CBER

11) BARDA Manufacturing

a) Discussions with Catalent regarding their capacity to fill additional AS03 in anticipation of material needed for COVID19 vaccines
b) Conducted TEP on 04/07/2020 for proposal from TAMUS CIADM
c) Phlow contract negotiations continue

SNS Hydroxychloroquine/Chloroquine Requests

Requestor/State	Clinical Trial Material	Hydroxychloroquine/ Chloroquine	# of Pills*	Date
Seminole Tribe of Florida		Hydroxychloroquine	9600	Shipped 04/06/2020
North Carolina Division of Public Health		Hydroxychloroquine	998,400	Received 04/05/2020(993,600) Shipped 04/06/2020(4800)
Nevada Public Health & Human Services		Hydroxychloroquine	14,400	Shipped 04/04/2020
Mississippi Dept of Public Health		Hydroxychloroquine	24,000	Shipped 04/05/2020(14,400) Shipped 04/06/2020(9600)
California Dept of Public Health		Hydroxychloroquine	3,297,400	Shipped 04/05/2020
Henry Ford Hospital, Detriot MI	Yes	Hydroxychloroquine	81,600	Received 4/05/2020
US Virgin Islands		Hydroxychloroquine	19,200	Received 04/03/2020
California, LA County Public Health		Hydroxychloroquine	28,800	Received 04/03/2020
New York, NYS Dept of Corrections and Community Supervision Central Pharmacy		Hydroxychloroquine	139,200	Received 04/03/2020

*Calculations of pills and bottles/blister packs are made by RQA based on data provided by SNS for cases of product. These amounts are based on assumptions and may not be exact.

HQ: 242,880 Bottles* Remain: (100 pills/bottle)
CHQ: 3,952 Blister Packs* Remain: (250 pills/pack)

16 Years

3rd Coronavirus Outbreak

No Licensed products

2019-nCoV Medical Countermeasures Task Force

Align MCM development across Interagency partners to avoid duplication of effort, identify opportunities for synergy, and fill potential gaps

NIH NIAID

BARDA Biomedical Advanced Research and Development Authority

ASPR Assistant Secretary for Preparedness and Response

CDC Centers for Disease Control and Prevention

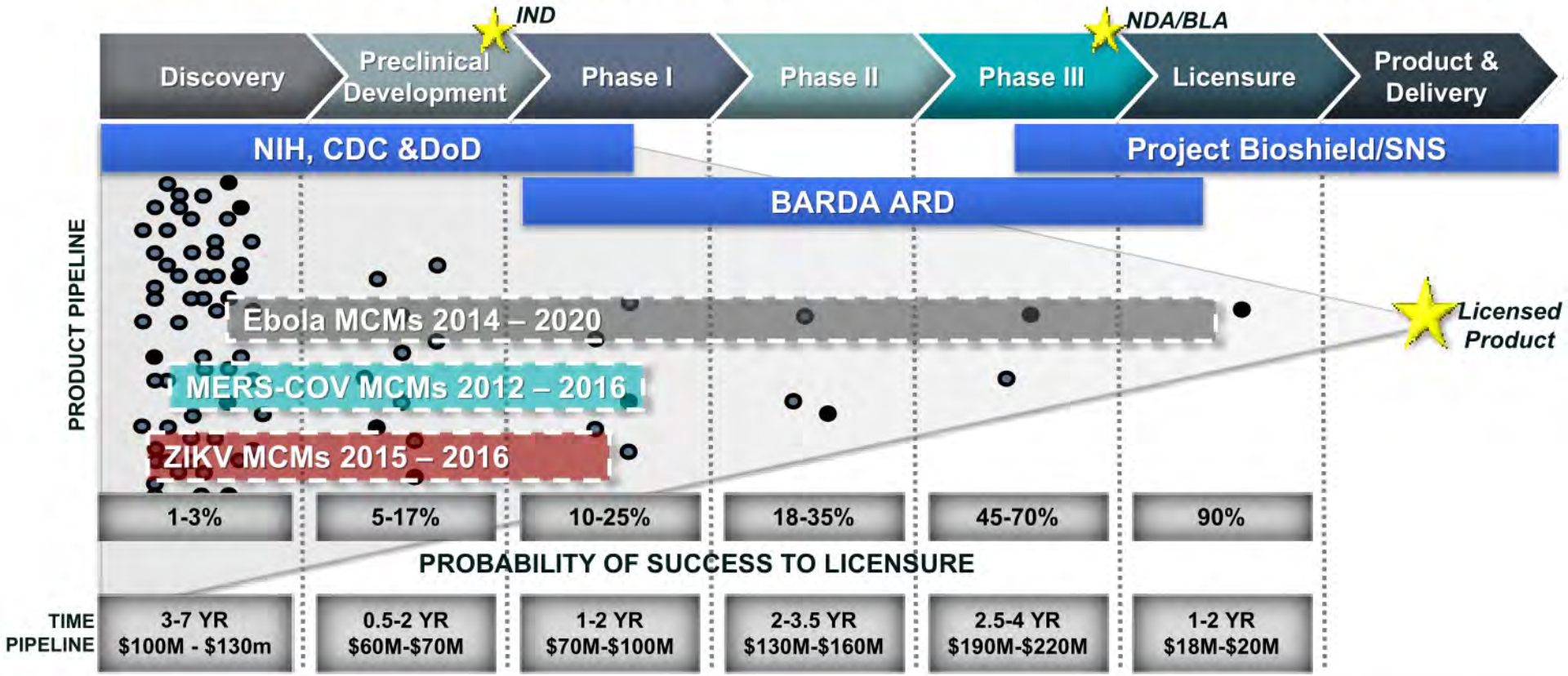
FDA

Department of Defense United States of America

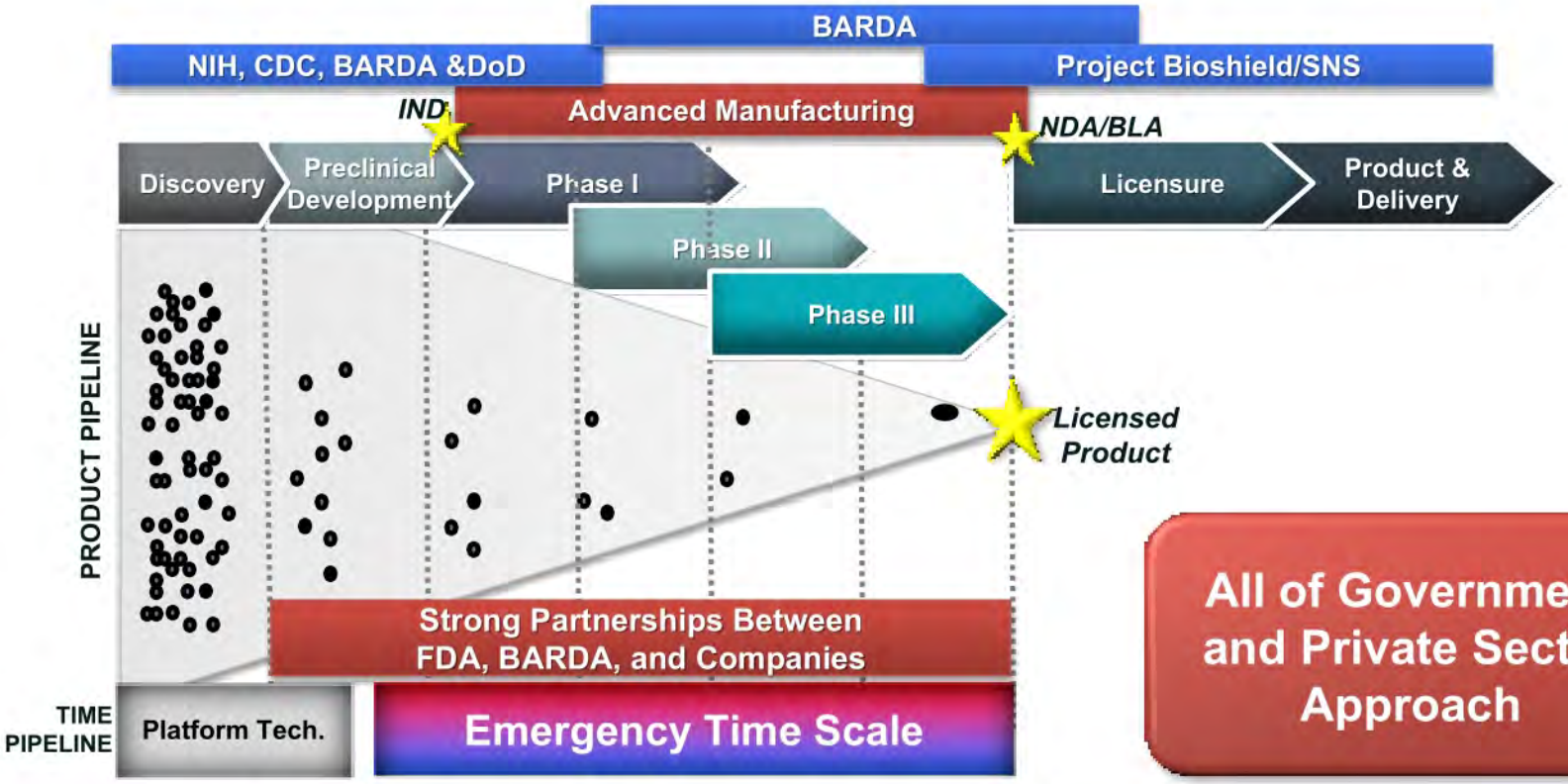
USDA

Homeland Security

Vaccine & Drug Development is Expensive, Risky and Lengthy



Emergency Vaccine & Drug Development



All of Government and Private Sector Approach

SARS COVID-19 MEDICAL COUNTERMEAUSRE DEVELOPMENT STRATEGY

ACCELERATE DEVELOPMENT

- Platform technologies
- Repurpose licensed products
- Parallel, not sequential, activities

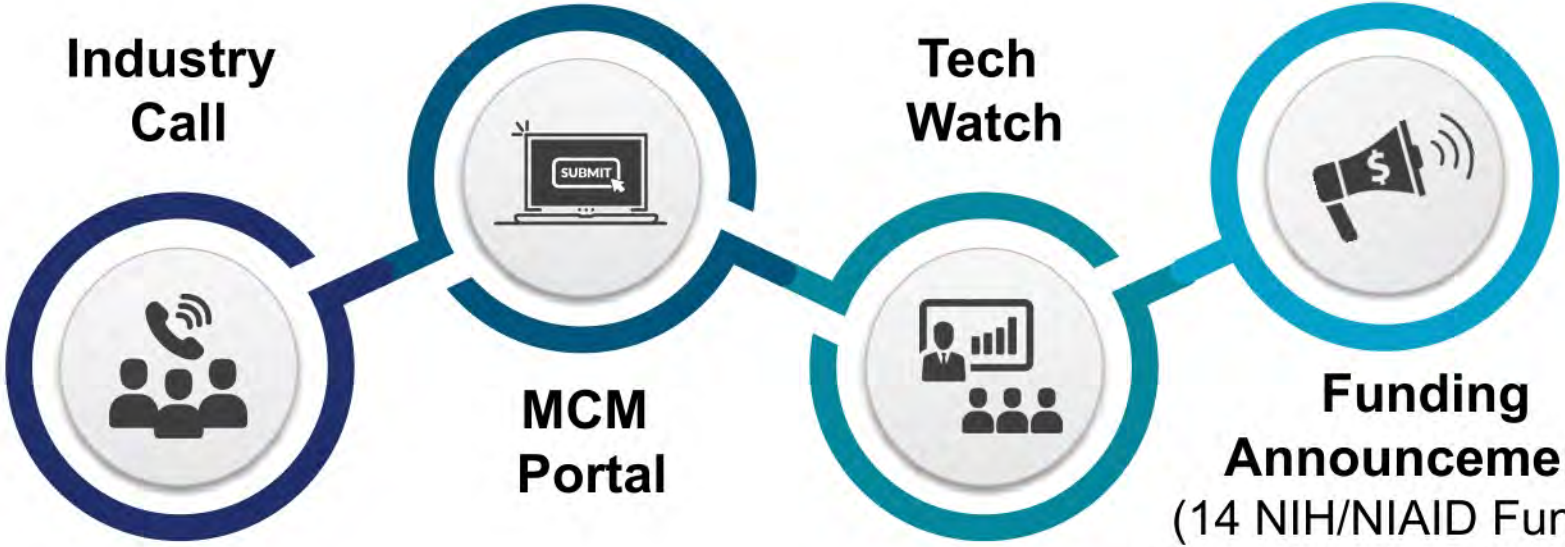
MITIGAGE RISK

- Multiple technologies
- Multiple targets
- Redundancy

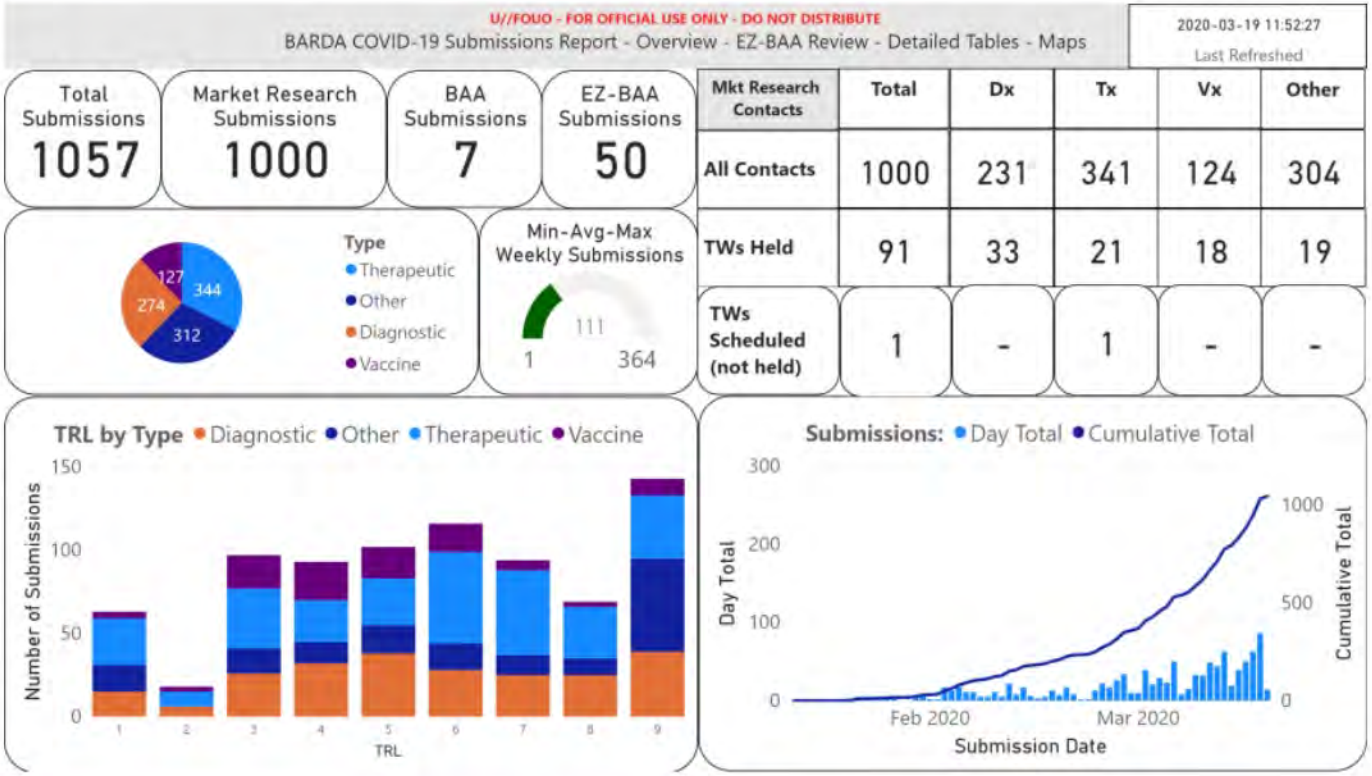
DOMESTIC MANUFACTURING

- Scale Up & Scale Out
- Raw materials and supply chains
- Leverage existing facilities

Agency-Wide Engagement with Developers



COVID-19 Market Research Portal Submissions



Therapeutics Development

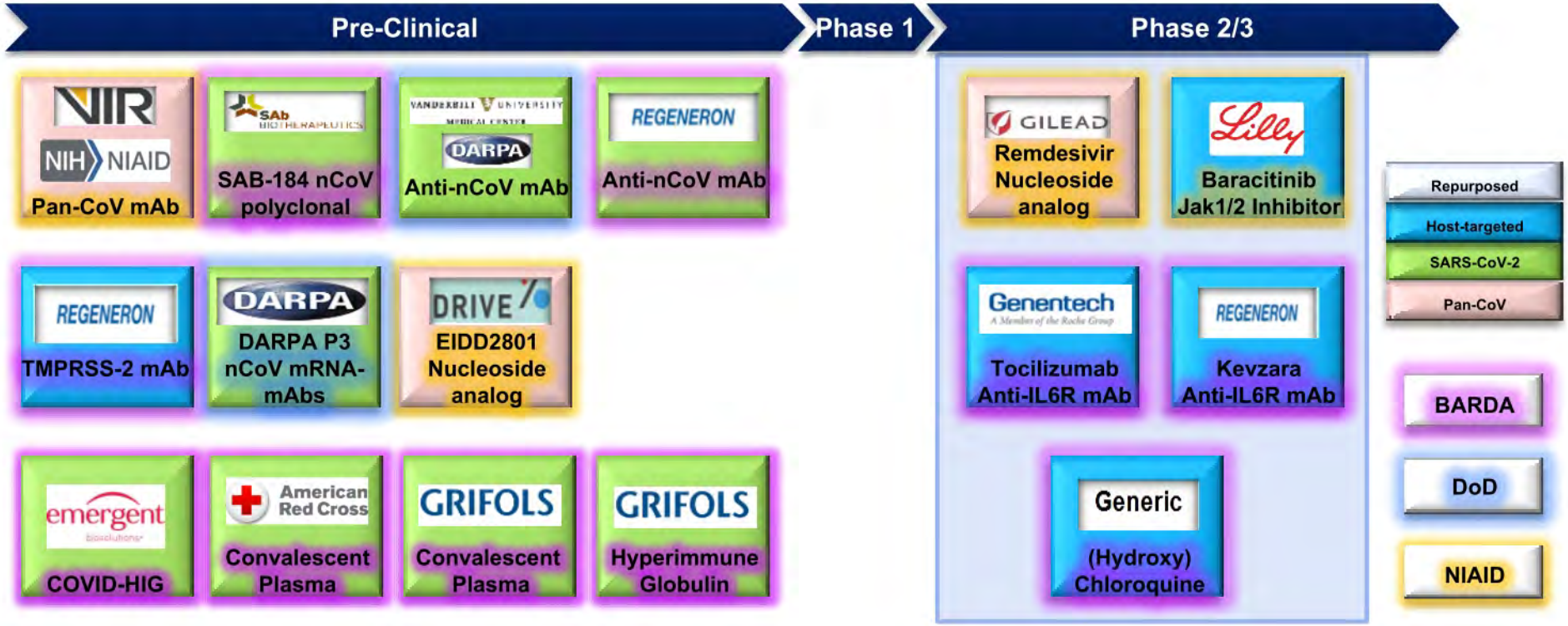
e.g., 2019-CoV specific monoclonal antibodies, small molecule antivirals, and immunoglobulins

e.g., inhibitors of viral activation, host pathway modulators

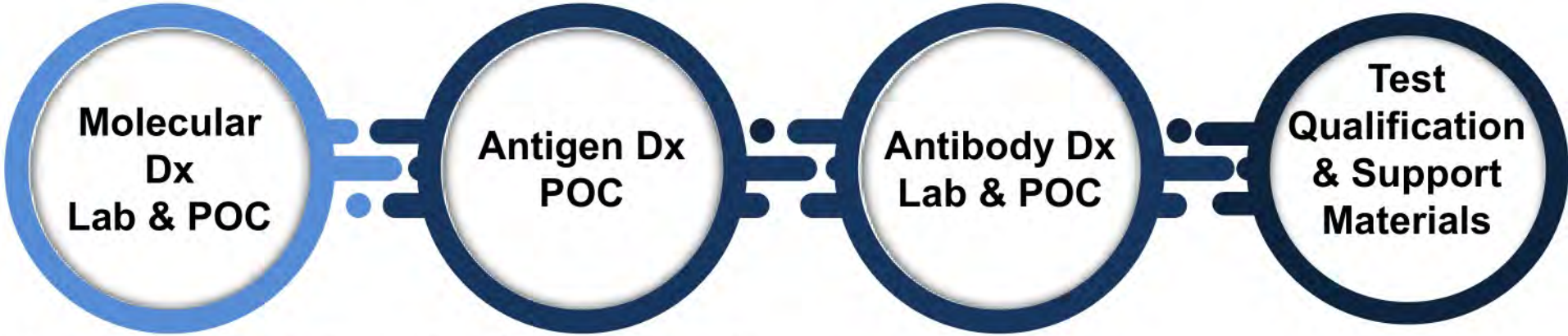
FDA-approved therapeutics licensed for other indications
- Ready for immediate clinical testing

Leverage existing infrastructure for rapid MCM generation and production through partnerships (contracts and OTA) including other USG agencies

USG-Supported SARS-CoV-2 Therapeutics



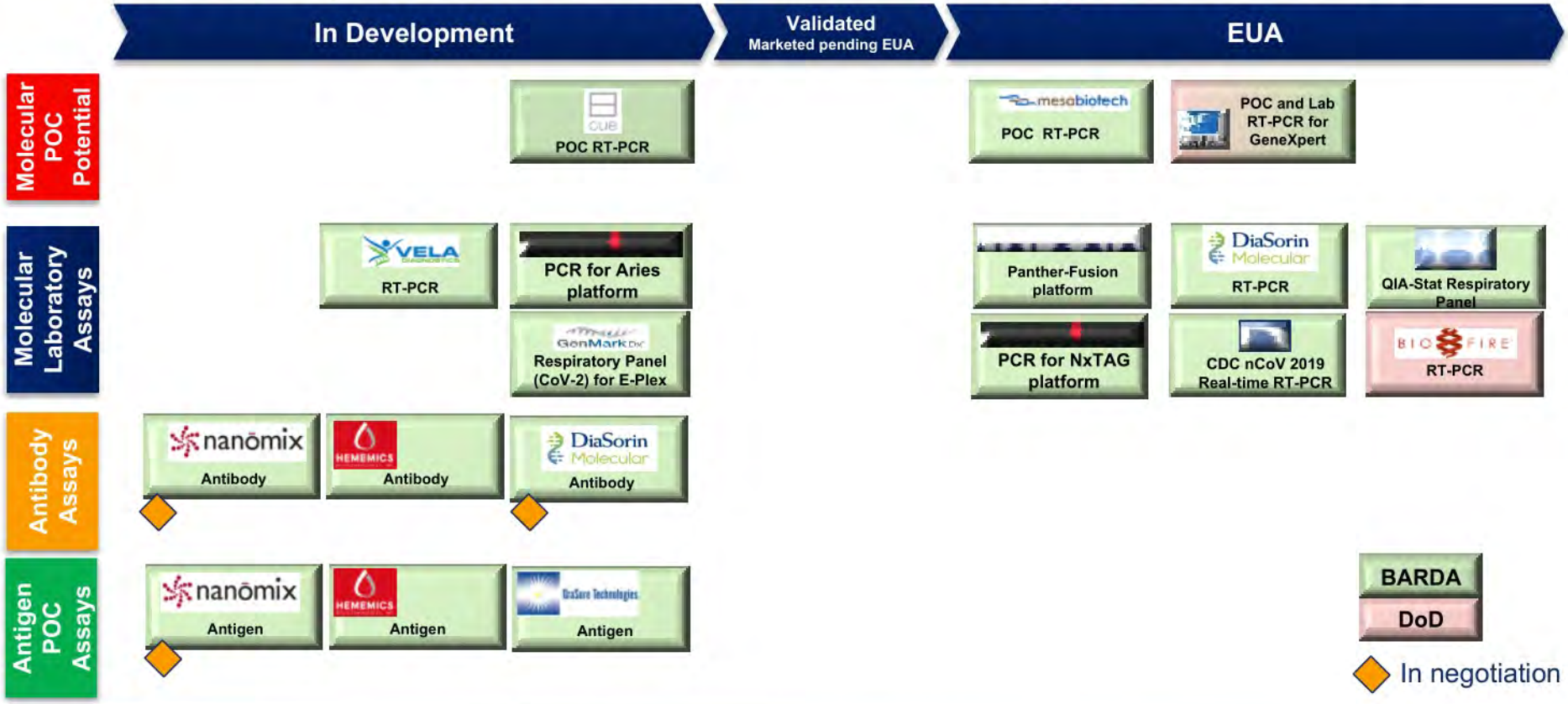
Diagnostics Development: Four-Pronged Approach



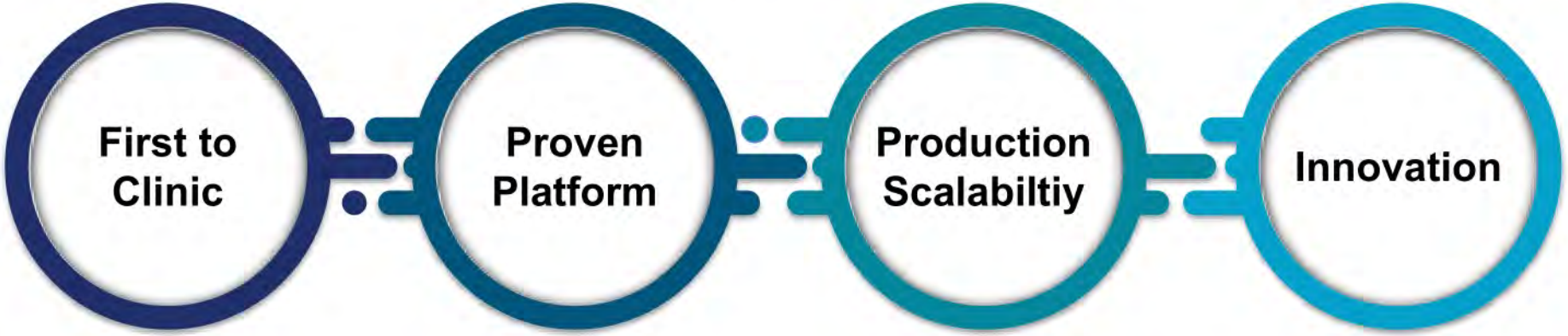
Leverage existing Laboratory Infrastructure & Equipment
Leverage Existing & Complete In-Development POC Equipment

04/02/20

USG-Sponsored SARS-CoV-2 Diagnostic Tests



Vaccine Development



e.g., mRNA based vaccines that allow rapid early development

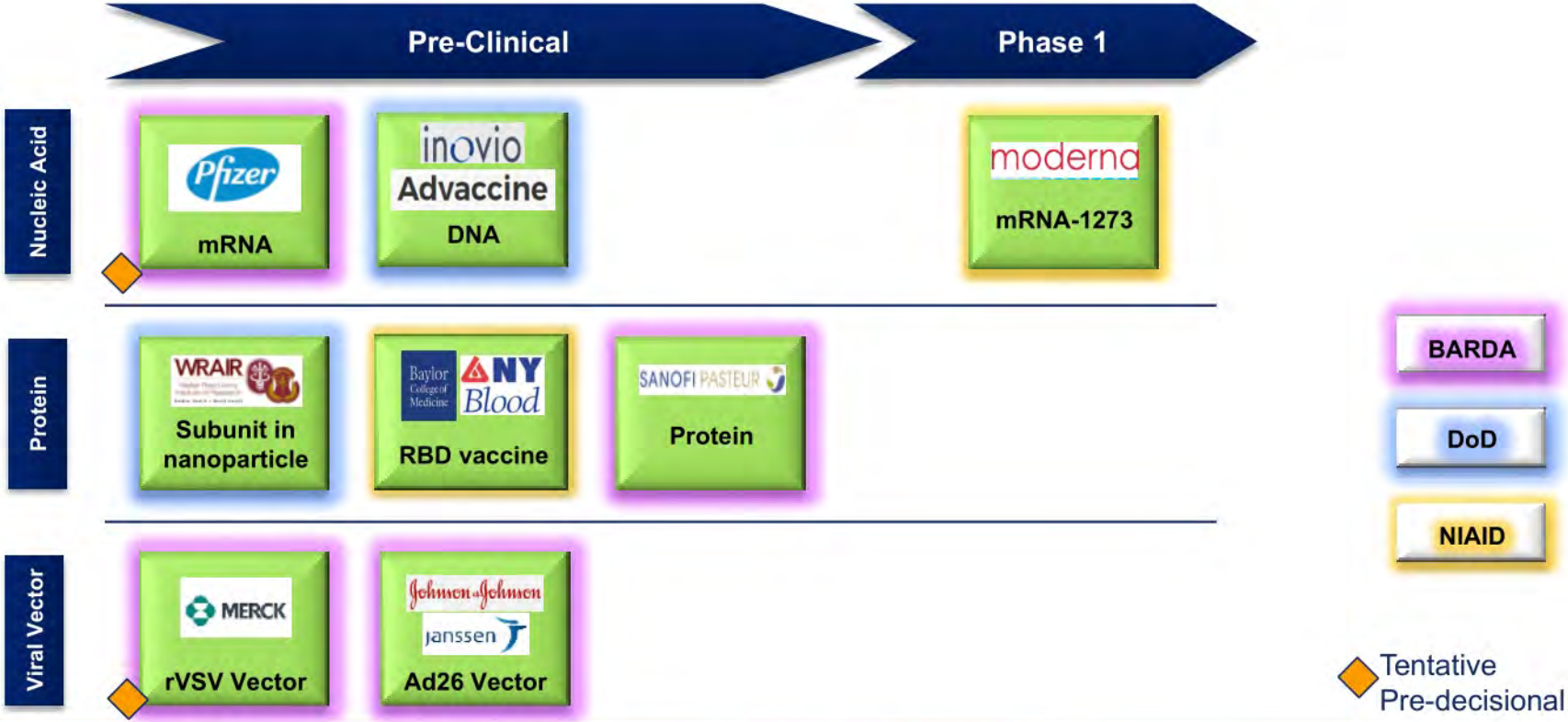
e.g., viral vectors with demonstrated safety and efficacy

e.g., Existing or readily amenable to large scale manufacturing, including experienced workforce

e.g., novel platforms, delivery approaches, or new thinking to transform the field

Leverage existing infrastructure for rapid MCM generation and production through partnerships (contracts and OTA) including other USG agencies

USG-Supported SARS-CoV-2 Vaccines



VACCINE APPROACH

Accelerate Development

Rapid Vaccine Platform Approaches
- Nucleic Acid
- Vectors
- Recombinant protein

Repurpose Licensed Products
- Viral Vector
- Recombinant Protein

Parallel Activities
- Overlapping clinical trials
- Scale up in parallel with clinical development

Mitigate Risk

Multiple Technologies
- Address potential yield risks
- Address potential dose risk

Multiple Targets
- Disease enhancement mitigation
- Alternative routes of delivery

Redundancy
- Take multiple products through large scale clinical trials
- Multiple manufacturing facilities for each product

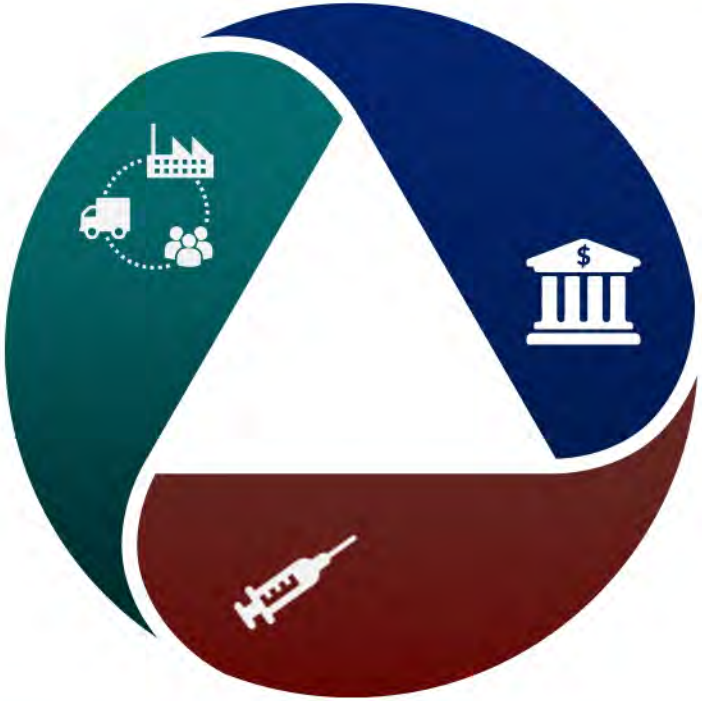
Domestic Manufacturing

Scale up & Scale out
- Validate larger scale process (i.e. larger tanks)
- Mutiple
- Technology Transfer to more facilities
- Increase fill/finish capacity

Raw Materials Supply Chains
- Remove bottlenecks
- Establish stockpiles

Leverage Existing Facilities
- CIADMs
- Facilities of large pharma partners
- CMOs

Moderna

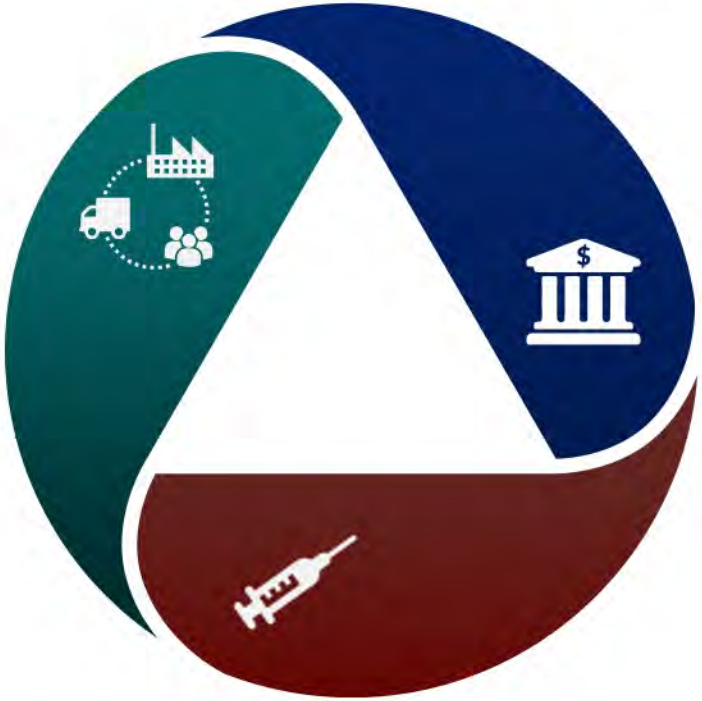


DEVELOPMENT
- First to clinic (1Q 2020)
- Phase 2 (2Q 2020)

RISK
- Unlicensed platform
- Scale-up constraints and limited experience
- Raw materials
- Required Dose

DOMESTIC MANUFACTURING
- Scale up (limited) and out
- Secure supply chain

Janssen

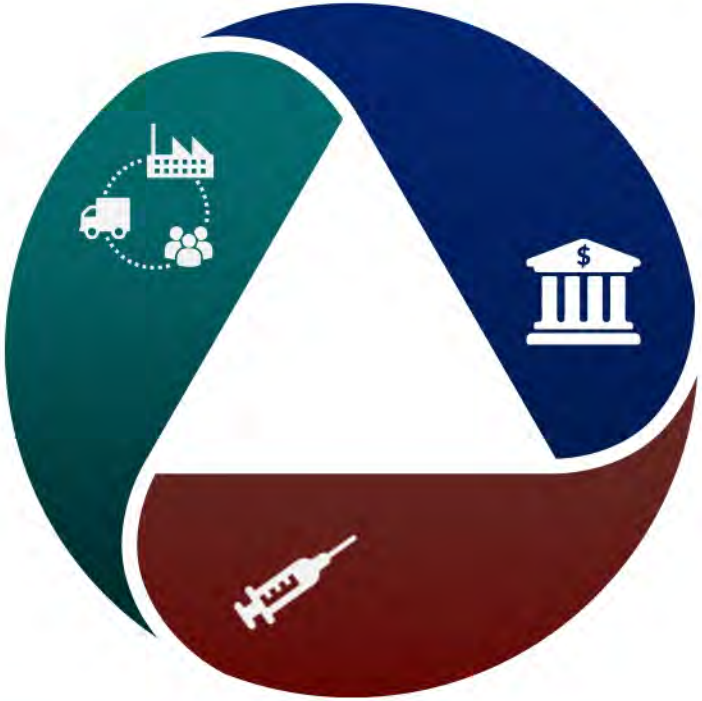


DEVELOPMENT
- Parallel Work Streams
- Robust preclinical screening
- Phase 1 by 3Q2020

RISK
- Production yield
- Required Dose

DOMESTIC MANUFACTURING
- Technology transfer to domestic facility
- Significant manufacturing experience mitigates risk

Sanofi Pasteur

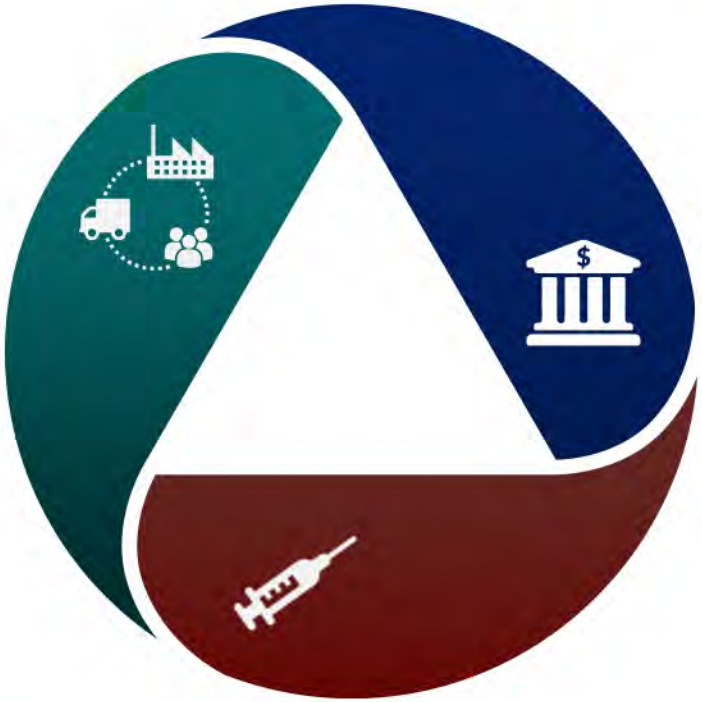


DEVELOPMENT
- FDA-licensed vaccine platform
- Parallel Work Streams
- Phase 1 by 3Q2020

RISK
- Multiple Vaccine Platforms
- Production yield
- Adjuvant likely required

DOMESTIC MANUFACTURING
- Licensed manufacturing facility available
- Production levels likely to be robust
- Experienced manufacturing team

Merck



DEVELOPMENT

- Parallel Work Streams
- FDA-licensed platform (VSV-vectored Ebola vaccine)

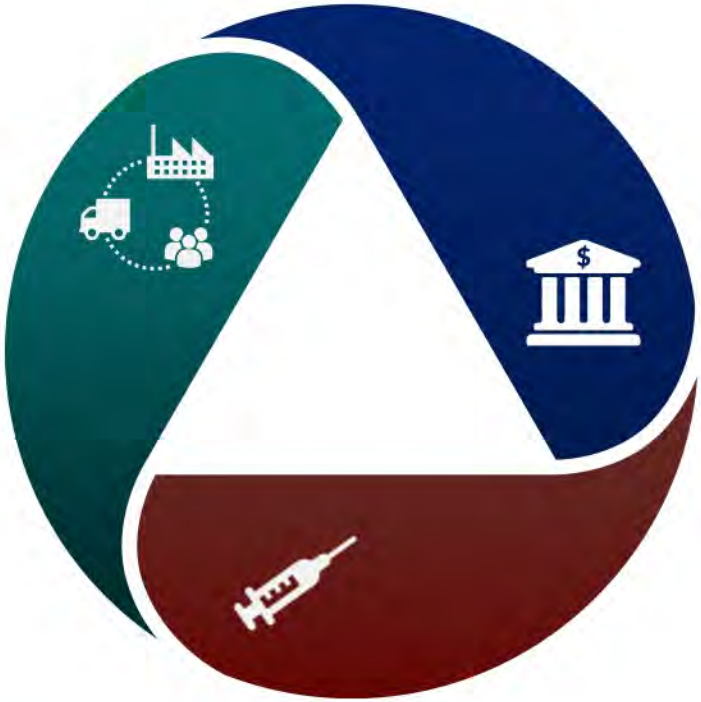
RISK

- Sufficient Scale up and out capability of the platform
- Phase 1 TBD
- Required Dose

DOMESTIC MANUFACTURING

- Scale Up or Out
- Experienced workforce
- Domestic facilities available

Pfizer

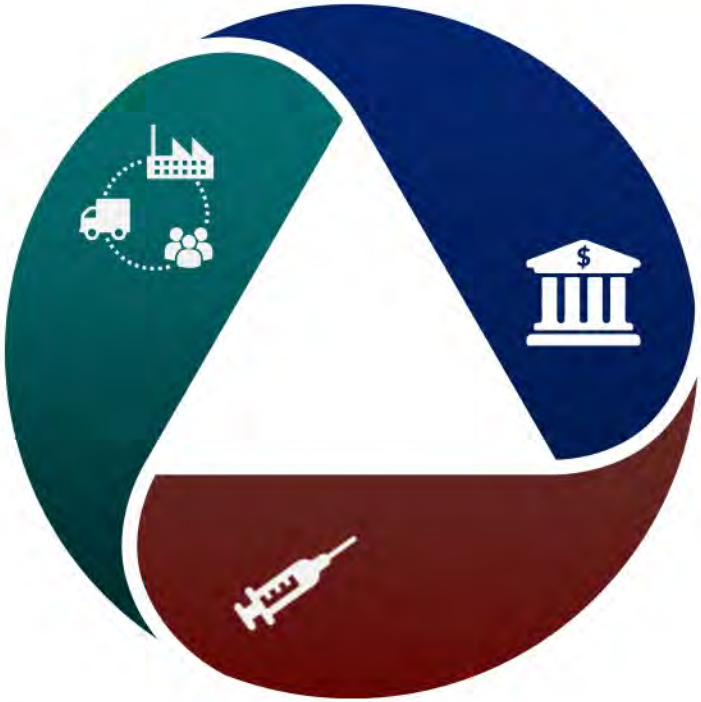


DEVELOPMENT
- Parallel work streams
- Phase 2 by 2Q 2020

RISK
- Multiple Vaccine Platforms could delay down-select
- Raw material needs (lipids are required)
- Maturity of technology

DOMESTIC MANUFACTURING
- Technology transfer to United States
- Large domestic facilities and experienced staff readily available
- Raw Materials Supply Chains

Innovation



AREAS OF INTEREST

- Product yield enhancement
- Faster time to protection
- Operational improvements

IDENTIFICATION

- Handoff from other Government agencies
- High ranking from MCM review panels
- Leveraging opportunities (within and outside of Government)

TARGETED STRATEGY

- Initial 'seed' funding to assess feasibility
- Flexible funding approaches
- Cost Share

From:	Kadlec, Robert (OS/ASPR/IO) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=A182EDA693D040D3832BAE6EFCF7A255-KADLEC, ROB <Robert.Kadlec@hhs.gov>
To:	Disbrow, Gary (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0fd5845defda4dc0bb45f8fac629cf09-Disbrow, Ga <Gary.Disbrow@hhs.gov>
CC:	Chang, William (HHS/OGC) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3cf70c842da144ab9bee61f353d932a0-Chang, Will <William.Chang@hhs.gov>; Redd, John (OS/ASPR/SPPR) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=9ba3fed4ee8646ec849a5a87136a24f6-Redd, John <John.Redd@hhs.gov>; Hassell, David (Chris) (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=aedbfb0ff96e4119ac7a3b3abaf71a3d-Hassell, Da <David.Hassell@hhs.gov>; Johnson, Lynn (ACF) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e08aee07c094419ab78da8fbb9b8be3e-Johnson, Ly <Lynn.Johnson@acf.hhs.gov>; Sherman, Susan (HHS/OGC) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=user161a2a33 <Susan.Sherman@HHS.GOV>; Stimson, Brian (HHS/OGC) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=338aa495176d4c92bb314f8f3f51d118-Stimson, Br <Brian.Stimson@hhs.gov>; Barry, Daniel J (HHS/OGC) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=user3e449ce0 <daniel.barry@hhs.gov>; Shuy, Bryan (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fdeb5ca04b6b4ed19fec2209b5f571e7-Shuy, Bryan <Bryan.Shuy@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0851e89240324306b78740a4a60745e2-Johnson, Ro <Robert.Johnson@hhs.gov>; Bright, Rick (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=53034752f35a4317aa74f46348442d39-Bright, Ric <Rick.Bright@hhs.gov>
Subject:	Re: Can you please send word doc for Remdesivir
Date:	2020/03/04 16:27:16
Priority:	Normal
Type:	Note

Thanks Gary

Sent from my iPhone

> On Mar 4, 2020, at 4:19 PM, Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov> wrote:
>
> Team,
>
> My edits/comments to the word document.
>
> Gary
>
> Gary L. Disbrow Ph.D.
> Deputy Assistant Secretary
> Director, Medical Countermeasure Programs

> Biomedical Advanced Research and Development Authority
> BARDA
> Assistant Secretary for Preparedness and Response ASPR
> Department of Health and Human Services
> 330 Independence Avenue, S.W. Room 640 G
> Washington, D.C. 20201
> Office: 202-260-0899
> Mobile: (b)(6)
> Fax: 202-205-0873
> email: Gary.Disbrow@HHS.gov
>
> Legally Privileged - This e-mail transmission and any documents attached to it may contain information that is legally privileged. If you are not the intended recipient, or a person responsible for delivering this transmission to the intended recipient, you are hereby notified that any disclosure, copying, distribution, or use of this transmission is strictly prohibited. If you have received this transmission in error, please immediately notify the sender and destroy the original transmission, attachments, and destroy any hard copies.
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> Note to contractors: nothing in this e-mail is intended to constitute contractual direction or to impact cost, price, or schedule contained in the contract. If the contractor believes there is an impact, the contractor must disregard that portion of the communication and contact the Contracting Officer for direction
>
>
> -----Original Message-----
> From: Chang, William (HHS/OGC) <William.Chang@hhs.gov>
> Sent: Wednesday, March 4, 2020 4:07 PM
> To: Kadlec, Robert (OS/ASPR/IO) <Robert.Kadlec@hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Redd, John (OS/ASPR/SPPR) <John.Redd@hhs.gov>; Hassell, David (Chris) (OS/ASPR/IO) <David.Hassell@hhs.gov>; Johnson, Lynn (ACF) <Lynn.Johnson@acf.hhs.gov>; Sherman, Susan (HHS/OGC) <Susan.Sherman@HHS.GOV>; Stimson, Brian (HHS/OGC) <Brian.Stimson@hhs.gov>; Barry, Daniel J (HHS/OGC) <daniel.barry@hhs.gov>
> Cc: Shuy, Bryan (OS/ASPR/IO) <Bryan.Shuy@hhs.gov>
> Subject: RE: Can you please send word doc for Remdesivir
>
> + Stimson and Barry
>
> Office of the General Counsel
> U.S. Department of Health and Human Services
> 202-690-7741 (o)
> (b)(6) (c)
>
> -----Original Message-----
> From: Kadlec, Robert (OS/ASPR/IO) <Robert.Kadlec@hhs.gov>
> Sent: Wednesday, March 4, 2020 3:59 PM
> To: Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Redd, John (OS/ASPR/SPPR) <John.Redd@hhs.gov>; Hassell, David (Chris) (OS/ASPR/IO) <David.Hassell@hhs.gov>; Johnson, Lynn (ACF) <Lynn.Johnson@acf.hhs.gov>; Sherman, Susan (HHS/OGC) <Susan.Sherman@HHS.GOV>; Chang, William (HHS/OGC) <William.Chang@hhs.gov>
> Cc: Shuy, Bryan (OS/ASPR/IO) <Bryan.Shuy@hhs.gov>
> Subject: FW: Can you please send word doc for Remdesivir

>
> All please edit and comment as needed. Please send back to Seth NLT 1800
>
> -----Original Message-----
> From: Jonas, Seth H. EOP/NSC <Seth.H.Jonas@nsc.eop.gov>
> Sent: Wednesday, March 4, 2020 3:52 PM
> To: Kadlec, Robert (OS/ASPR/IO) <Robert.Kadlec@hhs.gov>
> Cc: Cavanaugh, Brian J. EOP/NSC <Brian.J.Cavanaugh@nsc.eop.gov>
> Subject: RE: Can you please send word doc for Remdesivir
>
> Dear Bob,
>
> Attached is the current draft. Some elements are still in flux. Your comments are appreciated.
>
> Thanks,
> Seth.
>
> -----Original Message-----
> From: Kadlec, Robert (OS/ASPR/IO) <Robert.Kadlec@hhs.gov>
> Sent: Wednesday, March 4, 2020 3:12 PM
> To: Jonas, Seth H. EOP/NSC <Seth.H.Jonas@nsc.eop.gov>
> Cc: Cavanaugh, Brian J. EOP/NSC <Brian.J.Cavanaugh@nsc.eop.gov>
> Subject: Can you please send word doc for Remdesivir
>
> Seth have some comments and easiest way to transmit our suggested edits and comments. Best. Bob
>
> Sent from my iPhone
> <FOUO- DRAFT - Supply Chain Options - Remdesivir V8 ASPR Comments.docx>

Sender:	Kadlec, Robert (OS/ASPR/IO) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=A182EDA693D040D3832BAE6EFCF7A255-KADLEC, ROB <Robert.Kadlec@hhs.gov>
Recipient:	Disbrow, Gary (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0fd5845defda4dc0bb45f8fac629cf09-Disbrow, Ga <Gary.Disbrow@hhs.gov>; Chang, William (HHS/OGC) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3cf70c842da144ab9bee61f353d932a0-Chang, Will <William.Chang@hhs.gov>; Redd, John (OS/ASPR/SPPR) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=9ba3fed4ee8646ec849a5a87136a24f6-Redd, John <John.Redd@hhs.gov>; Hassell, David (Chris) (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=aedbfb0ff96e4119ac7a3b3abaf71a3d-Hassell, Da <David.Hassell@hhs.gov>; Johnson, Lynn (ACF) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e08aee07c094419ab78da8fbb9b8be3e-Johnson, Ly <Lynn.Johnson@acf.hhs.gov>; Sherman, Susan (HHS/OGC) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=user161a2a33 <Susan.Sherman@HHS.GOV>; Stimson, Brian (HHS/OGC) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=338aa495176d4c92bb314f8f3f51d118-Stimson, Br <Brian.Stimson@hhs.gov>; Barry, Daniel J (HHS/OGC) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=user3e449ce0 <daniel.barry@hhs.gov>; Shuy, Bryan (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fdeb5ca04b6b4ed19fec2209b5f571e7-Shuy, Bryan <Bryan.Shuy@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group

	(FYDIBOHF23SPDLT)/cn=Recipients/cn=0851e89240324306b78740a4a60745e2-Johnson, Ro <Robert.Johnson@hhs.gov>; Bright, Rick (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=53034752f35a4317aa74f46348442d39-Bright, Ric <Rick.Bright@hhs.gov>
Sent Date:	2020/03/04 16:27:15
Delivered Date:	2020/03/04 16:27:16

From:	Ventura, Christy (OS/ASPR/BARDA) (CTR) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=9BB949CACA464329823CA3CF77654A06-VENTURA, CH <Christy.Ventura@hhs.gov>
To:	Bright, Rick (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=53034752f35a4317aa74f46348442d39-Bright, Ric <Rick.Bright@hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0fd5845defda4dc0bb45f8fac629cf09-Disbrow, Ga <Gary.Disbrow@hhs.gov>; Lambert, Linda (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ce6824b6a92a4a4e893ea7b54e17eb3c-Lambert, Li <Linda.Lambert@hhs.gov>
CC:	MCM Task Force /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=49010f8ab3ab4aed868a72c707c08d08-MCM Task Fo <MCMTaskForce@hhs.gov>
Subject:	Saturday updates for the MCM Task Force
Date:	2020/04/10 19:54:19
Priority:	Normal
Type:	Note

Rick, Gary, Linda,

See below for tomorrow's updates for the MCM Task Force. Enrollment numbers for the ACTT trial and for EUAs will be updated when we receive them. Please let us know if you have any concerns.

- ACTT Clinical trial to test remdesivir for treatment of COVID-19: 604 (+44) new patients at 64 (+3) sites, including 5 military treatment facilities, in last 24 hrs (target = 700)
- Requests for chloroquine/hydroxychloroquine from the SNS
  - 2 clinical trial requests received, 1 fulfilled
  - 23 (+1) EUA requests received, 22 shipped
  - Frequently Asked Questions document posted on FDA website
- Emergency Use Authorizations granted by FDA: 32 (+2) molecular diagnostic tests, 6 (+1) laboratory-developed tests, 1 antibody test, and 2 repurposed treatments (chloroquine, hydroxychloroquine)
- 2099 (+39) market research submissions and 199 (+3) CoronaWatch meetings held
- National Animal Health Laboratory Network labs have tested samples from a variety of species, including pets and animals at zoological sites
  - National Veterinary Services Laboratory confirmed the Bronx Zoo tiger infection using PCR and partial sequencing on April 4. Whole genome sequencing of the isolate is ongoing at national veterinary labs.

Christy

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Christy L. Ventura, Ph.D.
Tunnell Government Services
Executive Secretary, SARS-CoV-2 Medical Countermeasures Task Force

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Sent Date:	2020/04/10 19:54:18
Delivered Date:	2020/04/10 19:54:19

We understand that Gilead—or an authorized distributor shipping on behalf of Gilead (hereinafter, "Gilead")—is prepared to transport remdesivir in interstate commerce, within the United States and its territories, in order to preposition remdesivir to respond to the spread of COVID-19. Transport that is for use under an existing IND, such as that held by NIAID or by Gilead itself, does not present any legal issues. We understand, however, that Gilead is concerned about prepositioning for use under potential individual patient INDs that may issue after the drug is prepositioned.

I am requesting that Gilead go forward with the proposed prepositioning. I understand that the transport, in response to this request, will be considered by the Food and Drug Administration (FDA) to be "on behalf of a government entity" and, so long as the prepositioned product is intended to be held and not used, and is in fact held and not used, until FDA authorizes the drug for use under an appropriate regulatory mechanism, such as an investigational use (IND) (including Expanded Access INDs, such as individual patient expanded access for emergency use), an emergency use authorization (EUA), or approval of a New Drug Application (NDA), the transport is permitted under Section 564B of the Federal Food, Drug, and Cosmetic Act. FDA has informed me that Gilead may transport the drug under this provision, without waiting for approval of the shipment, provided that the company maintains the necessary documentation, including records reflecting the intent to hold and not use the product until such time as it may be used under an appropriate regulatory mechanism. I understand that Gilead has agreed to keep FDA informed of any shipment occurring under this mechanism.

Robert Kadlec, M.D,

Assistant Secretary for Preparedness and Response

U.S. Department of Health and Human Services

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Subject:	MCM Task Force updates: 04/10/2020
Date:	2020/04/09 19:49:45
Priority:	Normal
Type:	Note

Rick, Gary, Linda,

MCM Task Force updates for tomorrow, 4/10/2020, are below. I will update the ACTT numbers when I receive them. Please let us know if you have any concerns.

- ACTT Clinical trial to test remdesivir for treatment of COVID-19: 560 (+34) new patients at 61 (+3) sites, including 5 military treatment facilities, in last 24 hrs (target = 700)
- 2060 (+45) market research submissions and 196 (+6) CoronaWatch meetings held
- USDA is working to identify the range of animals that can become infected with SARS-CoV-2 and to determine if mosquitoes and midge could be vectors that could transmit the virus
- Requests for chloroquine/hydroxychloroquine from the SNS
    - 2 clinical trial requests received, 1 fulfilled
    - 22 (+11) EUA requests received, 22 (+11) shipped
- Emergency Use Authorizations granted by FDA: 32 (+2) molecular diagnostic tests, 6 (+1) laboratory-developed tests, 1 antibody test, and 2 repurposed treatments (chloroquine, hydroxychloroquine)

Thanks
Christy
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Sent Date:	2020/04/09 19:49:44
Delivered Date:	2020/04/09 19:49:45

SARS-CoV-2 Medical Countermeasures Task Force
Date: April 1, 2020
FOR OFFICIAL USE ONLY

Agencies reporting: BARDA, NIAID, DoD, FDA, USDA
Agencies not reporting: CDC, DHS

Talking Points for 1200 SLB and 1230 VTC

Accomplishments

- Clinical trial to test remdesivir for treatment of COVID-19: 307 (+33) new patients in last 24 hrs (target = 440)
- Antibody therapeutic trial: 461 (+84) new patients dosed, 45 (+4) sites in last 24 hrs (target = 400)
- Verbal report only: FDA did not grant EUA to Bodysphere Inc for its fingerstick test for COVID-19 antibodies that provides results in 2 minutes

Currently Working

- Continuing to enroll patients in clinical trials to evaluate vaccines and therapeutics for COVID-19
- Identifying and prioritizing next therapeutics to be included in clinical trials
- USDA is investigating the stability of SARS-CoV-2 in foods that could become contaminated by food handlers with COVID-19

Updates for 1700 Operations Summary and SLB

Line of Effort: Clinical Trials
Activity: Ongoing and proposed clinical trials to test treatments for COVID-19 and to measure immune responses over time
Limiting Factors: Swabs for sample collection and PPE for healthcare workers

Line of Effort: Vaccines
Activity: Development and manufacturing of mRNA vaccine
Limiting Factors: Reagents (lipids) for vaccine production; vials for packaging of sterile vaccine products

Active USG-sponsored Clinical Trials

	Candidate	Sponsor	Target Enrollment	Number of Sites	Enrollment
Adaptive COVID-19 Treatment Trial (ACTT)	Remdesivir	NIAID, Gilead	440	46 (+2)	307 (+33)
Sarilumab (anti-IL-6R mAb)	Sarilumab	BARDA, Regeneron	400	45 (+4)	461 (+84)
COVACTA: tocilizumab (anti-IL-6R mAb)	Actemra	BARDA, Genentech	330	TBD	TBD
Moderna mRNA-1273 Vaccine Phase I	mRNA-1273	NIAID, Moderna	45	2	30
Epidemiology, Immunology and Clinical Characteristics (EpICC) Study	N/A	DoD	TBD	4	8

- Adaptive COVID-19 Treatment Trial - NIAID
  - Currently remdesivir vs. placebo control (with options to add additional arms as needed)
  - Target enrollment = 440
  - Inclusion criteria – Confirmed SARS-CoV-2 infection (efficacy, but a little gray area PEP too)
  - Primary endpoint:
    - 8pt ordinal scale scored at Day 15, ranging from death to discharged with no limitation on activities and no requirement for home oxygen

- Sarilumab (Anti IL-6R mAb, aka Kevzara), Regeneron/Sanofi
  - Sarilumab high dose vs. Sariluman low dose vs. placebo control
  - Target enrollment = 400
  - Inclusion criteria – Confirmed SARS-CoV-2 infection AND evidence of pneumonia and severe disease (a true efficacy study)
  - Primary endpoints:
    - Time to resolution of fever for at least 48 hours
    - 6pt ordinal scale scored on Day 15, ranging from death to discharged

- mRNA-1273, Moderna
  - Phase I safety/immunogenicity
  - Target enrollment = 45
  - NHV study
  - Cohorts (all n=15, including 4 sentinels):
    - Low dose = 25ug
    - Medium dose = 100ug
    - High dose = 250ug

- EpICC Study, IDCRP
  - Observational natural history study
  - Clinical parameters being evaluated: risk factors, outcomes, virology, immunology

Proposed Clinical Trials

Vaccine / Therapeutic Product	Date / Range for Entry into Clinic
Convalescent plasma	Approx. late April/early May
IVIg	Late Spring 2020
Regeneron SARS-CoV-2 specific mAbs	June-July 2020 for treatment study in COVID-19 patients
Janssen screening leads	Early Summer 2020 or later; highly dependent on leads identified
SAb	June to mid-Summer 2020
Janssen Ad26 Vaccine	Phase 1: Q3-2020
Moderna mRNA Vaccine	Phase 1 enrollment: March 16, 2020 Phase 2: Q2-2020 (likely about June 2020)
Sanofi-Pasteur Vaccine	Phase 1: Q1-2021 (September/October 2020 provided to CBER)

Operational Task Force Updates – 04-10-20	
Data Analysis	Accomplishments in last 24 Hours 1. State data for all (50) states and (6) territories is integrated into the HHS GeoHealth Common Operating Picture (COP) to support decision making. April 9, 2020. 2. Completed state-level analysis of ED alert thresholds, identifying those states observing consistent reductions in the number of patients presenting to the ED with COVID-like symptoms. April 9, 2020. Currently Working 1. Finalizing a resource and planning capability to inform government decisions based on projections from the John Hopkins Infectious Disease Dynamics (JHIDD) COVID-19 model. ETA is April 10, 2020. 2. Developing National and State ventilation usage projections for May 1, 2020 and May 15, 2020 in order to inform decision makers. ETA is April 10, 2020. 3. Developing a resource allocation dashboard to inform supply and demand decision-making. ETA to V.1 is April 14, 2020.
Community Mitigation	Accomplishments in last 24 Hours 1. *Tiger Team:* Adjudicated comments and incorporated into final draft of Framework for Reopening America. 2. *Guidance:* Launched several new webpages (1) providing a snapshot of guidance for homeless and meal service providers for emergency and day shelters to highlight the most important points from various guidance. (https://www.cdc.gov/coronavirus/2019-ncov/community/homeless-shelters/homeless-service-provider-guidance.html) and (2) new FAQ on homelessness and COVID-19 (https://www.cdc.gov/coronavirus/2019-ncov/community/homeless-shelters/faqs.html) 3. *SLTT Engagement:* Ongoing engagement on a variety of topics, including technical assistance to correctional facilities across IL/LA/AR; with Children's Healthcare of Atlanta to assist with planning for re-opening of summer camps; with transportation systems for both transit users and pedestrians (Transportation for America, National Complete Streets, Growth America). 4. *At Risk Individuals:* Prepared Dr. Redfield for African American stakeholder call at WH (with Pence). The call will focus on data and epi and the differences in outcomes for that group with COVID19. Currently Working 1. *Tiger Team:* Draft Framework for Reopening America is with HHS for clearance; hope to send to White House today. Collaborating with Data & Analytics team to develop dashboard for SLTT to evaluate their mitigation risk category when determining timing and adjustment strategies for easing community mitigation measures. 2. *Guidance:* a. Gathering feedback on draft CDC Minority Health Outreach Strategy b. Gathering feedback on draft Community and Behavioral Health plan c. Finalizing high risk conditions table for CDC website d. Collaborating with Environmental Protection Agency on cleaning and sanitation guidance for the cleaning and sanitation of buildings, facilities, and public spaces e. Identifying best ways to build capacity to handle community mitigation requests coming from the field 3. *SLTT Engagement:* NRCC Chief asked about Ohio correctional facility engagement. CDC following up. 4. *At Risk Individuals:* CDC is developing a minority health outreach plan in collaboration with interagency.

Health Care Resilience	Accomplishments in last 24 Hours 1. *Continued rapid progress in supporting healthcare workforce:* 1) Hosting urgently requested COVID-19 Extension for Community Healthcare Outcomes (ECHO) Peer to Peer Learning session on *Ventilation Support Strategies* to share best practices from Louisiana and Providence Health (WA, OR) on 4/10 2) Hosting a Peer to Peer Learning Session: *EMS Patient Care and Operations* on 4/10 3) Aligned with Centers for Medicare and Medicaid Services (CMS) Administrator on scope of *workforce virtual toolkit* and placement on multiple platforms to include the Assistant Secretary for Preparedness and Response (ASPR) Technical Resources, Assistance Center, and Information Exchange (TRACIE) (aligns with TF Goal 2: Healthcare Workforce) 2. *Continuing to identify areas where providers, facilities, and states need more flexibility:* The Centers for Medicare and Medicaid Services (CMS) announced (4/9/20) they had temporarily suspended a number of rules in order to reduce supervision and certification requirements so that practitioners can be hired quickly and perform work to the fullest extent of their licenses (aligns with TF Goal 2: Healthcare Workforce) Currently Working 1. *Stakeholder Communications*: Planning additional stakeholder engagements to amplify the national preservation messaging with American Hospital Association (AHA), American Medical Association (AMA), and other professional healthcare professional associations within the next week (Supports HRTF Goal 2: Healthcare Workforce) 2. *Healthcare Workforce and Delivery*: Actively pursuing multiple methods for a patient distribution and resource sharing concept, with options spanning from a full federal-level implementation to purely private solutions (Supports HRTF Goals: Optimizing Healthcare Delivery and Healthcare Workforce)
Laboratory Diagnostics	Accomplishments in last 24 hours 1. Provided equipment data at public health labs to help NRCC prioritize allocations of Qiagen QIAmp extraction kits. 2. Met with IRR and Regions to understand shortfalls and issues and path forward for clarifying guidance. Currently Working 1. NRCC to IRR requests transition: Following up and getting clarification to Regions and state labs on what to do with outstanding open, outstanding requests for reagents, swabs, and other diagnostics currently sitting in FEMA Resource Request Board and developing talking points and graphics to communicate to Regions 2. Abbott ID shipment to IRR: Confirming shipments of Abbott ID now to IRR and replenishment strategy; also working to get HHS guidance for how non-public labs can go to the commercial market, including information on the supply in commercial market now, process for ordering from the commercial market, and anticipated turnaround time for shipment and delivery. Need to put communicate this information to governors and state directors 3. Testing for Food Sector personnel: Tracking down what are the requirements for COVID-19 testing for the food sector personnel and identifying strategy to support 4. High demand diagnostics products: Working with NRCC/RSS to get this list of high demand diagnostics being requested by states so Supply Chain can plan to have products available before we run out. a. Especially if the products are made in China, Malaysia, Japan, Thailand, Vietnam, etc. Products might be; Abbott test cartridges, PCR products, vial transport tubes, swabs, lancets, blood collection products, biohazard bags, body bags (there is a shortage of these), etc. 5. Serology testing: Continuing to work on the strategy for serological testing (blood testing for COVID-19 antibodies) to help America get back to work safely. 6. Online Format for Testing Data: Tracking down if the online form for collecting testing data for hospitals is live. The FEMA team has been receiving hospital spreadsheets and manually consolidating data from over 1,000 facilities daily over the past week. The online system will replace this manual consolidation.

	7. Working with FEMA chief counsel on their PRA questions regarding FEMA's involvement in the above HHS data call to hospitals. 8. Developing informational products to help Regions and public better understand the diagnostics world and also putting together a fact sheet about the Lab Diagnostics Task Force
Community Based Testing Sites (CBTS)	Accomplishments in last 24 hours 1. Since 3/23/20, there have been 89,244 screened and 81,076 tested at CBTS locations. 2. Since 3/23/20, 75,639 tests processed and received by the call center with 15,054 positive, 593 indeterminate, 59,991 negative 3. Issued transition or extension letters to all CBTS 1.0 locations, 17 locations will be extending until 5/30/20 Currently Working 1. Coordinating reporting structure for continuation of CBTS 1.0 sites extending past 4/10 and CBTS 2.0 private sites. 2. Reorganizing and restructuring task force and battle rhythm to account for added functional requirements of 2.0 and shifting requirements of remaining state sites. 3. Continue socialization and training on pre-decisional draft self-swab CONOPS to launch self-swab concept at all sites 4. Executing UCG approved Transition Plan (4/10 transition date) including proactive messaging strategy through EA. 5. Coordinating with Data Analytics TF to integrate CBTS 2.0 tracking & site selection decision making.
Supply Chain	Accomplishments in last 24 Hours 1. Airbridge: 3 Flights (1 (b)(3):4 (1 (b)(3):4 and (1) (b)(3):. 26 flights complete. 54 remaining flights scheduled. a. The 24th Airbridge flight departed Kuala Lumpur 09 Apr 20 1250 (L) and arrived i (b)(3): (b)(3) 09 Apr 20 at 1453 (L). The cargo is 7,770,000 gloves. b. The 25th Airbridge flight departed Kuala Lumpur on 09 Apr 20 at 0630 (L) and arrived in (b)(3):42 09 Apr 20 at 1645 (L). The cargo is 21, 555,000 gloves. c. The 26th Airbridge flight departed Singapore 09 Apr 20 at 0605 (L) and arrived in (b)(3):4 (b)(3) 09 Apr 20 at 2225 (L). The cargo is 25,350,000 gloves. 2. Defense Production Act (DPA): a. With the WHTF Process: UCG recommended to authorize USACE to use its preexisting DPA Title I priority rating in future contracts for the construction of alternate care facilities (medical) required for the COVID-19 response. b. With the WHTF Process: UCG recommended to request DPA priority rating "DO" for ventilator orders for Combat Medical, similar to the previously designated ventilator producers. 3. (ALLOCATION) A second distribution of 10.1M HCQ shipped 09 Apr 20: 1M to the VA Consolidated Mail Outpatient Pharmacy; 1M to DoD; 100K to the Henry Ford Hospital in Detroit, MI; and 8M to St. Louis, MO, Philadelphia, PA, Pittsburg, PA, Baltimore, MD, Washington D.C., Milwaukee, WI, Miami, FL, Houston, TX, Indianapolis, IN, and Baton Rouge, LA. Currently Working 1. Airbridge: 4 Flights (1 (b)(3):42 (1) (b)(3):42 (1 (b)(3):4 and (1) (b)(3):42 a. The 27th Airbridge flight is scheduled to depart Shanghai 10 Apr 20 at 1755 (L) and arrive in (b)(3):42 at 2155 (L). The anticipated cargo is 256,850 gowns. b. The 28th Airbridge flight is scheduled to depart Kuala Lumpur 10 Apr 20 at 1755 (L) and arrive in (b)(3):4 10 Apr 20 at 2205 (L). The anticipated cargo is 7,050,000 gloves. c. The 29th Airbridge flight is scheduled to depart Kuala Lumpur 10 Apr 20 at 2000 and arrive in (b)(3):42 10 Apr 20 at 1720. The anticipated cargo is 18,330,000 gloves.

	d. The 30th Airbridge flight is scheduled to depart Guangzhou 10 Apr 20 and arrive in (b)(3): (b)(3):42 10 Apr 20. The anticipated cargo is 6,940 N95 masks. The SCTF will confirm departure and arrival times with the NRCC Movement Control Cell on 10 Apr 20. 2. (PRESERVATION) Washington State will return 427 ventilators to HHS to be cleaned, re-kitted, and added back to the SNS inventory. The UCG will determine the reallocation of these ventilators to States in need. 3. On April 9, DLA awarded a contract to Battelle on behalf of HHS for 60 N95 decontamination system units for sanitation and reuse of N95 respirators. Each unit can sterilize 80,000 masks daily. Five systems have already deployed to NY, WA, MA, IL. 55 additional units are planned for deployment across the U.S. by early May.
Medical Countermeasure (MCM)	Accomplishments in last 24 Hours 1. ACTT Clinical trial to test remdesivir for treatment of COVID-19: 604 (+44) new patients at 64 (+3) sites, including 5 military treatment facilities, in last 24 hrs (target = 700) 2. Phase 1 safety trial for mRNA vaccine: 34 (+4) healthy volunteers enrolled (target = 45) 3. Requests for chloroquine/hydroxychloroquine from the SNS a. 2 clinical trial requests received, 1 fulfilled b. 22 (+11) EUA requests received, 22 (+11) shipped 4. Emergency Use Authorizations granted by FDA: 32 (+2) molecular diagnostic tests, 6 (+1) laboratory-developed tests, 1 antibody test, and 2 repurposed treatments (chloroquine, hydroxychloroquine) 5. 2060 (+45) market research submissions and 196 (+6) CoronaWatch meetings held Currently Working 1. Continuing to enroll patients in clinical trials to evaluate vaccines and therapeutics for COVID-19 2. USDA is working to identify the range of animals that can become infected with SARS-CoV-2 and to determine if mosquitoes and midge could be vectors that could transmit the virus
Continuity	Accomplishments in last 24 hours 1. Over past 24 hours, 4 Wireless Emergency Alert (WEA) messages related to COVID-19 sent by local authorities. a. 4 of 4 were reminders to stay home. b. 1 also announced closure of public areas (beaches and parks).

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Subject:	MCM Task Force updates for 4/9/2020: For review
Date:	2020/04/08 19:19:56
Priority:	Normal
Type:	Note

Rick, Gary, Linda,

Tomorrow's MCM Task Force updates are shown here. The ACTT clinical trial numbers will be updated when I receive the new numbers from Hilary Marston. I've shared the last bullet with Kim Sciaretta. Please let us know if you have any concerns.

Talking Points for 1200 and 1700 SLBs and 1230 VTC

Accomplishments

- ACTT Clinical trial to test remdesivir for treatment of COVID-19: 526 (+29) new patients at 58 (+1) sites, including 5 military treatment facilities, in last 24 hrs (target = 700)
- Requests for chloroquine/hydroxychloroquine from the SNS
  - 2 clinical trial requests received, 1 fulfilled
  - 11 EUA requests received and 11 (+6) shipped
- Emergency Use Authorizations granted by FDA: 30 (+3) molecular diagnostic tests, 5 (+1) laboratory-developed tests, 1 antibody test, and 2 repurposed treatments (chloroquine, hydroxychloroquine)
- 1964 (+42) market research submissions and 185 (+7) CoronaWatch meetings held
- Entered into new partnership to deploy wearable biosensor devices to COVID-19 patients across the military health system

Christy

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Sender:	Ventura, Christy (OS/ASPR/BARDA) (CTR) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=9BB949CACA464329823CA3CF77654A06-VENTURA, CH <Christy.Ventura@hhs.gov>
Recipient:	Bright, Rick (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=53034752f35a4317aa74f46348442d39-Bright, Ric <Rick.Bright@hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0fd5845defda4dc0bb45f8fac629cf09-Disbrow, Ga <Gary.Disbrow@hhs.gov>; Lambert, Linda (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ce6824b6a92a4a4e893ea7b54e17eb3c-Lambert, Li <Linda.Lambert@hhs.gov>; MCM Task Force /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=49010f8ab3ab4aed868a72c707c08d08-MCM Task Fo <MCMTaskForce@hhs.gov>
Sent Date:	2020/04/08 19:19:55
Delivered Date:	2020/04/08 19:19:56

From:	Hassell, David (Chris) (OS/ASPR/IO) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=AEDBFB0FF96E4119AC7A3B3ABAF71A3D-HASSELL, DA <David.Hassell@hhs.gov>
To:	Stimson, Brian (HHS/OGC) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=338aa495176d4c92bb314f8f3f51d118-Stimson, Br <Brian.Stimson@hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0fd5845defda4dc0bb45f8fac629cf09-Disbrow, Ga <Gary.Disbrow@hhs.gov>; Chang, William (HHS/OGC) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3cf70c842da144ab9bee61f353d932a0-Chang, Will <William.Chang@hhs.gov>; Kadlec, Robert (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a182eda693d040d3832bae6efcf7a255-Kadlec, Rob <Robert.Kadlec@hhs.gov>; Redd, John (OS/ASPR/SPPR) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=9ba3fed4ee8646ec849a5a87136a24f6-Redd, John <John.Redd@hhs.gov>; Johnson, Lynn (ACF) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e08aee07c094419ab78da8fbb9b8be3e-Johnson, Ly <Lynn.Johnson@acf.hhs.gov>; Sherman, Susan (HHS/OGC) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=user161a2a33 <Susan.Sherman@HHS.GOV>; Barry, Daniel J (HHS/OGC) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=user3e449ce0 <daniel.barry@hhs.gov>
CC:	Shuy, Bryan (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fdeb5ca04b6b4ed19fec2209b5f571e7-Shuy, Bryan <Bryan.Shuy@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0851e89240324306b78740a4a60745e2-Johnson, Ro <Robert.Johnson@hhs.gov>; Bright, Rick (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=53034752f35a4317aa74f46348442d39-Bright, Ric <Rick.Bright@hhs.gov>; Amin, Stacy (FDA/OC) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8575c6e15e234834be21c0f7e315bddc-stacy.amin. <Stacy.Amin@fda.hhs.gov>; Charrow, Robert (HHS/OGC) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=00531138af454ce3ac0b5885bead345f-Charrow, Ro <Robert.Charrow@hhs.gov>
Subject:	RE: Can you please send word doc for Remdesivir
Date:	2020/03/04 17:17:17
Priority:	Normal
Type:	Note

I Concur with Gary's comments.
One question is how this would be coordinated with the Canadians. Their government has questioned some of our CFIUS Issues (a DoD program with a US prime and a CA sub), so I could imagine something similar here.

-----Original Message-----
From: Stimson, Brian (HHS/OGC) <Brian.Stimson@hhs.gov>
Sent: Wednesday, March 4, 2020 4:51 PM
To: Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Chang, William (HHS/OGC)

<William.Chang@hhs.gov>; Kadlec, Robert (OS/ASPR/IO) <Robert.Kadlec@hhs.gov>; Redd, John (OS/ASPR/SPPR) <John.Redd@hhs.gov>; Hassell, David (Chris) (OS/ASPR/IO) <David.Hassell@hhs.gov>; Johnson, Lynn (ACF) <Lynn.Johnson@acf.hhs.gov>; Sherman, Susan (HHS/OGC) <Susan.Sherman@HHS.GOV>; Barry, Daniel J (HHS/OGC) <daniel.barry@hhs.gov>
Cc: Shuy, Bryan (OS/ASPR/IO) <Bryan.Shuy@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) <Robert.Johnson@hhs.gov>; Bright, Rick (OS/ASPR/BARDA) <Rick.Bright@hhs.gov>; Amin, Stacy (FDA/OC) <Stacy.Amin@fda.hhs.gov>; Charrow, Robert (HHS/OGC) <Robert.Charrow@hhs.gov>
Subject: RE: Can you please send word doc for Remdesivir

+ Stacy Amin. I am consolidating HHS legal comments with Gary's technical comments.

Also, I have discussed with Brian Shuy and Gary. I will send our consolidated comments to Seth, Mike Sinclair (NSC Legal), and May Davis (WH Counsel) so that there is a common understanding that two HHS components (ASPR and OGC) and providing informal technical comments on an NSC document.

Thanks.

Brian

-----Original Message-----
From: Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>
Sent: Wednesday, March 4, 2020 4:20 PM
To: Chang, William (HHS/OGC) <William.Chang@hhs.gov>; Kadlec, Robert (OS/ASPR/IO) <Robert.Kadlec@hhs.gov>; Redd, John (OS/ASPR/SPPR) <John.Redd@hhs.gov>; Hassell, David (Chris) (OS/ASPR/IO) <David.Hassell@hhs.gov>; Johnson, Lynn (ACF) <Lynn.Johnson@acf.hhs.gov>; Sherman, Susan (HHS/OGC) <Susan.Sherman@HHS.GOV>; Stimson, Brian (HHS/OGC) <Brian.Stimson@hhs.gov>; Barry, Daniel J (HHS/OGC) <daniel.barry@hhs.gov>
Cc: Shuy, Bryan (OS/ASPR/IO) <Bryan.Shuy@hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) <Robert.Johnson@hhs.gov>; Bright, Rick (OS/ASPR/BARDA) <Rick.Bright@hhs.gov>
Subject: RE: Can you please send word doc for Remdesivir

Team,

My edits/comments to the word document.

Gary

Gary L. Disbrow Ph.D.
Deputy Assistant Secretary
Director, Medical Countermeasure Programs Biomedical Advanced Research and Development Authority
BARDA Assistant Secretary for Preparedness and Response ASPR Department of Health and Human Services
330 Independence Avenue, S.W. Room 640 G Washington, D.C. 20201
Office: 202-260-0899
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email: Gary.Disbrow@HHS.gov

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Note to contractors: nothing in this e-mail is intended to constitute contractual direction or to impact cost, price, or schedule contained in the contract. If the contractor believes there is an impact, the contractor must disregard that portion of the communication and contact the Contracting Officer for direction

-----Original Message-----
From: Chang, William (HHS/OGC) <William.Chang@hhs.gov>
Sent: Wednesday, March 4, 2020 4:07 PM
To: Kadlec, Robert (OS/ASPR/IO) <Robert.Kadlec@hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Redd, John (OS/ASPR/SPPR) <John.Redd@hhs.gov>; Hassell, David (Chris) (OS/ASPR/IO) <David.Hassell@hhs.gov>; Johnson, Lynn (ACF) <Lynn.Johnson@acf.hhs.gov>; Sherman, Susan (HHS/OGC) <Susan.Sherman@HHS.GOV>; Stimson, Brian (HHS/OGC) <Brian.Stimson@hhs.gov>; Barry, Daniel J (HHS/OGC) <daniel.barry@hhs.gov>
Cc: Shuy, Bryan (OS/ASPR/IO) <Bryan.Shuy@hhs.gov>
Subject: RE: Can you please send word doc for Remdesivir

+ Stimson and Barry

Office of the General Counsel
U.S. Department of Health and Human Services
202-690-7741 (o)
(b)(6) (c)

-----Original Message-----
From: Kadlec, Robert (OS/ASPR/IO) <Robert.Kadlec@hhs.gov>
Sent: Wednesday, March 4, 2020 3:59 PM
To: Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Redd, John (OS/ASPR/SPPR) <John.Redd@hhs.gov>; Hassell, David (Chris) (OS/ASPR/IO) <David.Hassell@hhs.gov>; Johnson, Lynn (ACF) <Lynn.Johnson@acf.hhs.gov>; Sherman, Susan (HHS/OGC) <Susan.Sherman@HHS.GOV>; Chang, William (HHS/OGC) <William.Chang@hhs.gov>
Cc: Shuy, Bryan (OS/ASPR/IO) <Bryan.Shuy@hhs.gov>
Subject: FW: Can you please send word doc for Remdesivir

All please edit and comment as needed. Please send back to Seth NLT 1800

-----Original Message-----
From: Jonas, Seth H. EOP/NSC <Seth.H.Jonas@nsc.eop.gov>
Sent: Wednesday, March 4, 2020 3:52 PM
To: Kadlec, Robert (OS/ASPR/IO) <Robert.Kadlec@hhs.gov>
Cc: Cavanaugh, Brian J. EOP/NSC <Brian.J.Cavanaugh@nsc.eop.gov>
Subject: RE: Can you please send word doc for Remdesivir

Dear Bob,

Attached is the current draft. Some elements are still in flux. Your comments are appreciated.

Thanks,
Seth.

-----Original Message-----
From: Kadlec, Robert (OS/ASPR/IO) <Robert.Kadlec@hhs.gov>
Sent: Wednesday, March 4, 2020 3:12 PM
To: Jonas, Seth H. EOP/NSC <Seth.H.Jonas@nsc.eop.gov>
Cc: Cavanaugh, Brian J. EOP/NSC <Brian.J.Cavanaugh@nsc.eop.gov>
Subject: Can you please send word doc for Remdesivir

Seth have some comments and easiest way to transmit our suggested edits and comments. Best. Bob

Sent from my iPhone

Sender:	Hassell, David (Chris) (OS/ASPR/IO) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=AEDBFB0FF96E4119AC7A3B3ABAF71A3D-HASSELL, DA <David.Hassell@hhs.gov>
Recipient:	Stimson, Brian (HHS/OGC) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=338aa495176d4c92bb314f8f3f51d118-Stimson, Br <Brian.Stimson@hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0fd5845defda4dc0bb45f8fac629cf09-Disbrow, Ga <Gary.Disbrow@hhs.gov>; Chang, William (HHS/OGC) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3cf70c842da144ab9bee61f353d932a0-Chang, Will <William.Chang@hhs.gov>; Kadlec, Robert (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a182eda693d040d3832bae6efcf7a255-Kadlec, Rob <Robert.Kadlec@hhs.gov>; Redd, John (OS/ASPR/SPPR) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=9ba3fed4ee8646ec849a5a87136a24f6-Redd, John <John.Redd@hhs.gov>; Johnson, Lynn (ACF) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e08aee07c094419ab78da8fbb9b8be3e-Johnson, Ly <Lynn.Johnson@acf.hhs.gov>; Sherman, Susan (HHS/OGC) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=user161a2a33 <Susan.Sherman@HHS.GOV>; Barry, Daniel J (HHS/OGC) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=user3e449ce0 <daniel.barry@hhs.gov>; Shuy, Bryan (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fdeb5ca04b6b4ed19fec2209b5f571e7-Shuy, Bryan <Bryan.Shuy@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0851e89240324306b78740a4a60745e2-Johnson, Ro <Robert.Johnson@hhs.gov>; Bright, Rick (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=53034752f35a4317aa74f46348442d39-Bright, Ric <Rick.Bright@hhs.gov>; Amin, Stacy (FDA/OC) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8575c6e15e234834be21c0f7e315bddc-stacy.amin. <Stacy.Amin@fda.hhs.gov>; Charrow, Robert (HHS/OGC) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=00531138af454ce3ac0b5885bead345f-Charrow, Ro <Robert.Charrow@hhs.gov>
Sent Date:	2020/03/04 17:17:17

Senior Leadership Brief COVID-19

March 30, 2020 12:00 p.m. ET

For the most up to date COVID-19 data: https://geohealth.hhs.gov/arcgis/home/

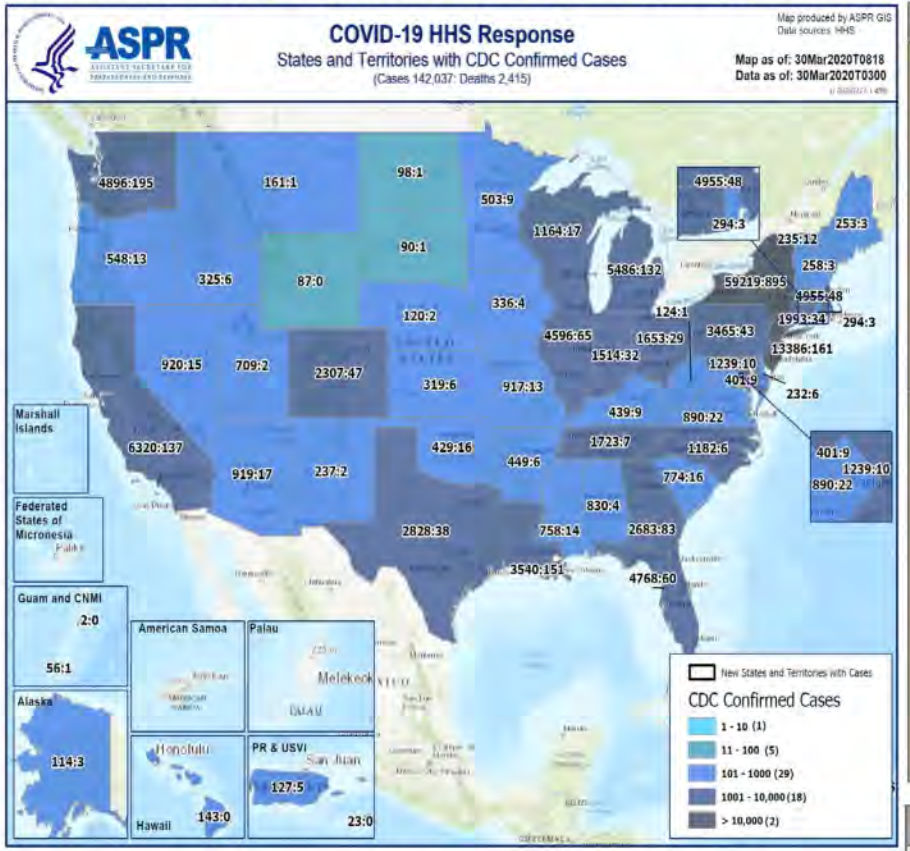
Current Situation: All 50 states, the District of Columbia, 5 territories, and 16 tribal nations are working directly with FEMA under the nationwide emergency declaration for COVID-19. FEMA is surging support to states seeing a steady increase of cases by using its Logistics Supply Chain Management System and working with HHS to deliver and track supplies and ventilators and expediting critical supplies from overseas to various US locations. FEMA is continuing to work with industry partners on distributing Personal Protective Equipment (PPE) as quickly as possible; prioritizing sending ventilators and Federal Medical Stations to areas in greatest need. FEMA Regional Administrators continue coordinating closely with governors, tribal leaders, state emergency managers, and state public health officials to address the COVID-19 threat. **CDC Update:** CDC confirmed and presumptive U.S. cases of COVID-19: 142,037 (+18,095) across 50 states and D.C., Guam, PR, CNMI, and USVI; Deaths: 2,415 (+276); Combined CDC and WHO reported global cases: 634,835 (+63,157); global deaths: 29,891 (+3,397); Countries with cases: 198 *(HHS Update, March 30, 2020, 8:06 a.m. ET)* **Testing:** 1,018,415 (+123,576) cumulative tests as of March 30.

Operational Task Forces

Medical Counter-Measure (MCM) Development	• FDA authorized emergency use of chloroquine and hydroxychloroquine to treat confirmed COVID-19 patients who cannot be enrolled in a clinical trial *(MCM TF Update, March 30 2020, 10:00 a.m. ET)* • Clinical trial to test antiviral remdesivir: 253 (+31) patients enrolled (440 target) at 37 sites *(MCM TF Update, March 30 2020, 10:00 a.m. ET)* • Antibody therapeutic trial: 259 (+100) patients dosed (400 target) at 39 (+4) sites *(MCM TF Update, March 30 2020, 10:00 a.m. ET)*
Health Care Resilience (HCR)	• Call with telehealth provider associations to assess current capacity, use patterns, and opportunities for engagement planned for March 30 *(HCR TF Update, March 30, 2020, 10:00 a.m. ET)* • Call with HHS and FEMA Regional Leadership on Alternate Care Strategies (ACS) implementation planned for March 30 *(HCR TF Update, March 30, 2020, 10:00 a.m. ET)*
Lab Diagnostics	• Coordinated with NIH and other partners to collect information from laboratories across the nation on reagents inventory, requirements, capacity, and burn rate *(LD TF Update, March 29, 2020, 3:45 p.m. ET)* • Engaged private sector to assess how UCG can support expanding test manufacturing capacity *(LD TF Update, March 29, 2020, 10:00 a.m. ET)*
Community Based Testing Sites (CBTS)	• 32,573 (+3,274) tested cumulatively since March 23 *(CBTS TF Update, March 30, 2020, 10:00 a.m. ET)* • Supplied additional barcodes to the sites and enabled all test results to be linked to testing sites *(CBTS TF Update, March 30, 2020, 10:00 a.m. ET)*
Supply Chain Stabilization	• 24 flights planned with 20 scheduled, and 1 complete. First flight departed Shanghai landed a(b)(3):4 March 29. Second flight departed Shanghai and will land in March 30 *(SC TF Update, March 30, 10:00 a.m. ET)* • Discussed overlapping tasks with HCR TF on March 29, Supply Chain TF will create strategic messaging campaign on the need to conserve PPE for healthcare facilities *(SC TF Update, March 30, 10:00 a.m. ET)* • Shipped 400K N95 mask rrived March 29 *(SC TF Update, March 30, 10:00 a.m. ET)* • Developing daily resource prioritization list for distribution allocation of nationally managed assets; priorities will be based on data modeling *(SC TF Update, March 30, 10:00 a.m. ET)*
Community Mitigation Measures	• Developing checklist for localities to identify their status in the community mitigation strategy, public health capacity, and medical capacity to enable the CDC to advise on mitigation strategies *(CMM TF Update, March 30, 2020, 10:00 a.m. ET)*
Continuity of Operations	• Restricted access to classified communications and IT capabilities limiting potential workflow *(COOP TF Update, March 28, 2020, 2:00 p.m. ET)*
Data and Analysis	• Provided state-level analysis of relative PPE burn rate, based on Emergency Department data *(DA TF Update, March 30, 2020, 10:00 a.m. ET)* • Proposed solution for acquiring estimated burn rate per state based on ICU occupancy and estimated PPEs per patient *(DA TF Update, March 30, 2020, 10:00 a.m. ET)*

(b)(3):42 U.S.C § 247d-6b(d)

(b)(3):42 U.S.C § 247d-6b(d)



Key Updates/Actions

FEMA HQ: National Watch Center Steady State; NRCC Level I (6:00 a.m. ET to 12:00 a.m. ET); Level 1: Region I, IX; Level 2: Regions II, III, IV, V, VI, VII, VIII, X; COVID-19 Major Declarations: 25 (+4) (GA, DC, KS, AL) *(FEMA Update, March 30, 2020, 8:30 a.m. ET)*

HHS: SOC at Level I (24/7) co-located with FEMA; CDC EOC activated, ACF OHSEPR at Level I *(FEMA National SITREP, March 21, 2020, 6:00 a.m. ET and HHS Update, March 20, 2020, 2:14 p.m. ET)*

Department of Homeland Security: 2,193 (+93) FEMA employees deployed to support COVID-19 Response; IMAT-A teams deployed to 25 states, territories, and DC; LNOs deployed to 37 states and territories *(FEMA Update, March 30, 2020, 8:30 a.m. ET)*

Health and Medical Lifeline

Public Health

Federal Assistance

- USACE received 8 (+1) mission assignments (MA) to design/build Alternate Care Sites (ACS) in NY (4 sites), CA (3 sites), IL (4 sites), WA (1 site), NJ, and MI; completed 218 (+37) ACS assessments; 1,121 (+48) USACE personnel supporting *(ESF-3 Update, March 30, 2020, 9:42 a.m. ET)*
- Immigration and Customs Enforcement monitoring 63 (-4) detainees across 22 (+1) facilities with 25 (+2) in isolation; 4 tested positive for COVID-19, detained population of 36,540 *(DHS Update, March 30, 2020, 9:41 a.m. ET)*

Medical Countermeasures

- FDA approved use of anesthesia machines as alternative intensive care unit (ICU) ventilators as a back-up option *(CISA Update, March 30, 2020, 5:00 a.m. ET)*
- First official testing of COVID-19 vaccine began March 27 by Emory University doctors, overseen by NIH *(CISA Update, March 30, 2020, 5:00 a.m. ET)*

Medical Care

Hospital Capacity

- HHS identified locations for thirty two 250 bed and nine 50 bed Federal Medical Stations (FMS) supporting 15 states with 8,450 beds; 6 delivered, 17 in route, 18 are processing *(HHS Update, March 28, 2020, 5:54 p.m. ET)*
- NY: Javits ACS in final preparation stages and expected to open March 30 with 1,000 beds *(HHS Update, March 29, 2020, 8:53 a.m. ET)*
- NY: USNS Comfort expected arrival in NY port March 30; initial operations begin March 31; providing 1,000 hospital beds and 1,200 medical personnel *(DoD Update, March 29, 2020, 1:44 p.m. ET)*
- CA: USNS Mercy hospital ship is in Port of Long Beach, CA and treating patients with 1,000 hospital beds *(CISA Update, March 30, 2020, 5:00 a.m. ET)*
- WA: 275 personnel from 62nd Medical Brigade plus augment units to staff ACS CenturyLink Field Event Center in Seattle; combined capability 248 total beds; initial operations March 31; fully operational April 7 *(DoD Update, March 29, 2020, 1:44 p.m. ET)*

Other Domestic Lifelines

Safety and Security

- Miami TSA and USCG working to repatriate 1,200 crew members from two cruise ships off the coast of Miami *(DHS Update, March 30, 2020, 9:45 a.m. ET)*
- 27 (+1) states and 12 tribes issued shelter-in-place orders *(CISA Update, March 30, 2020, 5:00 a.m. ET)*
- 588 U.S. Citizens and Lawful Permanent Residents repatriated from Peru, 558 from Honduras; as of March 27, 16,295 total repatriated; 30,617 potential repatriations remaining; 126 total flights planned *(International Affairs Advisor Update, March 30, 2020 9:30 a.m. ET)*

Transport

- Major U.S. Airlines beginning cargo-only flights *(CISA Update, March 30, 2020, 5:00 a.m. ET)*

FEMA

Senior Leadership Brief COVID-19

March 30, 2020 12:00 p.m. ET

For the most up to date COVID-19 data: https://geohealth.hhs.gov/arcgis/home/

Title 32 Status by State

Total Activated: 14,479 (+597)		T32 Approved: 11	T32 Requested: 23		
NGB Update, March 29, 1:47 p.m. ET					
State / Territory	# Personnel Activated	Title 32 Request Status	State / Territory	# Personnel Activated	Title 32 Request Status
AK	72	REQUESTED	MT	6	N/A
AL	N/A	N/A	NC	58	REQUESTED
AR	61	N/A	ND	27 (-4)	REQUESTED
AZ	1,023	REQUESTED	NE	45	N/A
CA	1028 (+61)	APPROVED	NH	65 (+20)	REQUESTED
CO	103	REQUESTED	NJ	277 (-11)	APPROVED
CT	12 (-88)	REQUESTED	NM	174 (+4)	REQUESTED
DC	256 (+50)	APPROVED*	NV	N/A	REQUESTED
DE	11	N/A	NY	2,015 (+152)	APPROVED
FL	1540 (+19)	APPROVED	OH	404 (+3)	REQUESTED
GA	310 (-35)	N/A	OK	29	REQUESTED
GU	55 (+2)	APPROVED	OR	26	N/A
HI	151 (+5)	N/A	PA	236 (-11)	N/A
IA	148	REQUESTED	PR	511	APPROVED
ID	37 (+1)	N/A	RI	481 (-36)	N/A
IL	310 (+140)	REQUESTED	SC	139	N/A
IN	305 (+160)	REQUESTED	SD	4	N/A
KS	60	N/A	TN	302 (+33)	REQUESTED
KY	78 (-14)	N/A	TX	N/A	N/A
LA	767 (+52)	APPROVED	UT	30	N/A
MA	297 (-4)	APPROVED	VA	123	REQUESTED
MD	1,634 (+42)	APPROVED	VI	N/A	REQUESTED
ME	43	REQUESTED	VT	78 (+11)	N/A
MI	291 (-33)	REQUESTED	WA	30	APPROVED
MN	112	REQUESTED	WI	447 (+9)	N/A
MO	82	REQUESTED	WV	31	REQUESTED
MS	151	REQUESTED	WY	4 (-3)	N/A

**District of Columbia is directly approved by the Secretary of the Army.*

Personal Protective Equipment

	N95 Respirators	Surgical Masks	Face Shield	Surgical Gowns	Coveralls	Gloves	Powered Air-Purifying Respirator (PAPR)	Ventilator	Federal Medical Station Beds
Quantity	11,637,877 (+4,518,641)	26,371,427 (+10,727,450)	5,275,920 (+2,332,707)	4,380,297 (+1,920,159)	144,011 (+131,895)	22,425,261 (+13,773,245)	50	7,140 (+640)	6,700 (+1,250)

Personal Protective Equipment distributed by Strategic National Stockpile to 63 locations including one tribe *(CDC Update, March 30, 2020, 5:25 a.m. ET)*

COVID-19 BARDA Overview

Date: March 31, 2020

1. Diagnostics
   - BARDA has partnered with Hologic, DiaSorin, Qiagen, MesaBioTech, GenMark, Cepheid, Luminex (NxTag and Aries), and Vela to develop diagnostic tests to detect 2019-nCoV
   - 20 Diagnostics with EUA

2. Therapeutics
   - Genentech Tocilizumab (α-IL-6R) clinical trial for COVID-19 targeting start early April
     i. Targeting shipment of drug product to clinical sites 03/31/2020
   - Regeneron adaptive phase 2/3 study of Sarilumab (α-IL-6R antibody) for COVID-19
     i. 40 sites activated (13 in NY, 4 in NJ, 3 NJ, 2 in CA, FL, GA, PA TX, WA, 1 each in CO, CT, DC, IL, MI, MN, OK, VA)
     ii. 301/400 Patients enrolled and dosed as of 03/29/2020
       1. Phase 2 enrollment complete
   - Regeneron has identified mAbs that neutralize SARs-CoV-2 virus in vitro
     i. 42 Lead mAbs candidates being further screened for neutralizing activity
     ii. Scaling up manufacturing of leads for additional screening
   - Janssen validation phase on going for high throughput screening
     i. Hit identified during validation

3. Vaccines
   - Sanofi Pasteur is pursuing a vaccine construct that is thought to be more stable.
     i. TEP scheduled for Monday 3/30
   - Janssen preliminary non-clinical data in immunogenicity mice and NHP virus challenge model

1. **BARDA Diagnostics**
    1. **Meeting 03/30/2020 at request of S1 regarding draft policy document for serology tests**
    2. **Current Diagnostic EUAs**
        i. 20 Diagnostics with (EUA):
            1. https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations#covid19ivd
        ii. Abbott COVID-ID test new point of care with results in less than 15 minutes
        iii. **Cepheid**, GenMark, **DiaSorin, Mesa BioTech** systems do not need the extraction reagents that are in short supply: "Sample to Answer" tests
    3. **Cepheid 2019-nCov diagnostic assay**
        i. **No Updates**
    4. **Cue**
        i. **No Updates**
    5. **[PROCUREMENT SENSITIVE] EZ-BAA submissions**
        i. **Hologic**
            1. **No update**
        ii. **DiaSorin Molecular**
            1. **EUA addendum approved to add transport media types**
            2. **A total of 1,219 kits (29,256 tests) shipped as of 03/30/2020**
        iii. **MesaBioTech Point of care (hand-held device)**
            1. **No update**
        iv. **Qiagen [Company Confidential]**
            1. **EUA submitted 03/26/2020**
        v. **Genmark**
            1. **SOW adds SARS-CoV-2 assay to existing respiratory panel**
        vi. **Luminex Corp**
            1. **Luminex NxTAG awarded 03/26/2020; EUA Awarded 03/27/2020**
            2. **Luminex Aries awarded 03/27/2020**
        vii. **Vela Diagnostics project kick off 03/31/200**
        viii. **Pending EZ-BAA contract actions**
            1. **Orasure and Rheonix: Stage 2 Negotiations**
2. **BARDA Therapeutics**
    1. **Regeneron**
        i. **2019-nCoV specific mAb on track to have leads by end of April and production in August 2020**
            1. **42 Lead mAbs candidates being further screened for neutralizing activity**
            2. **Scaling up manufacturing of leads for additional screening**
            3. **Manufacturing slots in place**
        ii. **Regeneron adaptive phase 2/3 study of Sarilumab (α-IL-6R antibody) for COVID-19**

1. 40 sites activated (13 in NY, 4 in NJ, 3 NJ, 2 in CA, FL, GA, PA TX, WA, 1 each in CO, CT, DC, IL, MI, MN, OK, VA)
2. 301/400 Patients enrolled and dosed as of 03/29/2020
3. Completed Phase 2 enrollment, DMC meeting 04/04/2020

2. Genentech IL-6R antibody (Tocilizumab) clinical trial in COVID-19 patients
   i. Targeting shipment of drug product to clinical sites 03/31/2020
   ii. Targeting a first subject dosed by 04/03/2020
3. Antiviral screening
   i. Janssen antiviral therapeutics screening
      1. Identified a hit, and follow up discussions held on 3/29/2020
         a. Possible phase 1 clinical trial with hit compound
4. SAb Biotherapeutics – Polyclonal antibody product
   i. Funds obligated to IAA
      1. Bovine immunogenicity studies underway
      2. Clinical trial planned for late June/July
5. Grifols (HIG)
   i. IAA signed by BARDA leadership; routed to DoD for signature
6. American Red Cross
   i. Letter contract signed 03/27/2020 to develop systems/procedures to collect/distribute convalescent plasma
7. UMSOM animal model and drug screening awarded 03/27/2020

3. BARDA Vaccines
   1. Two SSA briefings 03/30/2020: Inovio and Vaccitech
   2. Looking for guidance from FDA on preservative exemption
   3. Janssen Ad26 vaccine
      i. Modification on 03/27/2020 for vaccine ad26 vaccine development to licensure
      ii. Targeting to identify lead candidate(s) by end of March.
   4. Sanofi Pasteur
      i. SP indicated to FDA that they expect to enter Phase 1 study Sept/Oct 2020.
      ii. TEP scheduled for 3/30/2020 for proposal under Protein Sciences 5I IDIQ contract.
   5. Moderna
      i. Draft contract in review
   6. Merck and Pfizer proposals expected 03/30/2020
4. BARDA Rapidly Deployable Technology
   1. Reviewing draft MOU with VA
   2. 1 EZ BAA in negotiations/1 EZ BAA reviewing Stage II proposal/ 1 EZ BAA stage 1 under review
5. Sample Sharing Working Group engaging to identify PBMCs for product developers
   i. Established mechanism with NYU to deliver samples from COVID-19 patients
   ii. 15 acute patients have been enrolled at NYU
      1. one day-14 convalescent patient enrolled

2. Additional convalescent patients (day 14-28) expected to be enrolled this week.

6. **BARDA Clinical**
    1. Gilead Simple Trial (Remdesivir)
        i. Severe protocol: as of 3/27/2020, 400/400 enrolled.
            1. DSMB will now review study data now
        ii. Mild-moderate: as of 3/27/2020, 119/600 enrolled.
    2. **NIAID RCT Trial enrollment >150; blinded analysis of endpoints scheduled for April**
        i. **Engaging DSMB for guidance on sample size**
    3. **Chloroquine/Hydroxychloroquine EUA**
        i. **EUA letter of authorization was signed off by the FDA on 03/28/2020.**
        ii. **One million doses of chloroquine donated by Bayer arrived to the SNS**
7. **BARDA Non-clinical**
    1. **Nonclinical RTOR recommendation brief for leadership approval being developed**
        i. **4 Task Order base awards made 03/28, 29, 30/2020**
            1. **Base will cover reagents and assay preparation**
            2. **Options targeting to be awarded week of 03/30/2020 will include animal models**
            3. **Coordinating with NIAID to avoid redundancy in efforts**
    2. **Ensuring availability of NHPs for non-clinical studies (Embargo on species from China)**
8. **BARDA RQA**
    1. **Standing weekly meetings scheduled with CDER and CBER**
    2. **SAB Biotherapeutics. Meeting requested to discuss need for toxicology studies**
9. **BARDA Manufacturing**
    1. **TAMUS is reworking their proposal with IDRI and iBIO**
        i. **Targeting to submit through the BAA 03/30/2020**
    2. **Working with Phlow on potential OTA.**

From:	Mike Bowen <mike@prestigeam.com>
To:	Wallace, Rodney (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b4654f8f0c0f4623b9e47465e9e1037a-Wallace, Ro <Rodney.Wallace@hhs.gov>; Patel, Anita (CDC/DDID/NCIRD/OD) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=1281344f1dab4bd28aff1cf48cc25420-Patel, Anit <bop1@cdc.gov>; Bright, Rick (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=53034752f35a4317aa74f46348442d39-Bright, Ric <Rick.Bright@hhs.gov>; Wolf, Laura (OS/ASPR/SIIM) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=userb232d38c <Laura.Wolf@hhs.gov>
Subject:	Mask Fit Improvement - Used in the field by healthcare worker. Emergency CDC approval requested.
Date:	2020/03/24 06:20:20
Importance:	High
Priority:	Urgent
Type:	Note

Here are the patent sketches of the device I described in my previous email. I'm sending them in case the video link didn't work.

Figure 2 shows the construction of my simple device. Top and bottom layers are paper release liners. Middle layer is a double sided skin friendly pressure sensitive medical grade adhesive.

Peel off top layer, stick to mask, peel off bottom layer leaving only an adhesive perimeter seal around the edge of the mask.

This device will turn a high quality surgical mask into something close to an N95 respirators. Today's high quality surgical masks have high filtration, but they have loose fit. This device fixes the fit problem. It's quick, economical and effective.

The raw materials are plentiful and I can make millions of these devices per day. Please tell me how to get emergency CDC approval to sell it. The benefit is self-evident. The risks are low: Possible skin rash for people allergic to time-proven medical grade adhesive. We'll select a gentle adhesive that will adhere to skin but won't be hard to remove.

Sincerely,

Mike Bowen

Phone: (b)(6)
Fax: 817-886-2733

PRESTIGE AMERITECH
7201 Iron Horse Blvd.
North Richland Hills, TX 76180

From: Betsy Dowd <Betsy@bkdowdlaw.com>
Sent: Monday, March 23, 2020 4:16 PM
To: Mike Bowen <mike@prestigeam.com>
Subject: application for filing attached
Importance: High

Hi Mike,
Please take a look. I can file anytime up to midnight to get today's filing date, but I think I will file by 6:30 my time. If there are changes that need to be made and you have already disclosed it, I am not worried. We can just refile with the corrections or changes, and still have the benefit of what is disclosed here.
There is also a 1-year window for filing from "first use" , although we don't want to risk someone else filing before you.
I will prepare the documents for filing. In the meantime, read fast !!

Betsy Kingsbury Dowd, Esq.

65 AIR PARK DRIVE
SUITE 7
RONKONKOMA, NY 11779

PH: (631) 676-2047
Cell: (b)(6)

Betsy@BKDowdLaw.com

Sender:	Mike Bowen <mike@prestigeam.com>
Recipient:	Wallace, Rodney (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b4654f8f0c0f4623b9e47465e9e1037a-Wallace, Ro <Rodney.Wallace@hhs.gov>; Patel, Anita (CDC/DDID/NCIRD/OD) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=1281344f1dab4bd28aff1cf48cc25420-Patel, Anit <bop1@cdc.gov>; Bright, Rick (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=53034752f35a4317aa74f46348442d39-Bright, Ric <Rick.Bright@hhs.gov>; Wolf, Laura (OS/ASPR/SIIM) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=userb232d38c <Laura.Wolf@hhs.gov>
Sent Date:	2020/03/24 06:18:52
Delivered Date:	2020/03/24 06:20:20

From:	Oshansky, Christine (OS/ASPR/BARDA) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=D7BD764440B44B06AF644CDCD22E42D6-OSHANSKY, C <Christine.Oshansky@hhs.gov>
To:	Bright, Rick (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=53034752f35a4317aa74f46348442d39-Bright, Ric <Rick.Bright@hhs.gov>; Walker, Robert (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7a02e128c60f4a7195532a1545af9556-Walker, Rob <Robert.Walker@hhs.gov>; Armstrong, Kimberly (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5b778c7e17734740b14fbae4d3ed652c-Armstrong, <Kimberly.Armstrong@hhs.gov>; Houchens, Christopher (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7ac94a574bd04528b7c91bbd61893975-Houchens, C <Christopher.Houchens@hhs.gov>
CC:	Lambert, Linda (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ce6824b6a92a4a4e893ea7b54e17eb3c-Lambert, Li <Linda.Lambert@hhs.gov>; Blatner, Gretta (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=623cb123c2324236b1db6fb9153e0bbf-Blatner, Gr <Gretta.Blatner@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0851e89240324306b78740a4a60745e2-Johnson, Ro <Robert.Johnson@hhs.gov>
Subject:	RE: Gilead supersizes remdesivir trials, changes primary endpoint | FierceBiotech
Date:	2020/04/09 21:49:31
Priority:	Normal
Type:	Note

Hi Rick,

- I'm looking into a process to improve our tracking of COVID19 clinical trials. The article noted in your email below seem to have gleaned the information from monitoring the clinicaltrials.gov registry updates.
- On April 6, 2020, the clinicaltrials.gov trial pages for NCT04292899 (severe patients) and NCT04292730 (moderately severe patients) were updated (see table below)
- The change may allow greater power to detect an effect and/or may allow detection of modest positive effects using an ordinal scale

	Severe patient study (NCT04292899)		Moderately severe patient study (NCT04292730)	
	previous design	modified design	previous design	modified design
N	600	1600	400	2400
Primary Endpoint	normalization of temperature and oxygen saturation through Day 14	Clinical status assessed by a 7-point	time to discharge in participants with moderate	Clinical status assessed by a 7-point ordinal scale on Day 11

		ordinal scale on Day 14	coronavirus disease	

Thanks,
Christine

-----Original Message-----
From: Bright, Rick (OS/ASPR/BARDA) <Rick.Bright@hhs.gov>
Sent: Thursday, April 9, 2020 11:42 AM
To: Oshansky, Christine (OS/ASPR/BARDA) <Christine.Oshansky@hhs.gov>; Walker, Robert (OS/ASPR/BARDA) <Robert.Walker@hhs.gov>; Armstrong, Kimberly (OS/ASPR/BARDA) <Kimberly.Armstrong@hhs.gov>; Houchens, Christopher (OS/ASPR/BARDA) <Christopher.Houchens@hhs.gov>; Bright, Rick (OS/ASPR/BARDA) <Rick.Bright@hhs.gov>
Cc: Lambert, Linda (OS/ASPR/BARDA) <Linda.Lambert@hhs.gov>; Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) <Robert.Johnson@hhs.gov>
Subject: Gilead supersizes remdesivir trials, changes primary endpoint | FierceBiotech

Team. I need to be made aware of these things before they are in the media. Let's find a process that links updated to the clinical and therapeutics WGs where trials and therapeutics are being tracked. Thanks.

Please send me some insight and talking points on these changes as soon as possible today. Thanks. Rick.

https://www.fiercebiotech.com/biotech/gilead-supersizes-remdesivir-trials-changes-primary-endpoint

Sender:	Oshansky, Christine (OS/ASPR/BARDA) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=D7BD764440B44B06AF644CDCD22E42D6-OSHANSKY, C <Christine.Oshansky@hhs.gov>
Recipient:	Bright, Rick (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=53034752f35a4317aa74f46348442d39-Bright, Ric <Rick.Bright@hhs.gov>; Walker, Robert (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7a02e128c60f4a7195532a1545af9556-Walker, Rob <Robert.Walker@hhs.gov>; Armstrong, Kimberly (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5b778c7e17734740b14fbae4d3ed652c-Armstrong, <Kimberly.Armstrong@hhs.gov>; Houchens, Christopher (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7ac94a574bd04528b7c91bbd61893975-Houchens, C <Christopher.Houchens@hhs.gov>; Lambert, Linda (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ce6824b6a92a4a4e893ea7b54e17eb3c-Lambert, Li <Linda.Lambert@hhs.gov>; Blatner, Gretta (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=623cb123c2324236b1db6fb9153e0bbf-Blatner, Gr <Gretta.Blatner@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group

	(FYDIBOHF23SPDLT)/cn=Recipients/cn=0851e89240324306b78740a4a60745e2-Johnson, Ro <Robert.Johnson@hhs.gov>
Sent Date:	2020/04/09 21:49:28
Delivered Date:	2020/04/09 21:49:31

COVID-19 Daily News Summary
Office of Global Research
March 24, 2020; Current as of 4:00 p.m., EST

WHO Situation Report (compiled daily): March 24

372,757 confirmed cases globally (39,827 new)
16,231 deaths globally (1,772 new)

WHO Dashboard: Novel coronavirus (COVID-19) Situation*:

Globally: 195 countries
375,498 cases
16,362 deaths
*(ongoing compilation, but real-time reporting may lag)

U.S. CDC Update:

- Total U.S. Cases: 44,183
  - 479 are travel-related
  - 569 are person-to-person
  - 43,135 are under investigation
- **Total deaths:** 544

** **Includes date from** 50 states, DC, Puerto Rico, Guam, and US Virgin Islands); Data include both confirmed and presumptive positive cases of COVID-19 reported to CDC or tested at CDC since January 21, 2020, with the exception of testing results for persons repatriated to the United States from Wuhan, China and Japan. State and local public health departments are now testing and publicly reporting their cases. In the event of a discrepancy between CDC cases and cases reported by state and local public health officials, data reported by states should be considered the most up to date.

RESEARCH NEWS

Epidemiology/modeling

- A modelling study conducted in a simulated Singapore setting estimates that a combined approach of physical distancing interventions, including quarantine (for infected individuals and their families), school closure, and workplace distancing, is most effective at reducing the number of SARS-CoV-2 cases compared with other intervention scenarios included in the study. Quarantine plus workplace measures presented the next best option for reducing SARS-CoV-2 cases, followed by quarantine plus school closure, and then quarantine only. All intervention scenarios were more effective at reducing cases than no intervention. (Lancet Inf. Dis., March 23, 2020)
- The Chinese province of Hubei, where the coronavirus pandemic began, will allow most of its 60 million residents to leave starting March 25, ending nearly two months of lockdown and suggesting that the public measures imposed have worked to control the outbreak. (*New York Times*, March 24, 2020)
- An international team of researchers has developed a platform to aid the analysis and tracking of the COVID-19 epidemic. The researchers collected and curated individual-level data from national, provincial, and municipal health reports, as well as additional information from online reports. All data are geo-coded and, where available, include symptoms, key dates (date of onset, admission, and confirmation), and travel history. The researchers collected, and continue

to curate, a real-time database of individual-level epidemiological data and have designed an interactive web application that can be visualized at https://www.healthmap.org/covid-19/ (Bo Xu, Moritz U. G. Kraemer et al. *Scientific Data* **volume 7**, Article number: 106, 2020)

Clinical

- The American Academy of Otolaryngology Head & Neck Surgery has proposed adding anosmia (loss of sense of smell) and dysgeusia (distortion of the sense of taste) to the list of screening items for potential COVID-19 patients. Anecdotally, these symptoms have been reported among some patients who've tested positive, and in some cases, anosmia has been reported as the only symptom. At a news briefing on Monday, World Health Organization officials said they are investigating loss of smell and taste as potential early symptoms. (*NEJM*, March 23, 2020)

Vaccines

- On March 18, the U.S Food and Drug Administration and the European Medicines Agency (EMA) jointly chaired the first global regulators meeting to discuss regulatory strategies to facilitate the development of SARS-CoV-2 vaccines. The purpose of this discussion was to promote, to the extent possible, regulatory convergence with the goal of streamlining global SARS-CoV-2 vaccine development.
- Dynavax and Clover Biopharmaceuticals announced on March 24 that they have entered into a research collaboration to develop a vaccine candidate to prevent COVID-19. Clover is advancing evaluation of its protein-based coronavirus vaccine candidate (COVID-19 S-Trimer) in preclinical studies. Dynavax is providing technical expertise and the company's proprietary toll-like receptor 9 (TLR9) agonist adjuvant, CpG 1018, to support this initiative.
- Ology Bioservices Inc., and Inovio Pharmaceuticals Inc., (NASDAQ: INO) announced March 24 that the Department of Defense (DOD) has awarded Ology Bioservices an $11.9 million contract to work with Inovio to manufacture Inovio's COVID-19 DNA vaccine (INO-4800).

Treatments

- Gilead's experimental drug remdesivir, being studied as a potential treatment for COVID-19, received orphan drug designation from FDA on March 23. Orphan drug status provides a seven-year market exclusivity period, as well as tax and other incentives for drug companies developing treatments for rare diseases that affect fewer than 200,000 people. Gilead has temporarily emergency access to remdesivir on hold due to an exponential increase in compassionate-use requests for the drug. (*Reuters*, March 24, 2020)

Diagnostics

- Mesa Biotech announced March 24 that it has received Emergency Use Authorization (EUA) from the U.S. FDA for its Accula™ SARS-CoV-2 Test, which gives COVID-19 diagnostic results in 30 minutes. The testing platform, designed for point-of-care (POC) infectious disease diagnosis, enables 'near patient' testing outside of the central laboratory.

Technology/Resources

- The *New York Times* has developed an interactive tool for tracking COVID-19 deaths by country and U.S. state over time. The tool, which is updated daily, uses data from WHO, JHU, National

Health Commission of People's Republic of China, and local governments. https://www.nytimes.com/interactive/2020/03/21/upshot/coronavirus-deaths-by-country.html

- VirusTrack.live, a real-time pandemic tracker for COVID-19, was launched on March 24. The free and open-access tool cross-references data from repositories such as JHU Center for Science Systems and Engineering, BNO News, WHO COVID-2019 Situation Reports, U.S. CDC, Community Benefit Insight, and U.S. county data aggregators. VirusTrack is a non-commercial, non-advertising, open source project. The project, founded by software developers Eugene Ciurana and Andrew Lombardi of AI Smartech and Juvid Aryaman of Farad.ai, invites contributions from the general public, NGOs and government officials, health scientists, and technologists. https://virustrack.live
- *The Atlantic* has also launched a tracker to provide comprehensive information on the scope of the spread of COVID19 across the US. The website includes data on deaths and the number of people tested. (The COVID Tracking Project https://bit.ly/33GYolc)

RESEARCH PUBLICATIONS

NIAID-supported studies

- Tai, W., He, L., Zhang, X. *et al.* Characterization of the receptor-binding domain (RBD) of 2019 novel coronavirus: implication for development of RBD protein as a viral attachment inhibitor and vaccine. *Cell Mol Immunol* (2020). https://doi.org/10.1038/s41423-020-0400-4
  - Grants: **R01AI137472** and **R01AI139092**
- Zhang, C., Zheng, W., Huang, X., Bell, E.W., Zhou, X., and Zhang, Y. Protein structure and sequence re-analysis of 2019-n-CoV genome refutes snakes as its intermediate host or the unique similarity between its spike protein insertions and HIV-1. *J. Proteome Res.* 2020 March 22. DOI: 10.1021/acs.jproteome.0c00129
  - Grant: **AI134678**
- Hu, T. Y., Frieman, M., & Wolfram, J. (2020). Insights from nanomedicine into chloroquine efficacy against COVID-19. *Nature nanotechnology*, 10.1038/s41565-020-0674-9. Advance online publication. https://doi.org/10.1038/s41565-020-0674-9
  - Grant numbers: **AI122932 , AI113725 , AI126361, AI52318**
- Bedford, J., Enria, D., Giesecke, J., Heymann, D. L., Ihekweazu, C., Kobinger, G., **Lane, H. C.,** Memish, Z., Oh, M. D., Sall, A. A., Schuchat, A., Ungchusak, K., Wieler, L. H., & WHO Strategic and Technical Advisory Group for Infectious Hazards (2020). COVID-19: towards controlling of a pandemic. Lancet (London, England), S0140-6736(20)30673-5. Advance online publication. https://doi.org/10.1016/S0140-6736(20)30673-5
  - NIAID Director of Clinical Research, **Cliff Lane**, member of WHO Strategic and Technical Advisory Group for Infectious Hazards

PubMed queries

March 24, 2020 https://www.ncbi.nlm.nih.gov/pubmed/?cmd=historysearch&querykey=4

NON-PEER-REVIEWED PUBLICATIONS

Epidemiology/Modeling

- Jose Alvarez-Ramirez Sr., MONICA MERAZ. Role of meteorological temperature and relative humidity in the January-February 2020 propagation of 2019-nCoV in Wuhan, China. medRxiv 2020.03.19.20039164; doi: https://doi.org/10.1101/2020.03.19.20039164
- Alex Arenas, Wesley Cota, Jesus Gomez-Gardenes, Sergio Gómez, Clara Granell, Joan T. Matamalas, David Soriano-Panos, Benjamin Steinegger. A mathematical model for the spatiotemporal epidemic spreading of COVID19. medRxiv 2020.03.21.20040022; doi: https://doi.org/10.1101/2020.03.21.20040022
- Xiang Bai, Cong Fang, Yu Zhou, Song Bai, Zaiyi Liu, Qianlan Chen, Yongchao Xu, Tian Xia, Shi Gong, Xudong Xie, Dejia Song, Ronghui Du, Chunhua Zhou, Chengyang Chen, Dianer Nie, Dandan Tu, Changzheng Zhang, Xiaowu Liu, Lixin Qin, Weiwei Chen. Predicting COVID-19 malignant progression with AI techniques. medRxiv 2020.03.20.20037325; doi: https://doi.org/10.1101/2020.03.20.20037325Diego Caccavo. Chinese and Italian COVID-19 outbreaks can be correctly described by a modified SIRD model. medRxiv 2020.03.19.20039388; doi: https://doi.org/10.1101/2020.03.19.20039388
- Elizabeth T Chin, Benjamin Q Huynh, Nathan C Lo, Trevor Hastie, Sanjay Basu. Healthcare worker absenteeism, child care costs, and COVID-19 school closures: a simulation analysis. medRxiv 2020.03.19.20039404; doi: https://doi.org/10.1101/2020.03.19.20039404
- Flavio Codeco Coelho, Raquel Martins Lana, Oswaldo G Cruz, Claudia T Codeco, Daniel Villela, Leonardo S Bastos, Ana Pastory y Piontti, Jessica T Davis, Alessandro Vespignani, Marcelo F.C. Gomes. Assessing the potential impacts of COVID-19 in Brasil: Mobility, Morbidity and Impact to the Health System. medRxiv 2020.03.19.20039131; doi: https://doi.org/10.1101/2020.03.19.20039131
- Jacob Deasy, Emma Rocheteau, Katharina Kohler, Daniel J. Stubbs, Peitro Barbiero, Pietro Liò, Ari Ercole. Forecasting ultra-early intensive care strain from COVID-19 in England. medRxiv 2020.03.19.20039057; doi: https://doi.org/10.1101/2020.03.19.20039057
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- CDC Coronavirus Web Page: https://www.cdc.gov/coronavirus/2019-ncov/whats-new-all.html
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Compiled by Nancy Touchette

The information in this summary is compiled from publicly sourced information. The information in this report does not reflect the opinions of the National Institute of Allergy and Infectious Diseases (NIAID). NIAID shall not accept liability for any statements made that are the sender's own and not expressly made on behalf of the NIAID by one of its representatives.

From:	Walker, Robert (OS/ASPR/BARDA) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7A02E128C60F4A7195532A1545AF9556-WALKER, ROB <Robert.Walker@hhs.gov>
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Subject:	RE: Update on the HHS COVID-19 GL
Date:	2020/04/09 13:36:59
Priority:	Normal
Type:	Note

Rick
The relevant documents are attached (next to final). These are the treatment guidelines produced by the expert panel assembled by Cliff Lane, Henry Masur, and others that was mostly comprised of non-government experts. I've cut and pasted the bullets from the attached documents, as you can see there are quite a few. Highlighted text still evolving.

Bob

Summary Recommendations

- The Panel does not recommend the use of any agents for pre-SARS-CoV-2 exposure prophylaxis (PrEP) outside of a clinical trial **(AIII)**.
- The Panel does not recommend the use of any agents for post-SARS-CoV-2 exposure prophylaxis (PEP) outside of a clinical trial **(AIII)**.
- The Panel recommends no additional laboratory testing and no specific treatment for persons with suspected or confirmed asymptomatic/presymptomatic SARS-CoV-2 infection **(AIII)**.
- There are insufficient data to recommend either for or against any antiviral or immunomodulatory therapy in patients with COVID-19 and mild, moderate, severe or critical illness (AIII).

Summary Recommendations

Infection Control

- For healthcare workers performing aerosol-generating procedures on patients with COVID-19, the Panel recommends using fit-tested respirator masks (N-95 respirators) or powered air-purifying respirators (PAPRs) rather than surgical masks, in addition to other personal protective equipment (PPE) (i.e., gloves, gown, and eye protection such as a face shield or safety googles) **(AIII).**
- The Panel recommends that endotracheal intubation for patients with COVID-19 be done by healthcare providers with extensive airway management experience, if possible **(AIII)**.
- The Panel recommends that intubation be achieved by video laryngoscopy, if possible **(CIII)**.

Hemodynamic Support

- The Panel recommends norepinephrine as the first-choice vasopressor **(AII)**.
- The Panel recommends using dobutamine in patients who show evidence of persistent hypoperfusion despite adequate fluid loading and the use of vasopressor agents **(BII)**.

Ventilatory Support

- For adults with COVID-19 and acute hypoxemic respiratory failure despite conventional oxygen therapy, the Panel recommends high-flow nasal cannula (HFNC) oxygen over non-invasive positive pressure ventilation (NIPPV) **(BI)**.
- For adults with COVID-19 and acute hypoxemic respiratory failure for whom HFNC is not available, in the absence of an indication for endotracheal intubation, the Panel recommends a closely monitored trial of NIPPV **(BIII)**.
- For adults with COVID-19 who are receiving supplemental oxygen, the Panel recommends close monitoring for worsening of respiratory status and recommends early intubation by an experienced practitioner in a controlled setting **(AIII)**.
- The Panel recommends using low tidal volume (Vt) ventilation (Vt 4-8 mL/kg of predicted body weight) over higher tidal volumes (Vt>8 mL/kg) **(AI)**.
- For mechanically ventilated adults with COVID-19 and refractory hypoxemia despite optimizing ventilation, the Panel recommends prone ventilation for 12 to 16 hours per day over no prone ventilation **(BII)**.
- The Panel recommends a trial of inhaled pulmonary vasodilator as a rescue therapy; if no rapid improvement in oxygenation is observed, the patient should be tapered off treatment **(CIII)**.
- There are insufficient data to recommend either for or against the routine use of ECMO for patients with COVID-19 and refractory hypoxemia **(BIII)**.

Drug Therapy

- There are insufficient data for the Panel to recommend either for or against any antiviral or immunomodulatory therapy in patients with severe COVID-19 disease **(AIII)**.
- In patients with COVID-19 and severe or critical illness, in the absence of another indication there are insufficient data to recommend empiric broad-spectrum antimicrobial therapy **(BIII)**.

- The panel recommends against the routine use of systemic corticosteroids for the treatment of mechanically ventilated patients with COVID-19 without acute respiratory distress syndrome (ARDS) **(BIII)**.
- In mechanically ventilated adults with COVID-19 and ARDS, there are insufficient data to recommend either for or against corticosteroid therapy in the absence of another indication **(CI)**.
- In COVID-19 patients with refractory shock, low-dose corticosteroid therapy is preferred over no corticosteroid therapy **(BII).**

Panel's Recommendations

At present, no drug has been proven to be safe and effective for treating COVID-19*. There are no FDA-approved drugs to specifically treat patients with COVID-19. While reports have appeared in the medical literature and the lay press claiming successful treatment of patients with COVID-19 with a variety of agents, definitive clinical trial data are needed to identify optimal treatment for this disease. Recommended clinical management of these patients includes infection prevention and control measures and supportive care, including supplementary oxygen and mechanical ventilatory support when indicated. As always, treatment decisions ultimately reside with the patient and their healthcare provider.*

Antivirals

- There are insufficient clinical data to recommend for or against using **chloroquine** or **hydroxychloroquine** for the treatment of COVID-19 **(AIII)**.
  - If chloroquine or hydroxychloroquine is used, clinicians should monitor for adverse effects, especially prolonged QTc interval **(AIII)**.
- There are insufficient clinical data to recommend for or against using the investigational antiviral drug **remdesivir** for the treatment of COVID-19 **(AIII)**.
  - Remdesivir is currently in clinical trials and is also available through expanded access and compassionate use mechanisms for certain patient populations.
- The Panel recommends against the use of the following drugs for the treatment of COVID-19 except in a clinical trial:
  - The combination of **hydroxychloroquine + azithromycin (AIII)**, because of potential for toxicities
  - **Lopinavir/ritonavir** (AI) or **other HIV protease inhibitors (AIII),** because of unfavorable pharmacodynamics and negative clinical trial data.

Host Modifiers/Immune-Based Therapy

- There are insufficient data to recommend for or against the use of **convalescent plasma** or **hyperimmune immunoglobulin** for the treatment of COVID-19 **(AIII)**.
- There are insufficient data to recommend for or against the use of the following agents for the treatment of COVID-19 **(AIII)**.
  - IL-6 inhibitors (such as **sarilumab, siltuximab, or tocilizumab**)

- IL-1 inhibitors (such as **anakinra**)

- The Panel recommends against the use of other immunomodulators, except in a clinical trial, such as:
  - **Interferons (AIII),** because of lack of efficacy in SARS and MERS and toxicity.
  - **JAK inhibitors (such as baricitinib) (AIII),** because of their broad immunosuppressive effect

Summary Recommendations

Angiotensin-Converting Enzyme (ACE) Inhibitors and Angiotensin Receptor Blockers (ARBs)

- Persons with COVID-19 who are prescribed ACE inhibitors or ARBs for cardiovascular disease or other indications should continue these medications **(AIII).**

- The Panel recommends against the use of ACE inhibitors or ARBs for the treatment of COVID-19 outside of a clinical trial **(AIII).**

Corticosteroids

For Critically Ill Patients with COVID-19:

- The panel recommends against the routine use of systemic corticosteroids for the treatment of mechanically ventilated patients with COVID-19 without ARDS **(AIII).**

- For mechanically ventilated patients with ARDS, there is insufficient evidence to recommend for or against the use of systemic corticosteroids **(CI).**

- For adults with COVID-19 and refractory shock, the Panel recommends using low-dose corticosteroid therapy ("shock-reversal") over no corticosteroids **(BII)**.

For Hospitalized, Non-Critically Ill Patients with COVID-19:

- The Panel recommends against the routine use of systemic corticosteroids for the treatment of COVID-19 in hospitalized patients outside the ICU **(AIII).**

For Patients on Chronic Corticosteroids:

- Oral corticosteroid therapy used prior to COVID-19 diagnosis for another underlying condition, such as primary or secondary adrenal insufficiency or rheumatological diseases, should not be discontinued **(AIII)**. On a case-by-case basis, supplemental or stress-dose steroids may be indicated **(AIII)**.

- Inhaled corticosteroids used daily for patients with asthma and chronic obstructive pulmonary disease for control of airway inflammation should not be discontinued in patients with COVID-19 **(AIII)**.

Pregnancy considerations

- The antenatal corticosteroids betamethasone and dexamethasone are known to cross the placenta and therefore should be used only when administration for fetal benefit is required. Other systemic corticosteroids do not cross the placenta and pregnancy is not a reason to restrict use if otherwise indicated.

- ACOG recommends against offering antenatal corticosteroids for fetal benefit in the late preterm period (34 0/7 - 36 6/7) because the benefits of antenatal corticosteroids in the late preterm period are less well established.

- Modifications to care for these patients may be individualized, weighing the neonatal benefits of antenatal corticosteroid use with the risks of potential harm to the pregnant patient.

HMG-CoA Reductase Inhibitors ("Statins")

- Persons with COVID-19 who are prescribed statin therapy for the treatment or prevention of cardiovascular disease should continue these medications **(AIII).**
- The Panel recommends against the use of statins for the treatment of COVID-19 outside of a clinical trial **(AIII).**

Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)

- Persons with COVID-19 who are taking NSAIDs for a co-morbid condition should continue therapy as previously directed by their physician **(AIII).**

The Panel recommends that there be no difference in the use of antipyretic strategies (e.g., with acetaminophen or NSAIDs) between patients with or without COVID-19 **(AIII).**

From: Johnson, Robert (OS/ASPR/BARDA) <Robert.Johnson@hhs.gov>
Sent: Thursday, April 9, 2020 11:08 AM
To: Bright, Rick (OS/ASPR/BARDA) <Rick.Bright@hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Donis, Ruben (OS/ASPR/BARDA) <Ruben.Donis@hhs.gov>; Oshansky, Christine (OS/ASPR/BARDA) <Christine.Oshansky@hhs.gov>
Cc: Walker, Robert (OS/ASPR/BARDA) <Robert.Walker@hhs.gov>
Subject: RE: Update on the HHS COVID-19 GL

Looping in Bob to answer Rick's question.

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From: Bright, Rick (OS/ASPR/BARDA) <Rick.Bright@hhs.gov>
Sent: Thursday, April 9, 2020 10:26 AM
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Subject: Re: Update on the HHS COVID-19 GL

Thanks Bob. Any attachments or summaries of what is being discussed?

From: Robert Johnson <Robert.Johnson@hhs.gov>
Date: Thursday, April 9, 2020 at 10:08 AM
To: "Bright, Rick (OS/ASPR/BARDA)" <Rick.Bright@hhs.gov>, Gary Disbrow <Gary.Disbrow@hhs.gov>, Ruben Donis <Ruben.Donis@hhs.gov>, Christine Oshansky <Christine.Oshansky@hhs.gov>
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FYI

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To: BARDA SARS2 IMT Comms <BARDASARS2IMTComms@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) <Robert.Johnson@hhs.gov>; Tesfaya, Selamawit (OS/ASPR/BARDA) (CTR) <Selamawit.Tesfaya@hhs.gov>; Ventura, Christy (OS/ASPR/BARDA) (CTR) <Christy.Ventura@hhs.gov>
Subject: FW: Update on the HHS COVID-19 GL
Importance: High

FYI...this is regarding the HHS treatment guidelines. Want to ensure senior leadership is aware this AM.

From: Pau, Alice (NIH/NIAID) [E] <apau@niaid.nih.gov>
Sent: Thursday, April 9, 2020 9:54 AM
Subject: Update on the HHS COVID-19 GL

Dear Colleagues,

Just want to give you a quick update since our last communication. All 29 voting members submitted their votes, and 100% approved of the guidelines to move forward.

Tuesday night, Dr. Lane shared the Panel's work and recommendations with Dr. Fauci, who is very appreciative of everyone's work. This morning at 10am, Dr. Lane will join Dr. Fauci on a call to brief Secretary Azar. After that, this will be brought to the White House Coronavirus Task this afternoon.

We will provide you with more updated status later this afternoon or tomorrow.

Thanks for your dedication to this guidelines.

Alice

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Recipient:	Bright, Rick (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=53034752f35a4317aa74f46348442d39-Bright, Ric <Rick.Bright@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0851e89240324306b78740a4a60745e2-Johnson, Ro <Robert.Johnson@hhs.gov>; Donis, Ruben (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=af00dcf720cb429f8e2accbe06ee32ff-Donis, Rube <Ruben.Donis@hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0fd5845defda4dc0bb45f8fac629cf09-Disbrow, Ga <Gary.Disbrow@hhs.gov>; Oshansky, Christine (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d7bd764440b44b06af644cdcd22e42d6-Oshansky, C <Christine.Oshansky@hhs.gov>; Lambert, Linda (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ce6824b6a92a4a4e893ea7b54e17eb3c-Lambert, Li <Linda.Lambert@hhs.gov>
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Comments Regarding IL-6 Inhibitors for COVID-19

1. There is no data to date that has been suggestive of benefit. The RGN study has overenrolled and has 700 in a placebo controlled study and yet the IDMC is recommending a change in protocol---no public results. 2. The supply is limited and without guidance on who may benefit , how does one select the few pts out of 100s to offer this to? some have supplies that only would allow coverage for only 1-2% of total population. The FDA approved SC formulation of these drugs are not the same formulations in trials being studied for COVID. 3. These drugs are not benign. IL6RA are associated with GI perforations and bleeds that result in morbidity. 4. They also are associated with neutropenia that can result in prolonged stays in hospital while awaiting counts to recover and utilizing bed space needed by others 5. Anaphylaxis and serious hypersensitivity reactions may occur. Nurses have to be trained specifically to administer and some states require MOAB consents that must be signed by pt or family before they are administered. 6. These drugs are very costly 7. HCQ has the same recommendation assigned as the IL6R and IL1. But these drugs are different. Unlike HCQ, there is no EUA which protects physicians from using off label; HCQ side effects well known and less severe. QT can be resolved by stopping drug. IL6RA are in your system much longer and cannot reverse the cytopenias or GI bleed; There is more data on safety and potential benefit of HCQ, even if inadequate to provide a full recommendation, there are programs that do in fact endorse its use; there now is adequate supply, drug costs are affordable with some states providing for free and therefore can be prescribed more broadly and to most pts. We provide guidance on who to give and how to screen e.g. for HCQ yet we offer no guidance on who to offer biologic to. I am unclear why HCQ and IL6RA and IL1 would have same recommendation given the differences listed above. I do not believe we are offering appropriate guidance to say there is insufficient date for or against and leaving these types of complex and expensive drugs up to inexperienced users, some of which may not even know there are state regulations on their usage.

I missed call and discussion that led to this survey. I continue to struggle with distinction between "for or against" versus "against" because of the singling out of of HCQ + Azithro as "against" from all other options for which there are no strong efficacy data. Since I was led to understand that HCQ + Azithro is singled out amongst options for which there is no good data because of perceived higher toxicity risk, including chloroquine which has more QTc affect than HCQ, and the unknown clinical relevance of use of HCQ with Azithro impact on QTc not being defined and at least for admitted patients an AE than can be monitored for. My feeling is that we should be consistent for all of these options in which there is no good data for or against. With that background, I would suggest we be consistent with options and therefore IL-6 antagonists represents just another intervention that is used without data for efficacy and should be treated like other options in the "for or against" category.

In practical terms, this is a vote for 'insufficient data' vs 'recommend against' (which is an appropriate vote to have, BTW). The qualifier 'except in a clinical trial' is not practically relevant for IL-6 therapies in US. Although somewhat true for other medications in GL, EAP and IND/open protocol options are broadening access for remdesivir and convalescent plasma.

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very limited data to support use, including siltuximab real potential for toxicity: GI perforation, hepatic failure, neutropenia no guidance on when to administer it (most centers cannot follow IL-6 levels given long turnaround time) very limited supply

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Clinical trials may not be available at many clinics.

Based upon anecdotal NY experience; but that is the best we have.

I would need to see data to tilt toward recommending against use

Overview and Spectrum of Coronavirus Disease 2019 (COVID-19)

Summary Recommendations

- The Panel does not recommend the use of any agents for pre-SARS-CoV-2 exposure prophylaxis (PrEP) outside of a clinical trial **(AIII)**.
- The Panel does not recommend the use of any agents for post-SARS-CoV-2 exposure prophylaxis (PEP) outside of a clinical trial **(AIII)**.
- The Panel recommends no additional laboratory testing and no specific treatment for persons with suspected or confirmed asymptomatic/presymptomatic SARS-CoV-2 infection **(AIII)**.
- There are insufficient data to recommend either for or against any antiviral or immunomodulatory therapy in patients with COVID-19 and mild, moderate, severe or critical illness **(AIII)**.

Epidemiology

The coronavirus disease 2019 (COVID-19) pandemic has exploded since cases were first reported in China in January 2020. As of April 6, 2020, more than 1.3 million reported cases of COVID-19 caused by SARS-CoV-2 infection had occurred globally, including more than 70,000 deaths. Cases have been reported in approximately 200 countries and 55 jurisdictions, including all 50 states, of the United States (WHO situation report and CDC report).

Individuals of all ages are at risk for infection and severe disease. However, the probability of fatal disease is highest in people age 65 years and older and those living in a nursing home or long-term care facility. Others at highest risk are people of any age with certain underlying conditions, especially when not well-controlled, including

- Hypertension
- Cardiovascular disease
- Diabetes
- Chronic respiratory disease
- Cancer
- Renal disease
- Obesity

Clinical Presentation

The estimated incubation period for COVID-19 is up to 14 days from the time of exposure, with a median incubation period of 4-5 days. The spectrum of illness can range from asymptomatic infection to severe pneumonia with acute respiratory distress syndrome (ARDS) and death. In a

Commented [DL([1]: Add the CDC link/ref: https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-at-higher-risk.html

Commented [PA([2R1]: Wu - doi:10.1001/jamainternmed.2020.0994

Commented [PA([3R1]: Guan - https://www.ncbi.nlm.nih.gov/pubmed/32109013 https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3556658

Commented [PA([4]: Guan NEJM 2020 and Li NEJM January 2020

summary of 72,314 persons with COVID-19 in China, 81% of cases were reported to be mild, 14% were severe, and 5% were critical (Wu NEJM). In an early report of 138 hospitalized patients with COVID-19 in Wuhan, China, the most common presenting signs and symptoms were: fever (>90%), fatigue (70%), dry cough (59%), myalgia (35%), and dyspnea (31%) (Guan NEJM). Other reported symptoms have included but were not limited to sputum production, headache, dizziness, rhinorrhea, anosmia, dysgeusia, sore throat, abdominal pain, anorexia, nausea, vomiting, and diarrhea.

Commented [PA([5]: *Wu Z. JAMA published on line 2/24/20*

Commented [PA([6]: https://www.ncbi.nlm.nih.gov/pubmed/32109013

Common laboratory findings include leukopenia and lymphopenia. Other laboratory abnormalities have included elevations in aminotransferase levels, C-reactive protein, D-dimer, ferritin, and lactate dehydrogenase.

Abnormalities in chest X-ray (CXR) vary, but typically reveal bilateral multi-focal opacities. Abnormalities seen in computed tomography (CT) of the chest also vary, but typically reveal bilateral peripheral ground-glass opacities with the development of areas of consolidation later in the clinical course. (Shi, Lancet) Imaging may be normal early in infection and can be abnormal in the absence of symptoms.

Commented [PA([7]: Shi - Lancet

Diagnosis of SARS CoV-2 Infection

Ideally, diagnostic testing would be conducted for all suspected patients, people with known high-risk exposures, and people likely to be at repeated risk of exposure, such as healthcare workers and first responders. https://www.cdc.gov/coronavirus/2019-ncov/lab/guidelines-clinical-specimens.html

The CDC recommends that nasopharynx samples be used to detect SARS-CoV2. Nasal swabs or oropharyngeal swabs may be acceptable alternatives. Lower respiratory tract samples have a higher yield than upper tract samples, but often they are not obtained because of concerns about aerosolization of virus during the procedures.

Commented [PA([8]: https://www.cdc.gov/coronavirus/2019-ncov/lab/guidelines-clinical-specimens.html

While initial tests have relied on reverse transcriptase polymerase chain reaction (RT-PCR) platforms, more recent tests have included a variety of additional platforms. More than 20 diagnostic tests for SARS-CoV-2 have received Emergency Use Authorization (EUA) by the FDA. Formal comparisons of these tests are in progress.

Commented [PA([9]: https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations#covid19ivd

Commented [UTM(10R9]:

The CDC has established a priority system for testing based on the availability of tests. This list is updated periodically.

- Priority 1: hospitalized patients, symptomatic healthcare workers (to reduce the risk of nosocomial infections and maintain the healthcare system)
- Priority 2: individuals with symptoms who live in long-term care facilities, who are 65 years or older, those with underlying conditions, and symptomatic first responders (to ensure those at highest risk of complications of infection are rapidly identified and triaged)

Commented [PA([11]: https://www.cdc.gov/coronavirus/2019-nCoV/hcp/clinical-criteria.html

- Priority 3: Critical infrastructure workers and other individuals with symptoms, healthcare workers and first responders, and individuals with mild symptoms in communities experiencing high COVID-19 hospitalizations (to decrease community spread and ensure the health of essential workers)

Of note, false negative test results can occur. In people with a high likelihood of infection based on exposure history and/or clinical presentation, a single negative test does not completely exclude SARS-CoV-2 infection, and testing should be repeated.

Routes of SARS-CoV-2 Transmission and Standard Means of Prevention

The onset and duration of viral shedding and period of infectiousness are not completely defined. Asymptomatic/pre-symptomatic individuals infected with SARS-CoV-2 may have viral RNA detected in upper respiratory specimens before the onset of symptoms (Pan). Transmission of SARS-CoV-2 from asymptomatic individuals has been described (Rothe, Yu, Bai). The extent to which this occurs remains unknown.

Commented [PA(12]: Pan Y Lancet Infect Dis 2020

Commented [PA(13]: Rothe NEJM 2020
Yu JID 2020
Bai Y JAMA 2020

PERSONS AT RISK FOR INFECTION WITH SARS-CoV-2

Pre-exposure prophylaxis
The Panel does not recommend the use of any agents for pre-SARS-CoV-2 exposure prophylaxis (PrEP) outside of a clinical trial (AIII).

At present, no agent when given before an exposure, i.e., as PrEP, is known to be effective in preventing SARS-CoV-2 infection. Clinical trials are in development or underway using hydroxychloroquine, chloroquine, or HIV protease inhibitors as PrEP.

Post-exposure prophylaxis
The Panel does not recommend the use of any agents for post-SARS-CoV-2 exposure prophylaxis (PEP) outside of a clinical trial (AIII).

At present, no agent is known to be effective for preventing SARS-CoV-2 infection after an exposure, i.e., as PEP. Potential options for PEP currently under investigation in clinical trials include hydrochloroquine, chloroquine, or lopinavir/ritonavir.

MANAGEMENT OF PERSONS INFECTED WITH SARS-CoV-2

Patients infected with SARS-CoV-2 can experience a range of clinical manifestations, from no symptoms to critical illness. This section discusses the clinical management of patients according to the severity of their illness. Currently, no FDA-approved drugs exist to specifically treat patients with COVID-19. Chloroquine and hydroxychloroquine, which are not FDA approved for COVID-19, are available from the Strategic National Stockpile for hospitalized

adults and adolescents (>50 kg) under an EUA. An array of drugs approved for other indications as well as multiple investigational agents are being studied for the treatment of COVID-19 in several hundred clinical trials around the globe. Some drugs can be accessed through expanded access or compassionate use mechanisms. Available clinical data for these drugs under investigation are discussed in the Therapeutic Considerations Section. **As noted there, no drug has been proven to be safe and effective for the treatment of COVID-19.**

In general, patients can be divided into the following illness categories:

Asymptomatic/Pre-symptomatic infection: individuals who tested positive for SARS-CoV-2 but have no symptoms

Mild illness: any of various signs and symptoms (fever, cough, sore throat, malaise, headache, muscle pain) without shortness of breath/dyspnea or abnormal imaging

Moderate illness: evidence of lower respiratory disease by clinical assessment or imaging with SaO2 >93% on room air

Severe illness: respiratory frequency ≥30 breaths per minute, SaO2 ≤93% on room air, ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO2/FiO2) <300, or lung infiltrates >50%

Critical illness: respiratory failure, septic shock, and/or multiple organ dysfunction

Asymptomatic/Presymptomatic Infection

Asymptomatic infection can occur, although the percentage of patients who remain truly asymptomatic for the course of their infection is unknown. A significant percentage of asymptomatic infections may progress to clinical disease. Some asymptomatic individuals have been reported to have objective radiographic findings consistent with COVID-19 pneumonia. Eventually the availability of widespread testing for SARS-CoV-2 and the development of serologic assays for antibodies to the virus will help determine the true prevalence of asymptomatic/presymptomatic infections.

Commented [LC([14]: Wang Y, Liu Y, Liu L, et al. Clinical outcome of 55 asymptomatic cases at the time of hospital admission infected with SARS-Coronavirus-2 in Shenzhen, China. J Infect Dis 2020.

Persons who test positive for SARS-CoV-2 and who are asymptomatic should self-isolate. If they remain asymptomatic, they can discontinue isolation 7 days after the date of their first positive SARS-CoV-2 test. If they become symptomatic, they should contact their healthcare provider for further guidance. For healthcare workers who test positive and are asymptomatic, there may be additional guidance from their occupational health service. For detailed information, see https://www.cdc.gov/coronavirus/2019-ncov/hcp/guidance-prevent-spread.html

Commented [PA([15]: (https://www.cdc.gov/coronavirus/2019-ncov/hcp/disposition-in-home-patients.html)

The Panel recommends no additional laboratory testing and no specific treatment for persons with suspected or confirmed asymptomatic/presymptomatic SARS-CoV-2 infection (AIII).

Mild Illness

Patients may have mild illness defined by any of various signs and symptoms (fever, cough, sore throat, malaise, headache, muscle pain, malaise) without shortness of breath/dyspnea or abnormal imaging. Most mildly ill patients can be managed in an ambulatory setting or at home through telemedicine or remote visits.

All patients with symptomatic COVID-19 and risk factors for severe disease should be closely monitored. In some patients the clinical course may rapidly progress. (Guan. NEJM 2020 Feb 28. PMID 32109013; Huang. Lancet. 2020 Feb 15;395(10223):497-506.)

No specific laboratory evaluations are indicated in otherwise healthy patients with mild disease.

There are insufficient data to recommend either for or against any antiviral or immunomodulatory therapy in patients with mild illness (AIII).

Moderate Illness

Moderate illness is defined as evidence of lower respiratory disease by clinical assessment or imaging with SpO2 >93% on room air at sea level. Given that pulmonary disease can rapidly progress in patients with COVID-19, patients with moderate COVID-19 should be admitted to a healthcare facility for close observation. If bacterial pneumonia or sepsis is strongly suspected, administer empiric antibiotic treatment for community-acquired pneumonia, re-evaluate daily, and if no evidence of bacterial infection, de-escalate or stop antibiotics.

Most patients with moderate to severe illness will require hospitalization. Hospital infection prevention and control measures include use of personal protective equipment (PPE) for droplet and contact precautions (such as masks, face shields, gloves, gowns, etc.), including eye protection (face shields or goggles) and single-patient dedicated medical equipment (stethoscopes, blood pressure cuffs, thermometers, etc.). The number of individuals and providers entering the room should be limited. If necessary, confirmed COVID-19 patients may be cohorted. If available, airborne Infection Isolation Rooms should be used if the patient will be undergoing any aerosol-generating procedures. N95 masks or PAPRs should be worn by all staff during these procedures in place of the surgical mask.

Commented [UTM(16]: Can link to CDC infection prevention and control recommendations.
https://www.cdc.gov/coronavirus/2019-ncov/hcp/infection-control-recommendations.html

https://www.cdc.gov/coronavirus/2019-ncov/hcp/ppe-strategy/index.html

The optimal pulmonary imaging technique for people with COVID-19 is yet to be defined. Initial evaluation may include chest x-ray, ultrasound, or if indicated, CT. Electrocardiogram (ECG) should be performed if indicated. Laboratory testing includes CBC with differential; metabolic profile, including liver and renal function tests. Measurements of inflammatory markers such as CRP, D-dimer and ferritin, while not part of standard care, may have prognostic value.

There are insufficient data for the Panel to recommend either for or against any antiviral or immunomodulatory therapy in patients with moderate illness (AIII).

Clinicians can refer to the **Therapeutic Options for COVID-19 Currently Under Investigation** section and Tables 2a and 3a of these Guidelines to review the available clinical dataregarding investigational drugs being evaluated for treatment of this disease.

Severe Illness

Patients are considered to have severe illness if they have, SpO2≤93% on room air at sea level, respiratory rate >30, ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO2/FiO2)<300, or lung infiltrates >50%. These patients may experience rapid clinical deterioration and are likely to need to undergo aerosol-generating procedures. They should be placed in airborne Infection Isolation Rooms, if available. Administer oxygen therapy immediately using nasal cannula or high-flow oxygen.

If secondary bacterial pneumonia or sepsis is suspected, administer empiric antibiotics, re-evaluate daily, and if no evidence of bacterial infection, de-escalate or stop antibiotics.

Evaluation should include pulmonary imagining (chest x-ray, ultrasound, or if indicated, CT) and EKG, if indicated. Laboratory evaluation includes CBC with differential ad metabolic profile, including liver and renal function tests. Measurements of inflammatory markers such as CRP, D-dimer, and ferritin, while not part of standard care, may have prognostic value.

There are insufficient data for the Panel to recommend either for or against any antiviral or immunomodulatory therapy in patients with severe illness (AIII).

Clinicians can refer to the **Therapeutic Options for COVID-19 Currently Under Investigation** section and Tables 2a and 3a of these Guidelines to review the available clinical data regarding drugs being evaluated for treatment of this disease.

Critical Illness (Additional details – refer to the **Managing the Critically Ill Patient with COVID-19** section)

Commented [PA([17]: link

COVID-19 is primarily a pulmonary disease. Severe cases may be associated with ARDS, septic shock that may represent virus-induced distributive shock, cardiac dysfunction, elevations in multiple inflammatory cytokines giving a picture of "cytokine storm," and/or exacerbation of underlying co-morbidities. In addition to pulmonary disease, patients with COVID-19 may also experience cardiac, hepatic, renal, and CNS disease

Since patients with critical illness are likely to undergo aerosol-generating procedures, they should be placed in airborne Infection Isolation Rooms if available.

Most of the recommendations for the management of critically ill patients with COVID-19 are extrapolated from experience with other life-threatening infections. Currently, there is limited information to suggest that the critical care management of patients with COVID-19 should differ substantially from the management of other critically ill patients, although special precautions about environmental contamination by SARS-CoV-2 is warranted.

Commented [PA([18]: From Andrea - https://www.sccm.org/getattachment/Disaster/SSC-COVID19-Critical-Care-Guidelines.pdf?lang=en-US

The Surviving Sepsis Campaign (SSC), an initiative supported by the Society of Critical Care Medicine and the European Society of Intensive Care Medicine, issued Guidelines on the Management of Critically Ill Adults with Coronavirus Disease 2019 (COVID-19) in March 2020 (ref). The Panel members have relied heavily on these Guidelines in making our recommendations and gratefully acknowledge the work of the SSC COVID-19 Guidelines panel.

Commented [LA([19]: https://www.sccm.org/getattachment/Disaster/SSC-COVID19-Critical-Care-Guidelines.pdf?lang=en-US

As with any patient in the intensive care unit (ICU), successful clinical management depends on attention to the primary process leading to ICU admission, but also to other co-morbidities and nosocomial complications.

There are insufficient data for the Panel to recommend either for or against any antiviral or immunomodulatory therapy in critically ill patients with COVID-19 (AIII).

Clinicians can refer to the **Therapeutic Options for COVID-19 Currently Under Investigation** section and Tables 2a and 3a of these Guidelines to review the available clinical dataregarding drugs being evaluated for treatment of this disease.

Special Considerations in Pregnancy and Post-partum

Commented [PA([20]: editor – please note the reference list can be found after the "Special Consideration" section

There is current guidance from the CDC, the American College of Obstetricians and Gynecologists (ACOG), and the Society for Maternal Fetal Medicine (SMFM) on the management of pregnant patients with COVID-19.(1-4) This document complements that guidance and focuses on pregnancy considerations related to treatment.

Limited information is available regarding the effect of COVID-19 on obstetric or neonatal outcomes. Initial reports of COVID-19 disease acquired in the third trimester were largely reassuring, but most data are limited to case reports and case series.(5-6) In one of the larger series from Wuhan, China, pregnant women did not appear to be at risk for more severe

disease. Among 147 pregnant women (64 confirmed, 82 suspected, and 1 asymptomatic), 8% had severe disease and 1% had critical disease, compared to the general population where 13.8% had severe disease and 6.1% had critical disease.(7) To date, there are no reports of neonatal disease due to perinatal transmission.(5,8)

ACOG has developed algorithms to evaluate pregnant outpatients with suspected or confirmed COVID-19.(9) As with non-pregnant patients, a wide range of clinical manifestations of the disease occurs, from mild symptoms that can be managed with supportive care at home to severe disease and respiratory failure requiring ICU admission. As with other patients, in the pregnant patient with symptoms compatible with COVID-19, the illness severity, underlying co-morbidities, and clinical status should all be assessed to determine if in-person evaluation for potential hospitalization is needed.

If hospitalization is indicated, ideally the care should be provided in a facility with the ability to conduct close maternal and fetal monitoring. The principles of management of COVID-19 in the pregnant patient may include

- fetal and uterine contraction monitoring
- individualized delivery planning
- a team-based approach with multispecialty consultation

Other recommendations, as outlined for the non-pregnant patient, will apply in pregnancy as well.

Timing of Delivery

- In most cases, the timing of delivery should be dictated by obstetric indications rather than maternal diagnosis of COVID-19. For women with suspected or confirmed COVID-19 early in pregnancy who recover, no alteration to the usual timing of delivery is indicated.
- For women with suspected or confirmed COVID-19 in the third trimester, it is reasonable to attempt to postpone delivery (if no other medical indications arise) until a negative test is obtained or quarantine status is lifted in an attempt to avoid virus transmission to the neonate.
- In general, a diagnosis of COVID-19 in pregnancy is not an indication for early delivery (https://www.acog.org/clinical-information/physician-faqs/covid-19-faqs-for-ob-gyns-obstetrics).
- Based on limited data on primarily cesarean deliveries, there appears to be no risk of vertical transmission of the virus via the transplacental route. https://www.acog.org/clinical-information/physician-faqs/covid-19-faqs-for-ob-gyns-obstetrics).

Treatment for COVID-19 in the setting of pregnancy

Commented [UTM(21]: See this recent small case series from New York:
Breslin N, Baptiste C, Miller R, Fuchs K, Goffman D, Gyamfi-Bannerman C,
D'Alton M. COVID-19 in pregnancy: early lessons. *American Journal of Obstetrics & Gynecology MFM* (2020). doi: https://doi.org/10.1016/j.ajogmf.2020.100111.

- There are no FDA-approved medications for the treatment of COVID-19.
- Most clinical trials to date have excluded pregnant and lactating women.
- Treatment considerations must be made with shared decision-making, considering the safety of the medication but also the risk and seriousness of maternal disease.
- Involvement of a multidisciplinary team in these discussion, including, among others obstetrics, maternal fetal medicine and pediatrics, is recommended.
- Enrollment of pregnant and lactating women in clinical trials (if eligible) is encouraged.

Post delivery

- Currently the CDC recommends temporary infant separation from mothers who are persons under investigation (PUI) or COVID-infected because of concern for transmission of the virus to the infant via respiratory droplets.
- ACOG supports breastfeeding for infants. They recommend that, for women who are PUI or confirmed with SARS-CoV-2 infection, the decision about whether and how to start or continue breastfeeding be made by the mother, in coordination with her family and healthcare practitioners.[10]
- The CDC has developed interim guidance on breastfeeding, recommending that women who intend to breastfeed and who are temporarily separated from their infant express their breastmilk ideally from a dedicated pump, practice good hand hygiene before and after, and consider having a well person feed the infant.
- They advise that women who choose to room with their infant should take precautions against transmission of the virus to the infant via respiratory droplets during breastfeeding by practicing good hand hygiene and wearing a facemask.[1] Virus has not been isolated from breast milk.[5]

Special Considerations in Children

Data on disease severity and pathogenesis of SARS-CoV-2 infection in children are limited. Overall, several large epidemiologic studies suggest that disease manifestations are substantially less severe in children compared to adults, though there are reports of children requiring ICU-level care[1-5]. Without widespread testing, including for mild symptoms, it is not clear what the true incidence of severe disease is. Data on perinatal vertical transmission to neonates are limited to small case series with conflicting results; some studies have demonstrated lack of transmission, whereas others have not been able to definitively rule out this possibility[6-8].

Commented [PA(|22|:
https://www.cdc.gov/mmwr/volumes/69/wr/mm6914e4.htm

No specific data are available establishing risk factors for severe disease in children. Based on adult data and extrapolation from other pediatric respiratory viruses, severely immunocompromised children and those with underlying cardiopulmonary disease may be at higher risk for severe disease. Children with risk factors recognized in adults, including obesity,

diabetes, and hypertension, may also be at risk, although there are no published data supporting this association and insufficient data to guide therapy. As data emerge on risk factors for severe disease, it may be possible to provide more directed guidance for specific populations at high risk and to tailor treatment recommendations accordingly.

As above, there is insufficient data to recommend for or against the use of specific antivirals or immunomodulatory agents for the treatment of SARS-CoV-2 in pediatric patients. General considerations such as underlying conditions, disease severity, and potential for drug toxicity or interactions may inform management decisions on a case-by-case basis. Enrollment in clinical trials should be prioritized if trials are available. Disease categories outlined in the overall guidance may require specific consideration in pediatrics, as a number of different classification schemes have been used to stratify patients based on illness severity and/or primary site of infection.

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5. Dong, Y., *et al.* Epidemiological Characteristics of 2143 Pediatric Patients With 2019 Coronavirus Disease in China. *Pediatrics* (2020).
6. Chen, H., *et al.* Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. *Lancet* **395**, 809-815 (2020).
7. Fan, C., *et al.* Perinatal Transmission of COVID-19 Associated SARS-CoV-2: Should We Worry? *Clin Infect Dis* (2020).
8. Zeng, L., *et al.* Neonatal Early-Onset Infection With SARS-CoV-2 in 33 Neonates Born to Mothers With COVID-19 in Wuhan, China. *JAMA Pediatr* (2020).

THERAPEUTIC OPTIONS FOR COVID-19 CURRENTLY UNDER INVESTIGATION

Panel's Recommendations

At present, no drug has been proven to be safe and effective for treating COVID-19*. There are no FDA-approved drugs to specifically treat patients with COVID-19. While reports have appeared in the medical literature and the lay press claiming successful treatment of patients with COVID-19 with a variety of agents, definitive clinical trial data are needed to identify optimal treatment for this disease. Recommended clinical management of these patients includes infection prevention and control measures and supportive care, including supplementary oxygen and mechanical ventilatory support when indicated. As always, treatment decisions ultimately reside with the patient and their healthcare provider.*

Antivirals

- There are insufficient clinical data to recommend for or against using **chloroquine** or **hydroxychloroquine** for the treatment of COVID-19 **(AIII)**.
  - If chloroquine or hydroxychloroquine is used, clinicians should monitor for adverse effects, especially prolonged QTc interval **(AIII)**.
- There are insufficient clinical data to recommend for or against using the investigational antiviral drug **remdesivir** for the treatment of COVID-19 **(AIII)**.
  - Remdesivir is currently in clinical trials and is also available through expanded access and compassionate use mechanisms for certain patient populations.
- The Panel recommends against the use of the following drugs for the treatment of COVID-19 except in a clinical trial:
  - The combination of **hydroxychloroquine + azithromycin (AIII)**, because of potential for toxicities
  - **Lopinavir/ritonavir** (AI) or **other HIV protease inhibitors (AIII),** because of unfavorable pharmacodynamics and negative clinical trial data.

Host Modifiers/Immune-Based Therapy

- There are insufficient data to recommend for or against the use of **convalescent plasma** or **hyperimmune immunoglobulin** for the treatment of COVID-19 **(AIII)**.
- There are insufficient data to recommend for or against the use of the following agents for the treatment of COVID-19 **(AIII)**.
  - IL-6 inhibitors (such as **sarilumab, siltuximab, or tocilizumab**)
  - IL-1 inhibitors (such as **anakinra**)
- The Panel recommends against the use of other immunomodulators, except in a clinical trial, such as:
  - **Interferons (AIII),** because of lack of efficacy in SARS and MERS and toxicity.
  - **JAK inhibitors (such as baricitinib) (AIII),** because of their broad immunosuppressive effect

Commented [PA([1]: Laurie suggested combining these 2 sentences –
At present, no drug has been proven to be safe and effective for treating COVID-19 or approved by the FDA to specifically treat patients with COVID-19.

Commented [RMG2R1]: I would keep them separate.

Commented [PA([3R1]: Cliff agreed as well. We don't want the 2 sentences to be lumped together

Antiviral Therapy with Potential for Treatment of COVID-19

Chloroquine or Hydroxychloroquine

Panel's Recommendation:

- There are insufficient clinical data to recommend for or against using **chloroquine** or **hydroxychloroquine** for the treatment of COVID-19 **(AIII)**.
    - If **chloroquine or hydroxychloroquine** is used, clinicians should monitor for adverse effects, especially prolonged QTc interval **(AIII)**.

Rationale for Panel's Recommendation:
Chloroquine and hydroxychloroquine have been used in small randomized trials and in some case series with conflicting study reports (as described below). Both drugs are available through the U.S. National Stock Pile for hospitalized adults and adolescents weighing ≥ 50kg.

Background
Chloroquine is an antimalarial drug first developed in 1934. Hydroxychloroquine, an analogue of chloroquine, was developed in 1946 and is used to treat autoimmune diseases such as systemic lupus erythematosus (SLE), rheumatoid arthritis (RA); in general, it has less toxicity (including less propensity to prolong the QT interval) and fewer drug-drug interactions than chloroquine.

Proposed Mechanism of Action and Rationale for Use in COVID-19

- Both chloroquine and hydroxychloroquine increase the endosomal pH, inhibiting fusion of the virus and the host cell membrane. (Wang)
- Chloroquine inhibits glycosylation of the cellular ACE2 receptor, which may interfere with binding of the virus to the cell receptor. (Vincent MJ 2005)
- In vitro, both drugs may block the transport of SARS-CoV-2 from early endosomes to endolysosomes, which may be required for release of the viral genome. (Liu J)
- Several studies have demonstrated in vitro activity of chloroquine against SARS-Co-V. (Keyaerts E, 2004) (Vincent MJ 2005)
- Both drugs have immunomodulatory effects.

Clinical Data in COVID-19 - The clinical data available to date for chloroquine and hydroxychloroquine have been mostly in patients with mild, and in some cases moderate disease and there are very limited safety and clinical efficacy data in patients with severe and critical illnesses. The clinical data are summarized below.

Chloroquine:

- In a small randomized controlled trial in China, 22 hospitalized patients (none critically ill) were randomized to chloroquine 500mg PO twice daily or lopinavir/ritonavir 400mg/100mg twice daily for 10 days. Patients with history of heart (chronic disease and history of arrhythmia), kidney, liver or hematologic diseases were excluded from participation. Primary study outcome was SARS-CoV-2 PCR negativity at days 10 and 14, secondary outcomes included improvement of lung CT at days 10 and 14, discharge at day 14, and clinical recovery at day 10, as well as study drug related adverse effects.

  Results:

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- 10 patients received chloroquine and 12 patients received lopinavir/ritonavir. Patients had good SpO2 at baseline (97-98%)
- The chloroquine treated patients had a shorter duration from symptom onset to initiation of treatment (2.5 days vs. 6.5 days, p<0.001).
- Though not statistically significant, patients in the chloroquine arm were younger (median age 41.5 vs. 53.0 years, p=0.09). Few patients had comorbidities.
- At day 10, 90% of chloroquine and 75% of lopinavir/ritonavir-treated patients had negative SARS-CoV-2 PCR. At day 14, it was 100% and 91.2% respectively.
- At day 10, 20% of chloroquine and 8.3% of lopinavir/ritonavir-treated patients had CT scan improvement. At day 14, it was 100% and 75% respectively.
- At day 14, 100% of the chloroquine-treated patients and 50% of the lopinavir/ritonavir-treated patients were discharged from the hospital.
- The risk ratios of these outcome data cross 1 and the results were not statistically significant.
- Both drugs were generally well tolerated.

Limitations:

- Very small sample size of a fairly young group of patients.
- Chloroquine-treated patients were younger and had less symptoms prior to treatment initiation – these could have impacted the patients' clinical outcomes.
- Patients with chronic co-morbidities and critically ill patients were excluded from the study.

Hydroxychloroquine:

- In a randomized controlled trial from China, 62 hospitalized patients with "mild" (SaO2/SPO2 ratio >93% or PaO2/FIO2 ratio >300 mmHg) and CT confirmed COVID-19 pneumonia were randomized to hydroxychloroquine 200 twice daily x 5 days plus standard treatments "standard treatment" only. Standard treatment included oxygen therapy, "antiviral" and antibacterial therapy, and immunoglobin, with or without corticosteroids.

Commented [AAA11]: Chen Z. Efficacy of hydroxychloroquine in patients with COVID-19: results of a randomized clinical tri

Commented [PA([12R11]: https://www.medrxiv.org/content/10.1101/2020.03.22.20040758v2

Results:

- Mean duration of fever (2.2 vs 3.2 days) and cough (2.0 vs 3.1 days) was 1 day shorter among hydroxychloroquine-treated patients than among controls.
- 13% of control patients and none of the hydroxychloroquine-treated patients experienced progression of illness.
- 80.6% of hydroxychloroquine-treated patients experienced either moderate or significant improvement in chest CT compared to 54.8% of controls.
- Adverse effects occurred among 2 (6.4%) (1 rash, 1 headache) hydroxychloroquine-treated patients; none occurred among the controls.

Limitations:

- Small sample size and short follow-up.
- Control and hydroxychloroquine group were not well matched.
- Standard treatment is complex and not well defined.
- Presence and distribution of associated co-morbidities (e.g., HTN, DM, lung disease) is not reported.
- No indication that radiologists were blinded to treatment status of patients, which could have biased determination of the chest CT outcome.

- A pilot trial from China randomized hydroxychloroquine 400 mg per day x 5 days vs "conventional treatment" among 30 patients with COVID-19 demonstrated no difference in viral clearance of NP swabs at day 7 between hydroxychloroquine (86.7%) and the control arm (93.3%).(Chen J 2020)
    - One patient in the hydroxychloroquine arm progressed to severe pneumonia. All patients clinically improved in subsequent follow-up.

- 26 hospitalized adults with SARS -CoV-2 categorized as asymptomatic or with upper or lower respiratory tract infection received hydroxychloroquine 200 mg 3x daily x 10 days were compared to 16 "controls" (who refused treatment, did not meet eligibility criteria or from a different clinic).(Gautret P 2020)
    - Six patients in the hydroxychloroquine group were not included from the analysis for the following reasons:
        - 1 died
        - 3 were transferred to the ICU
        - 1 stopped drug due to nausea
        - 1 withdrew from the study
    - Six patients also received azithromycin
    - By day 6, (NP PCRs were negative in 14/20 (70%) hydroxychloroquine patients and 2/16 (12.5%) controls.
    - Among the hydroxychloroquine patients, 8/14 (57.1%) who received hydroxychloroquine alone and 6/6 (100%) who received hydroxychloroquine + azithromycin had negative NP PCRs by day 6.
    - Clinical outcomes for those patients were not reported.
    - Of note, there are several methodologic concerns with this case series, which include:
        - Small sample size
        - Unclear criteria for enrollment of cases and controls
        - Asymptomatic individuals were enrolled.
        - Exclusion of 6 hydroxychloroquine patients include 1 death and 2 ICU transfers
        - No clinical outcomes reported; the clinical significance of a negative PCR is unknown.
        - The reason for the addition of azithromycin in some patients is unclear

Monitoring/adverse events/drug-drug interactions:

Chloroquine/Hydroxychloroquine: These drugs have a similar toxicity profile, although hydroxychloroquine is better tolerated and has a lower incidence of toxicity than chloroquine.

Special considerations:

- Cardiac
    - QTc prolongation, torsade de pointe, ventricular arrythmia and cardiac deaths
    - QTc prolongation risk is higher for chloroquine than hydroxychloroquine.
    - Concomitant medications that are moderate to high risk for QT prolongation (e.g. antiarrhythmics, antipsychotics, antifungals, macrolides [including azithromycin] and fluoroquinolone antibiotics) should only be used if necessary. Consider using doxycycline in place of azithromycin as empiric therapy for atypical pneumonia.

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- Baseline and follow-up EKG are recommended if there are potential drug interactions with concomitant medications (e.g., azithromycin) or underlying cardiac diseases.
- The risk-benefit ratio should be closely assessed for patients with cardiac disease, history of ventricular arrhythmia, bradycardia (<50 beats per minute), or uncorrected hypokalemia and/or hypomagnesemia.

- Other adverse effects
  - Hypoglycemia, nausea, and rash. Daily divided doses may reduce these effects.
  - Retinopathy, bone marrow suppression with long-term use; not likely for short-term use.
- There is no evidence that G6PD deficiency is relevant for the use of hydroxychloroquine, and G6PD testing is not recommended.
- With chloroquine use, there is a greater risk for hemolysis in G6PD deficient patients. Obtain G6PD testing before initiation. Consider using hydroxychloroquine until results are available. If the patient is found to be G6PD deficient, hydroxychloroquine should be continued.
- Chloroquine and hydroxychloroquine are moderate inhibitors of CYP2D6 and are also P-gp inhibitors. Use caution when co-administering with concomitant medications metabolized by CYP2D6 (such as certain antipsychotics, beta-blockers, SSRIs, and methadone) or transported by P-gp (such as certain direct-acting oral anticoagulants or digoxin)

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Commented [PA([17]: https://www.covid19-druginteractions.org/

Considerations in Pregnancy

Chloroquine and Hydroxychloroquine:

- Anti-rheumatic doses of chloroquine and hydroxychloroquine have been used safely during pregnancy in mothers with SLE
- Hydroxychloroquine has not been associated with adverse pregnancy outcomes in more than 300 exposed human pregnancies.
- Chloroquine is used for malaria prophylaxis in pregnancy at a lower dose of 500mg per week.
- Animal studies with chloroquine (rats, monkeys) had toxicity only in very high doses.
- Dosing/PK/PD: No dosing changes in pregnancy

Considerations in Children

- Chloroquine and hydroxychloroquine have been used routinely in pediatric populations for the treatment/prevention of malaria and in rheumatologic conditions.

Drug Availability

- Hydroxychloroquine is FDA-approved for treatment of malaria, lupus erythematosus, and rheumatoid arthritis and is available commercially. It is not approved for treatment of COVID-19.
- The FDA issued an Emergency Use Authorization (EUA) for the use of chloroquine and hydroxychloroquine that was donated to the Strategic National Stockpile (SNS). The EUA authorizes the use of these drugs from the SNS for treatment of hospitalized adolescent and adult COVID-19 patients who weigh 50 kg or more and for whom a clinical trial is not available, or participation is not feasible.

Hydroxychloroquine + Azithromycin

Panel's Recommendation:

- The Panel recommends against the use of **hydroxychloroquine + azithromycin** for the treatment of COVID-19 except in a clinical trial **(AIII).**

Rationale for Panel's Recommendation: Chloroquine and hydroxychloroquine have been used in small randomized trials and in some case series with conflicting study reports (as described above). The combination of hydroxychloroquine and azithromycin was associated with QTc prolongation in patients with COVID-19.

Clinical Data in COVID-19

- In a case series of 80 hospitalized patients with COVID-19 (including 6 patients from a previous study), patients were treated with hydroxychloroquine sulfate 200 mg 3x daily for 3 to 10 days + azithromycin 500 mg x 1 day followed by 250 mg daily x 4 days. Mean time from symptom onset to treatment was 4.9 ± 3.6 days. Outcomes evaluated: need for oxygen therapy or ICU transfer after ≥3 days of therapy; NP PCR, SARS-Co-V-2 culture; length of hospitalization.

  Results:
  - Clinical
    - 1 (1.2%) died, 3 (3.8%) required ICU transfer, 12 (15%) required oxygen therapy
    - 65 (81.2%) discharged (to home or "transferred to other units for continuing treatment"); 14 (17.4%) remained hospitalized at time of publication.
  - Laboratory
    - 40/60 (66.7%) patients tested on day 6 had negative NP PCR
    - All patients tested had negative PCRs by days 12-14.
    - Culture positivity decreased over time among the smaller numbers of patients for whom cultures were obtained.
  - Methodologic limitations include:
    - Lack of a control group. This is particularly important because many people with mild disease improve in the absence of treatment.
    - Criteria for selection of cases was not reported.
    - Missing data for PCR and culture results.
    - Definition of "discharge" varied and was unclear.
    - Lack of complete or longer-term follow-up.

- A prospective case series from France of 11 consecutive hospitalized patients with COVID-19 (8 with significant co-morbid conditions: obesity in 2; solid cancer in 3; hematological cancer in 2; HIV-infection in 1). 10/11 patients were receiving supplemental oxygen upon treatment initiation. All were treated with hydroxychloroquine 600 mg daily for 10 days and azithromycin 500 mg x 1 day followed by 250 mg daily x 4 days.

  Results:
  - Within 5 days, 3 patients worsened, including 1 who died and 2 who were transferred to the ICU
  - Adverse effects: hydroxychloroquine discontinued in 1 patient due to QTc prolongation
  - Qualitative NP PCR remained positive at days 5-6 after treatment initiation in 8/10 patients (repeat testing not done in one patient because of death)

Commented [PA([18]: https://www.sciencedirect.com/science/article/pii/S0924857920300996

Commented [AAA19]: Gautret P. Clinical and microbiological effect of a combination of hydroxychloroquine and azithromycin in 80 COVID-19 patients with at least a six-day follow up: an observational study.

Commented [PA([20R19]: https://doi.org/doi:10.1016/j.medmal.2020.03.006

Commented [AAA21]: Molina JM. No Evidence of Rapid Antiviral Clearance or Clinical Benefit with the Combination of Hydroxychloroquine and Azithromycin in Patients with Severe COVID-19 Infection. Medecine et Maladies Infectieuses. 2020. https://doi.org/doi:10.1016/j.medmal.2020.03.006

- A case series in the United States reported changes in QTc interval in 84 patients who received the combination of hydroxychloroquine and azithromycin.

  Results:
  - 84 patients, 74% male, mean age 63 ± 15 years, 65% had hypertension, baseline serum creatinine 1.4 mg/dL, 13% required vasopressors, 11% had coronary artery disease.
  - Concomitant drugs that may prolong QTc interval - 11% on neuropsychiatric drugs and 8% received levofloxacin, lopinavir/ritonavir or tacrolimus.
  - 4 patients died, without arrhythmia
  - Mean baseline QTc was 435 ± 24 ms, mean maximum QTc was 463 ± 35 ms.
  - Mean time to maximum QTc was 3.6 ±1.6 days, ECG follow-up was done for a mean of 4.3 days.
  - 11% developed QTc > 500 ms; in 18% QTc increased by 40-60 ms, and 12% QTc increased by > 60 ms.
  - Baseline QTc was not a predictor of subsequent QTc increase during therapy.
  - In multivariate analysis, acute kidney injury (in 5 patients) was a significant predictor of severe QTc prolongation (OR 19.45 , 95% CI 2.06-183.88, p=0.01).

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Available clinical trials:
Clinical trials are in development in the United States and internationally to test the safety and efficacy of chloroquine or hydroxychloroquine with or without azithromycin in people with or at risk for COVID-19. Please check clinicaltrials.gov for the latest information (https://clinicaltrials.gov/ct2/results?cond=&term=hydroxychloroquine+and+covid-19;

Lopinavir/ritonavir and other HIV Protease Inhibitors:

Panel's Recommendation:

- The Panel recommends against the use of **lopinavir/ritonavir or other HIV protease inhibitors** for the treatment of COVID-19 except in a clinical trial **(AIII).**

Rationale for Panel's Recommendation: The pharmacodynamics of HIV protease inhibitors do not support their therapeutic use for COVID-19. Also, lopinavir/ritonavir was studied in a small randomized controlled trial in patients with COVID-19 with negative results (see below).

Lopinavir/Ritonavir (LPV/r)
Proposed mechanism of Action and Rationale for Use in COVID-19

- Replication of SARS-CoV-2 depends on the cleavage of polyproteins into an RNA- dependent RNA polymerase and a helicase.(1) The enzymes responsible for this cleavage are two proteases, 3-chymotrypsin-like protease (3CLpro) and papain like protease (PLpro).
- Lopinavir/ritonavir (LPV/r) is an inhibitor of SARS-CoV 3CLpro in vitro, and this protease appears highly conserved in SARS-CoV-2.

Commented [PA([23]: 1. Zumla A, Chan JFW, Azhar EI, Hui DSC, Yuen K-Y. Coronaviruses — drug discovery and therapeutic options. Nature Reviews Drug Discovery. 2016;15(5):327-47.

Commented [PA([24]: https://www.sciencedirect.com/science/article/pii/S2095177920301271 andhttps://www.biorxiv.org/content/10.1101/2020.01.29.924100v1.full.pdf.

- LPV/r has in vitro activity against SARS-CoV, though it was thought to have a poor selectivity index, indicating that higher than tolerable levels might be required to achieve meaningful inhibition in vivo.
- Lopinavir is excreted in the gastrointestinal tract, and thus coronavirus-infected enterocytes might be exposed to higher concentrations.

Clinical data on COVID-19

- In a Chinese cohort of 55 pre-symptomatic patients identified early (RT-PCR positive after a family member or close contact was found to have COVID-19), all of whom were given LPV/r for 7 days, all recovered and none required ICU admission.(4)
- In a clinical trial where 199 patients were randomized to 14 days of LPV/r 400mg/100mg orally twice daily or standard of care (SOC), patients randomized to the LPV/r arm did not have a shorter time to clinical improvement.
    - There was a lower, but not statistically significant, mortality rate (LPV/r 19.2%, on SOC 25.0%) and shorter ICU stay compared to those given standard of care (6 days vs. 11 days; difference = -5 days; 95% CI, -9 to 0) (5)
    - The duration of hospital stay and time to clearance of viral RNA from respiratory tract samples did not differ between lopinavir/ritonavir and SOC.
    - Nausea, vomiting, and diarrhea were all more frequent in the LPV/r treated group.
    - The study was powered only to show a ~~substantial~~ fairly large effect.
- A trial of 44 hospitalized patients with mild-to-moderate COVID-19, randomized 21 to LPV/r, 16 to the broad-spectrum antiviral Arbidol (available in Russia), and 7 to SOC.(6)
    - The time to a negative SARS-CoV-2 nucleic acid pharyngeal swab was not shorter for LPV/r (8.5 days [IQR: 3, 13]) vs. SOC (4 days [IQR: 3, 10.5]).
    - Progression to severe/critical status occurred among 8 (38%) patients receiving LPV/r compared to 1 (14%) on SOC.
- A small randomized study from China compared LPV/r to chloroquine. Please refer to the chloroquine section for study description.

Available clinical trials in the United States: none

Monitoring/Adverse Effects/Drug interactions

- Adverse events include
    - Nausea, vomiting, diarrhea (common)
    - QT prolongation
    - Hepatotoxicity
- LPV/r is a potent inhibitor of CYP3A and many medications metabolized by this enzyme may cause severe toxicity. Please refer to https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/284/pi-drug-interactions for list of potential drug interactions.

Considerations in Pregnancy:

- Wide experience with LPV/r use in pregnancies in persons with HIV with good safety profile.
- No evidence of human teratogenicity (can rule out a 1.5-fold increase in overall birth defects).
- Low placental transfer to the fetus. (USDHHS Perinatal HIV Guidelines)
- Dosing:

Commented [PA([25]: Chen F, Chan KH, Jiang Y, Kao RYT, Lu HT, Fan KW, et al. In vitro susceptibility of 10 clinical isolates of SARS coronavirus to selected antiviral compounds. Journal of Clinical Virology. 2004;31(1):69-75

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Commented [PA([27]: *The Journal of Infectious Diseases*, jiaa119, https://doi.org/10.1093/infdis/jiaa119

Commented [PA([28]: Cao B, Wang Y, Wen D, Liu W, Wang J, Fan G, et al. A trial of lopinavir–ritonavir in adults hospitalized with severe Covid-19. New England Journal of Medicine, DOI: 10.1056/NEJMoa2001282

Commented [PA([29]: Li Y, Xie Z, Lin W, Cai W, Wen C, Guan Y, Mo X, Wang J, et al. An exploratory randomized, controlled study on the efficacy and safety of lopinavir/ritonavir or arbidol treating adult patients hospitalized with mild/moderate COVID-19 (ELACOI), https://doi.org/10.1101/2020.03.19.20038984

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- LPV/r oral solution contains 42.4% (volume/volume) alcohol and 15.3% (weight/volume) propylene glycol and **is not recommended** for use during pregnancy (USDHHS Perinatal HIV Guidelines).
- Once daily LPV/rdosing is not recommended during pregnancy.

Considerations in Children:

- LPV/r is approved for the treatment of HIV in infants, children, and adolescents.
- No data on the efficacy of lopinavir/ritonavir treating SARS-CoV-2 in pediatric patients is available

Darunavir/cobicistat (DRV/c) or Darunavir/ritonavir

Rationale for use/proposed mechanism of action for COVID-19

- Inhibition of the 3CLpro enzyme of SARS-CoV-2 and possibly also inhibition of the PLpro.
- Results from an unpublished randomized controlled trial of 30 patients in China showed that darunavir/cobicistat (DRV/c) was not effective in the treatment of COVID-19.

Available clinical trials in the United States: None

Other HIV Protease Inhibitors, including atazanavir:

There are no data from clinical trials supporting the use of other HIV protease inhibitors for treatment of COVID-19.

Remdesivir

Panel's Recommendation: There are insufficient clinical data to recommend for or against using the investigational antiviral agent **remdesivir** for the treatment of COVID-19 **(AIII)**.

Rationale for Panel's Recommendation: Remdesivir is an investigational antiviral drug with no currently available clinical trial data on COVID-19.

Proposed mechanism of Action and Rationale for Use in COVID-19

Remdesivir is an intravenous investigational nucleotide prodrug of an adenosine analog. It has demonstrated in vitro activity against SARS-CoV-2 [Wang, et al], and in vitro and in vivo activity (based on animal studies) against SARS-CoV and MERS-CoV. [Sheahan, Sheahan, DeWit]. It binds to the viral RNA-dependent RNA polymerase, inhibiting viral replication through premature termination of RNA transcription.

Preclinical studies show that remdesivir improves disease outcomes and reduces SARS-CoV (the virus that caused SARS) levels in mice (Sheahan TP et al, Sci Transl Med 2017). When given as prophylaxis or therapy, remdesivir also reduces MERS-CoV levels and lung injury in mice. In a rhesus macaque model of MERS-CoV infection, prophylactic remdesivir prevented MERS-CoV clinical disease (de Wit et al, PNAS, 2020). When given 12 hours after MERS-CoV infection to rhesus macaques, remdesivir reduced viral replication and the severity of lung disease compared to control animals.

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Commented [PA([33]: https://www.jnj.com/lack-of-evidence-to-support-darunavir-based-hiv-treatments-for-coronavirus

Commented [PA([34]:
1. Wang M, et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. Cell Res. 2020 Mar;30(3):269-271.

5. Accessed at: https://clinicaltrials.gov/ct2/show/NCT04257656?cond=NCT04257656&draw=2&rank=1
6. Accessed at: https://clinicaltrials.gov/ct2/show/NCT04252664?term=NCT04252664&cond=remdesivir&draw=2&rank=1

Commented [PA([35]: Sheahan TP, Sims AC, et al. Broad-spectrum antiviral GS-5734 inhibits both epidemic and zoonotic coronaviruses. Sci Transl Med. 2017 Jun 28;9(396).

Sheahan TP, Sims AC, et al. Comparative therapeutic efficacy of remdesivir and combination lopinavir, ritonavir, and interferon beta against MERS-CoV. Nat Commun. 2020 Jan 10;11(1):222.

de Wit E, et al. Prophylactic and therapeutic remdesivir (GS-5734) treatment in the rhesus macaque model of MERS-CoV infection. Proc Natl Acad Sci U S A. 2020 Feb 13. pii: 201922083. doi: 10.1073/pnas.1922083117.]

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Remdesivir is administered by IV infusion at 200 mg on day 1 followed by 100 mg/day for up to 10 days; the infusion is usually given over 30-60 minutes.

Clinical data to date: Only anecdotal data are available.

Clinical Trials: Multiple clinical trials are currently underway or in development. https://clinicaltrials.gov/ct2/results?cond=&term=remdesivir+and+covid-19

In areas without access to clinical trials in the United States, remdesivir may be available through an expanded access program: https://remdesivircu.gilead.com/external icon. for a subset of patients

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Monitoring/adverse effects/drug-drug interactions: Remdesivir can cause gastrointestinal symptoms, (including nausea, vomiting), elevated transaminases and prothrombin time elevation (without change in INR). Remdesivir is a CYP3A4, CYP2C8, and CYP2D6 substrate in vitro. Coadministration of remdesivir with inhibitors of these enzymes is not expected to have a significant impact on remdesivir concentrations. Remdesivir concentration may be affected by strong CYP inducers, but the interaction is not expected to be clinically significant.

Commented [PA([39]: Remdesivir (GS-5734™) Investigator's Brochure. Edition 5. Dated 21 February 2020. Gilead Sciences, In

Because remdesivir formulation contain s renally cleared sulfobutylether beta-cyclodextrin sodium (SBECD), patients with eGFR <50 mL/min are excluded from some clinical trials (note some trials have a cutoff of eGFR < 30 mL/min).

Considerations in Pregnancy:

- Remdesivir is available for pregnant women through the compassionate access program.
- In a randomized controlled Ebola treatment trial, among 98 females in the remdesivir arm, 6 had a positive pregnancy test, the obstetric and neonatal outcomes were not reported in the study.

Considerations in Children:

- Currently, remdesivir is only available for compassionate use for <18 years of age
- There is no published clinical data on remdesivir use in pediatric patients

Host modifiers and Immune-Based Therapy for COVID-19

Several immune therapies directed at modifying the course of COVID-19 are currently under investigation or are used off-label. These agents may target the virus (such as convalescent plasma) or modulate the immune response (such as IL-1 or IL-6 blockade).

Convalescent Plasma and Specific Immune Globulins

Panel's Recommendation: There are insufficient data to recommend for or against the use of convalescent plasma or hyperimmune immunoglobulin for the treatment of COVID-19 (AIII).

Rationale for Panel's Recommendation: While convalescent plasma and hyperimmune immunoglobulin have been used in other viral infections, sufficient clinical data are lacking for COVID-19 and theoretical

risks exist of antibody-dependent enhancement (ADE) of infection and transfusion-associated acute lung injury (TRALI).

Rationale for Use in Patients with COVID-19:

Plasma donated from individuals who have recovered from COVID-19, which includes antibodies to SARS-CoV-2, may help suppress the virus and may modify the inflammatory response. SARS-CoV-2 Immune Globulin Intravenous (IVIG) is a concentrated antibody preparation derived from plasma of people who have recovered from COVID-19.

Clinical Experience in Patients with ~~Coronavirus~~Viral Infections:

- Data supporting the use of convalescent plasma for COVID-19 and SARS are limited to case reports and case series. There are no clinical data on the use of specific immune globulin or hyperimmune immunoglobulin in COVID-19, SARS, or MERS.
- The use of convalescent plasma has been evaluated in other viral diseases, with some evidence of potential benefit. No such products are currently licensed by the FDA.
- Several specific immune globulin products are licensed for preventing post-transplant CMV disease (Cytogam) and post-exposure prophylaxis of varicella in high-risk individuals (VariZig).
- Risks associated with plasma transfusion include antibody-mediated enhancement of infection, transfusion-related acute lung injury (TRALI), transfusion-associated circulatory overload (TACO), and allergic transfusion reactions (ATR). Rare complications include transmission of infectious diseases and red cell alloimmunization.
- Clinical trials are in development to evaluate both convalescent plasma and SARS-CoV-2 IVIG for the treatment of COVID-19.
- The FDA has provided guidance for the use of COVID-19 Convalescent Plasma under Emergency IND. https://www.fda.gov/vaccines-blood-biologics/investigational-new-drug-ind-or-device-exemption-ide-process-cber/investigational-covid-19-convalescent-plasma-emergency-inds
- The FDA has approved a national expanded access program for the use of convalescent plasma for the treatment of Patients with COVID-19. Clinicians can refer to link [https://ccpp19.org/about/index.html] for more information. People who have fully recovered from COVID-19 for at least two weeks who are interested in donating plasma can contact their local blood donor or plasma collection center or refer to the American Red Cross website [link www.redcrossblood.org/plasma4covid]

Considerations in Pregnancy:

- Pathogen-specific immunoglobulins are used clinically during pregnancy to prevent varicella zoster virus and rabies, and have been used in clinical trials of congenital CMV infection.

Considerations in Pediatrics:

- Hyperimmune globulin has been used in the treatment of several viral infections in children, including VZV, RSV, and CMV; efficacy data for other respiratory viruses is limited
- The efficacy and/or side effects associated with administration of convalescent plasma has not been well established.

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Interleukin-1 (IL-1) and Interleukin-6 Inhibitors and Other Immunomodulators

The cytokine profiles of serum from some patients with moderate to severe COVID-19 overlap with those seen in macrophage activation syndrome (MAS) and secondary hemophagocytic lymphohistiocytosis (sHLH) (Petersen). MAS is characterized by hyperinflammation and manifests as fever, elevated ferritin levels and pulmonary involvement, with a spectrum of presentation that includes sHLH (Ramos-Casals). Viruses are known triggers of MAS/sHLH, and high ferritin levels are associated with both MAS and mortality in COVID-19 (Seguin2016; Huang 2020). Endogenous IL-1, a proinflammatory cytokine, potently induces IL-6 in monocytes and macrophages and is elevated in COVID-19, MAS, and other conditions such as severe chimeric antigen receptor T-cell (CAR-T) mediated cytokine release syndrome (CRS).(Shakoory) The JAK family of enzymes regulate signal transduction in immune cells and JAK inhibitors play a major role in inhibiting and blocking cytokine release. IL-6 and IL-1 blockades and JAK inhibition have each been proposed as an approach to treat the systemic inflammation associated with severe COVID-19 and are reviewed below.

IL-1 Inhibitor (such as Anakinra)

Panel's Recommendation: There are insufficient data to recommend for or against the use of an IL-1 antagonist such as anakinra for treatment of COVID-19 (AIII).

Rationale for Panel's Recommendation: There are no data from clinical trials using anakinra in COVID-19.

Anakinra is a recombinant human IL-1 receptor antagonist (rhIL-1ra). It is approved for a variety of inflammatory conditions ranging from RA to familial Mediterranean fever and is also used off-label for the severe CAR-T mediated CRS and MAS/sHLH.

Proposed Mechanism of Action and Rationale for Use: Endogenous IL-1 is elevated in COVID-19 and other conditions such as severe chimeric antigen receptor T-cell (CAR-T) mediated cytokine release syndrome (CRS).

Clinical data for COVID-19: There are no published studies to date on the use of anakinra in COVID-19 infection, or for other novel coronavirus infections (SARS or MERS).

Clinical trial: An open label randomized trial of IV administered Anakinra for COVID-19 compared with emapalumab (an interferon gamma (IFNγ)–blocking antibody) is being conducted in Italy.

Adverse effects and monitoring: Anakinra was not associated with any significant safety concerns in trials of sepsis. Increased rates of infection were reported with prolonged use in combination with TNF-alfa blockade, but not with short-term use.

Pregnancy Consideration. Limited evidence on which to base a recommendation in pregnancy, but unintentional first trimester exposure is unlikely to be harmful.

Considerations in Children:

- Anakinra has been used extensively in the treatment of severely ill children with complications of rheumatologic conditions, including macrophage activating syndrome.
- Pediatric data for its use in ARDS/sepsis are limited.

Drug Availability: Procurement of anakinra may be a challenge at some hospitals in the U.S. Anakinra is approved only in a SC formulation.

Commented [PA([43]: Petersen and Ho: https://www.jci.org/articles/view/137647

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IL-6 Inhibitors (sarilumab, siltuximab, tocilizumab)

Panel's Recommendation: There are insufficient data to recommend for or against the use of IL-6 or IL-6R inhibitors (such as sarilumab, siltuximab, or tocilizumab) for the treatment of COVID-19 (AIII).

Rationale for Panel's Recommendation: There are no data from clinical trials on the use of IL-6 antagonist in COVID-19.

Rationale for IL-6 (interleukin-6) blockade

- IL-6 is a pleiotropic, pro-inflammatory cytokine produced by a variety of cell types, including lymphocytes, monocytes and fibroblasts.
- Infection by the related SARS-CoV induces a dose-dependent production of IL-6 from bronchial epithelial cells [Yoshikawa et. al. Journal of Virology 2009;83(7):3039]. Elevations in IL-6 levels may be an important mediator when severe systemic inflammatory responses occur in patients infected with SARS-CoV-2.
- COVID-19-associated systemic inflammation and hypoxic respiratory failure is associated with heightened cytokine release as indicated by elevated blood levels of IL-6 , CRP, D-dimer, and ferritin but typically not procalcitonin.

Commented [PA([55]: Zhou et. al. Lancet 2020, Huang et. al. Lancet 2020, Wang et. al. CID in press]

Sarilumab

Sarilumab is a recombinant humanized anti-IL-6R monoclonal antibody that is FDA- approved for use in patients with RA. It is dosed SC and is not approved for cytokine release syndrome. A placebo-controlled clinical trial is evaluating the use of an IV formulation administered as a single dose for COVID-19.

Clinical data. There are currently no data from randomized clinical trials or large observational cohorts describing the efficacy of sarilumab among patients with COVID-19.

Potential adverse effects and monitoring. Primary lab abnormalities reported with sarilumab treatment are transient/reversible elevations in liver enzymes that appear dose dependent and rare occurrences of neutropenia and thrombocytopenia. Risk for serious infections (e.g., TB, other bacterial) have been reported only in the context of long-term use of sarilumab.

Pregnancy Considerations: There are insufficient data to determine if there is a drug-associated risk for major birth defects or miscarriage.

Drug availability. The SC formulation is not approved for cytokine release syndrome and the IV formulation is not FDA approved, but is being studied in a clinical trial of hospitalized patients with COVID-19 (https://clinicaltrials.gov/ct2/results?cond=&term=sarilumab+and+COVID-19)

Siltuximab

Siltuximab is a recombinant human-mouse chimeric monoclonal antibody that binds IL-6, and is FDA-approved for use in patients with Castleman's disease. Siltuximab prevents the binding of IL-6 to both soluble and membrane-bound IL-6R and thereby inhibits IL-6 signaling. Siltuximab is dosed as an IV infusion.

Clinical data. There are limited data describing the efficacy of siltuximab among patients with COVID-19. There are also no data describing clinical experiences using siltuximab for patients with other novel coronavirus infections (e.g., SARS or MERS).

Potential adverse effects and monitoring. The primary adverse effects reported have been related to rash. Additional adverse events such as risk for serious bacterial infections have been reported only in the context of long-term dosing of siltuximab every three weeks.

Pregnancy Considerations: There are insufficient data to determine if there is a drug-associated risk for major birth defects or miscarriage.

Drug availability. Procurement of siltuximab may be a challenge at some hospitals in the U.S.

Tocilizumab

Tocilizumab is a recombinant humanized anti-IL-6R monoclonal antibody that is FDA-approved for use in patients with rheumatologic disorders and cytokine release syndrome-induced by CAR T-cell therapy. Tocilizumab can be dosed IV or SC. For cytokine release syndrome, the IV formulation should be used.

Clinical data for COVID-19.

- There are no data from randomized clinical trials or large observational cohort studies describing the efficacy of tocilizumab among patients with COVID-19.
- There are anecdotal reports of improved oxygenation in patients with COVID-19, systemic inflammation and hypoxic respiratory failure.

Potential adverse effects and monitoring. The primary laboratory abnormalities reported with tocilizumab treatment are elevated liver enzymes that appear to be dose dependent. Neutropenia or thrombocytopenia are uncommon. Additional adverse events such as risk for serious infections (e.g., TB, other bacterial) have been reported only in the context of continuous dosing of tocilizumab.

Considerations in Pregnancy: There are insufficient data to determine whether there is a risk for major birth defects and miscarriage. Monoclonal antibodies are actively transported across the placenta in the third trimester and may affect immune responses in utero in the exposed infant.

Considerations in Children: Tocilizumab is frequently used in cytokine release syndrome following CAR T-cell therapy (Gardner, Blood 2019), and occasionally for macrophage activating syndrome in children. (Yokota, 2015). Pediatric data for its use in ARDS/sepsis are limited.

Drug availability. Procurement of IV tocilizumab may be a challenge at some hospitals in the U.S.

Clinical Trial: Ongoing trials can be found in this link:
https://clinicaltrials.gov/ct2/results?cond=&term=tocilizumab+and+covid-19

Commented [PA([56]: https://www.medrxiv.org/content/10.1101/2020.04.01.20048561v1

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Macrophage Activation Syndrome in Patients with Systemic Juvenile Idiopathic Arthritis under Treatment with Tocilizumab.
Yokota S[1], Itoh Y[2], Morio T[2], Sumitomo N[2], Daimaru K[2], Minota S[2].

Other immunomodulators

Interferons (Alpha, Beta)

Panel's Recommendation: The Panel recommends against the use of interferons for treatment of COVID-19 except in a clinical trial (AIII).

Rationale for Panel's Recommendation: The lack of benefit when interferons were used in other coronavirus infections MERS and SARS, and no clinical trial results in COVID-19, as well as significant toxicities of interferons outweighs the potential for benefit.

Rationale for Use: Interferons, a family of cytokines with antiviral properties, have been suggested as a potential treatment of COVID-19 for their in vitro and in vivo antiviral properties.

Clinical data:

- Interferon-beta alone and in combination with ribavirin in SARS and MERS has failed to show a significant positive effect on clinical outcomes [1-5].
- In a retrospective observational analysis of 350 critically ill patients with MERS[2] from 14 hospitals in Saudi Arabia, mortality was higher for those who received ribavirin and interferon (-beta-1a, alfa-2a, or alfa-2b) compared to those who did not.
- In a randomized clinical trial that included 301 patients with ARDS[6], there was no benefit of IV interferon β-1a compared with placebo as measured by ventilator-free days over a 28-day period (median, 10.0 vs 8.5 days) or mortality (26.4% vs 23.0%).
- INF- alfa-1b (not available in the US) has been used in patients with COVID-19 in China, but it has been primarily used by atomization inhalation and the clinical data have not yet been presented.

Adverse events and monitoring. The most frequent adverse effects of interferon-alfa include flu-like symptoms, hematological toxicities (cytopenias) including elevated transaminases, nausea, fatigue, weight loss, and psychiatric problems (depression and suicidal ideation). Interferon-beta is better tolerated.

Drug-drug Interactions. The most serious interactions are the potential for added toxicity with other immunomodulators and chemotherapeutic agents

Considerations in Pregnancy: 63 pregnancies were studied in which IFN-B1b was used for MS and no major birth defects were observed. The average birth weight was reduced. (Weber-Schoendorfer 2008)

Considerations in Children: There are limited data on the use of interferons for treatment of respiratory viral infections.

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Janus Kinase (JAK) Inhibitors (such as baricitinib)

Panel's Recommendation: The Panel recommends against the use of JAK inhibitors for the treatment of COVD-19 except in a clinical trial (AIII).

Rationale for Panel's Recommendation: At present, the broad immunosuppressive effect of JAK inhibitors outweigh the potential for benefit.

Baricitinib is an oral Janus Kinase (JAK) inhibitor that works by inhibiting the JAK-STAT pathway. Baricitinib is FDA-approved to treat RA and can ameliorate the chronic inflammation seen in interferonopathies.

Rationale for Use in COVID-19: Baricitinib is a potent anti-inflammatory with activity against interferon-associated inflammation. It has also been postulated to have an antiviral effect. A related drug, ibrutinib, has been showed to decrease lung inflammation in a mouse model of influenza.

Clinical data for COVID-19: There are no clinical data reported to date.

Adverse effects: Side effects with prolonged use include upper respiratory infections (>10%), increased LDL, herpesvirus infections, increased LFTs and thrombocytosis.

Pregnancy Considerations:

- In animal studies of embryo-fetal development, there was increased embryolethality in some species at very high doses, well above the recommended dose for humans. (baricitinib package insert).
- Limited human data on the use of baricitinib are not enough to inform a drug-associated risk for major birth defects or miscarriage. (Package insert)

CORTICOSTEROIDS

The role of corticosteroid as concomitant therapy in persons with COVID-19 will be discussed in the Special Considerations for Concomitant Use of Certain Medications section.

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First published March 8, 2018;
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Table 2a: Potentially Direct Acting Antiviral Agents Under Evaluation for Treatment of COVID-19: Clinical Data to Date

Information presented in this table may include data from pre-print/non-peer reviewed articles. This table will be updated as new information becomes available.

Drug Name	FDA Approved Indications	Pre-clinical Data / Mechanism of Action	Clinical Data to Date Find clinical trials on www.clinicaltrials.gov
Azithromycin (+ HCQ)	• Mycobacterial (nontuberculous) infection • Sexually transmitted infections, and various bacterial infections	• Proposed antiviral effects: induction of IFN-stimulated genes, attenuating viral replication • Immunomodulatory effect: enhanced neutrophil activation • Anti-inflammatory effects: attenuation of inflammatory cytokines (IL-6 and IL-8) in epithelial cells and inhibition of fibroblast growth factor in airway smooth muscle cells	Azithromycin is only studied for treatment of COVID-19 in the context of combination with hydroxychloroquine. Please see description of study results below under "Hydroxychloroquine and Azithromycin", and in the **Therapeutic Options Under Investigation** section
Chloroquine	• Malaria • Extraintestinal amebiasis	• *In vitro* antiviral activity by increasing the pH of intracellular vacuoles and altering protein degradation pathways thereby interfering with the virus/cell fusion and glycosylation of cellular receptors • Inhibits glycosylation of the cellular ACE2 receptor, which may interfere with binding of the virus to the cell receptor • Immunomodulatory effects may lead to a reduction in pro-inflammatory cytokines	In a small RCT in China, 22 hospitalized patients (none critically ill) were randomized to chloroquine 500mg PO twice daily or LPV/r 400mg/100mg twice daily for 10 days. Ten patients received chloroquine and 12 patients received LPV/r. The chloroquine treated patients had a shorter duration from symptom onset to initiation of treatment (2.5 days vs. 6.5 days, $p<0.001$). Outcomes included SARS-CoV-2 negative PCR at days 10 and 14, CT scan improvement at days 10 and 14, and discharge at day 14. The risk ratios of these outcome results were not statistically significant between groups.
Hydroxychloroquine	• Lupus erythematosus • Malaria • Rheumatoid arthritis	• *In vitro* antiviral activity by increasing the pH of intracellular vacuoles and altering protein degradation pathways thereby interfering with the virus/cell fusion and glycosylation of cellular receptors • Immune modulating effect may lead to a reduction in pro-inflammatory cytokines	In a small RCT in China, 62 hospitalized patients with "mild" COVID-19 pneumonia were randomized to HCQ 200 mg PO twice daily x 5 days vs "standard treatment" (including O_2, antivirals, antibacterials, immunoglobulin, with or without steroids). Mean duration of fever and cough was 1 day shorter among HCQ-treated patients than among controls. 13% of control patients and none of the HCQ-treated patients experienced progression of illness. 80.6% of HCQ-treated patients experienced either moderate or significant improvement in chest CT, compared to 54.8% of controls. Limitations include small sample size and short follow up, standard treatment and progression of illness were not well defined, and distribution of comorbidities and whether radiologists were blinded was not reported. Prospective trial of 30 patients with mild COVID-19 randomized 1:1 to HCQ 400 mg daily for 5 days plus conventional treatment (alpha interferon [100%], Arbidol (umifenovir) [80%], LPV/r [2%]) versus conventional treatment alone. On day 7, nasopharyngeal swab was negative in 86.7% (13/15) in HCQ group vs. 93.3% (14/15) in control, $p>0.05$. No difference in hospitalization. One patient in hydroxychloroquine group progressed to severe pneumonia.

Commented [KS([2]: Ref: Eur Respir J. 2010 Sep;36(3):646-54. doi: 10.1183/09031936.00095809. https://erj.ersjournals.com/content/36/3/646

Commented [KS([3]: REF: Eur J Pharmacol. 2002 Aug 30;450(3):277-289. https://www.ncbi.nlm.nih.gov/pubmed/12208321

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Commented [KS([10]: REF: Package insert. https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/009768s037s045s047lbl.pdf

Commented [KS([12]: https://www.nature.com/articles/s41422-020-0282-0 REF: Cell Res. 2020 Mar;30(3):269-271. doi:

Commented [KS([14]: REF:http://www.zjujournals.com/med/EN/10.3785/j.issn.1008-9292.2020.03.03

			Case series in 42 patients with COVID-19: 26 received HCQ 200 mg three times daily for 10 days and 16 control patients. Six patients who received HCQ were not included in the analysis due to death, ICU transfer, adverse effects, or withdrawal. 14 patients received hydroxychloroquine alone; 6 patients received hydroxychloroquine + azithromycin. See text for details on significant methodological concerns regarding these data.
Hydroxychloroquine plus azithromycin	see azithromycin and HCQ	See azithromycin and HCQ	In a single center case series of 80 patients with generally mild COVID-19 who received HCQ 200 mg three times daily and azithromycin for ≥ 3 days and had ≥ 6 days of data. 66% had negative NP PCR by Day 6. See text for details on significant methodological concerns regarding these data. In a prospectively studied case series from France of 11 consecutive hospitalized patients with COVID-19, all were treated with HCQ 600 mg daily for 10 days and azithromycin 500 mg x 1 day followed by 250 mg daily x 4 days. Within 5 days, 3 patients worsened, including 1 who died and 2 who were transferred to the ICU. Adverse effects: hydroxychloroquine discontinued in 1 patient due to QTc prolongation. Qualitative NP PCR remained positive at days 5-6 after treatment initiation in 8/10 patients (repeat testing not done in one patient because of death). In a case study evaluating QTc before and after initiation of HCQ + azithromycin in 84 patients, noted that 11% oof the patients had peak QTc > 500 ms; 30% had increase by > 30ms from baseline; peak QTc occurred at 3.6 ± 1.6 days after beginning of treatment. Acute kidney injury was a strong predictor of severe QTc prolongation.
HIV Protease Inhibitors LPV/r and DRV/c have been studied in patients with COVID-19	• HIV Infection	• No data on *in vitro* activity against SARS-CoV-2 • Possible inhibition of SARS-CoV-2 protease 3CLpro	In an open label RCT, 199 participants with COVID-19 were randomized to LPV/r 400/100mg twice daily for 14 days versus standard of care. Participants enrolled a median of 13 days after symptom onset. No difference in primary outcome (time to clinical improvement) was observed and 28-day mortality was similar between groups. About 50% of participants in each group experienced adverse effects; 13.8% in the LPV/r group could not complete treatment due to adverse effects. In an exploratory RCT of 44 participants with mild-moderate COVID-19, 21 participants were randomized to LPV/r, 16 to Arbidol (umifenovir) and 7 to control. No differences were observed in the primary outcome (time to conversion of SARS-CoV-2 nucleic acid from treatment initiation to day 21) or in clinical measures (rates of antipyretic treatment, cough alleviation, improvement in chest CT, or deterioration rate). 23.8% (5

Commented [KS([15]: Molina JM. No Evidence of Rapid Antiviral Clearance or Clinical Benefit with the Combination of Hydroxychloroquine and Azithromycin in Patients with Severe COVID-19 Infection. Medecine et Maladies Infectieuses. 2020. https://doi.org/doi:10.1016/j.medmal.2020.03.006

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			participants) in the LPV/r experienced adverse effects versus none in Arbidol (umifenovir) or control group. Results from an unpublished study in China showed that darunavir/cobicistat is not effective in the treatment of COVID-19.
Remdesivir (GS-5734)	• Not FDA approved • Investigational antiviral agent	• Adenosine nucleotide analog prodrug that undergoes hydrolysis to active form which inhibits viral RNA-dependent RNA polymerase • Potent *in vitro* activity demonstrated in SARS-CoV-2 infected Vero E6 cells	Single case report of a 35-year-old man with COVID-19 who progressed to pneumonia by day 9 requiring supplemental oxygen. Remdesivir started on day 11 with improvement observed by day 12, and afebrile and asymptomatic except for cough by day 15.

Key: ACE2 = angiotensin-converting enzyme 2; COVID-19 = coronavirus-19 disease; FDA = Food and Drug Administration; IL = interleukin; IFN = interferon; HCQ = hydroxychloroquine; LPV/r = lopinavir/ritonavir; RCT = randomized controlled trial; SARS-CoV- =: severe acute respiratory syndrome coronavirus 2

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Commented [KS([22]: https://www.ncbi.nlm.nih.gov/pubmed/26934220 Nature. **2016** Mar 17;531(7594):381-5. doi: 10.1038/nature17180. Epub **2016**

Commented [KS([24]: https://www.nejm.org/doi/full/10.1056/NEJMoa2001191 **N Engl J Med**. 2020 Mar 5;382(10):929-936. doi: 10.1056/NEJMoa2001191. Epub 2020 Jan 31.

Commented [KS([23]: Clinical Features of 69 Cases with Coronavirus Disease 2019 in Wuhan, China. **Wang** Z, Yang B, Li Q, Wen L, Zhang R. **Clin Infect Dis**. 2020 Mar 16. pii: ciaa272. doi: 10.1093/cid/ciaa272. [Epub ahead of print] PMID: 32176772

Table 2b. Characteristics of Potential Direct-Acting Antiviral Agents Under Evaluation for Treatment of COVID-19

- The information in this table is derived from data on the use of these drugs for FDA-approved indications or from investigational trials, and it is supplemented with data from patients with COVID-19 where available.
- The effective dosing of these drugs for treatment of COVID-19 is unknown. Therefore, the doses listed below are primarily derived from FDA-approved indications or from clinical trials investigating therapies for COVID-19.
- There is limited or no data on dose modifications for patients with organ failure or those who require extracorporeal devices; please refer to product labels, when available.
- Treatment-related AEs in patients with COVID-19 are not well defined; the validity of extrapolation between patient populations (i.e., FDA-approved use vs. COVID-19 use) is unknown, especially in critically ill patients. Reported AEs of these drugs that are associated with long-term therapy (i.e., months to years) are not included in this table because treatment for COVID-19 is not long term. Please refer to product labels, when available.
- The safety of using treatments for COVID-19 concurrently with other medications is unknown. When using concomitant medications with similar toxicity profiles, consider additional safety monitoring.
- The potential additive, antagonistic, or synergistic effects and the safety of combination therapies for treatment of COVID-19 are unknown. Clinicians are encouraged to report adverse events to the FDA *Medwatch* program.
- For drug interaction information, please refer to product labeling and visit the Liverpool COVID-19 Drug Interactions website.
- For information on drugs that prolong the QT interval, please visit *CredibleMeds.org*.

Drug Name (Generic)	Dosing Regimens *There are no approved doses for the treatment of COVID-19. The doses listed here are for approved indications, from reported experiences or clinical trials.*	Adverse Effects	Monitoring Parameters	Drug-Drug Interaction Potential	Panel's Recommendation/ Comments / Clinical Trials Link
Azithromycin (when used with hydroxychloroquine in reported cases)	500 mg PO once on Day 1, then 250 mg PO daily on Days 2-5	• Gastrointestinal effects (e.g., diarrhea, nausea, vomiting) • Hepatotoxicity	• Baseline/follow-up ECG • Hepatic panel, S.Cr., potassium, magnesium	• Additive effect with other drugs that prolong the QT interval (including hydroxychloroquine and chloroquine)	Panel recommends against use of HCQ + azithromycin except in a clinical trial **(AIII)** For clinical trials, click here: Azithromycin
Chloroquine	Suggested dose in Emergency Use Authorization (EUA)[1] for adults/adolescents ≥50 kg: 1 gram PO one time dose on Day 1, then 500 mg PO once daily for 4-7 days of total treatment based on clinical evaluation. Per EUA: some experts recommend a dose reduction of 50% for GFR < 10 mL/min, hemodialysis, or peritoneal dialysis; no dose reduction is recommended if GFR > 10 mL/min	• Prolonged QT interval, Torsades de Pointes, AV block, ventricular arrhythmia • Gastrointestinal effects (e.g., nausea, vomiting, diarrhea, hepatitis) • Hypoglycemia • Hemolysis (esp if G6PD deficient) • Myopathy	• CBC, hepatic panel, blood glucose, S.Cr., potassium, magnesium • Baseline/follow-up ECG if given with concomitant QTc prolonging drugs or if underlying cardiac diseases	• Additive effect with other drugs that prolong the QT interval (including azithromycin) or cause hypoglycemia • CYP2D6 inhibitor (moderate) • P-gp inhibitor	Insufficient data for the Panel to recommend for or against use of chloroquine **(AIII)** Available through Emergency Use Authorization for hospitalized patients who cannot access chloroquine via clinical trials

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Table 3b also has biologic products listed, should it be added here, as well?

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There are currently not enough data to determine whether certain medications can be safely coadministered with treatment for COVID-19.

Or

There is a lack of data on the safety of coadministering treatments for COVID-19 and many other medications.

Commented [KS([4R3]: I think I like the second option – because it says "certain" meds instead of implying there is no safety data with any meds. Many drugs in this table have been around for a long time

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Commented [JM7]: http://www.covid19-druginteractions.org/

Commented [JM8]: www.crediblemeds.org

		• Rash	• G6PD testing, Not recommended in patients with G6PD deficiency - consider using HCQ instead of chloroquine while awaiting G6PD result.		Dose dependent toxicity. For clinical trials, click here: Chloroquine
Hydroxychloroquine	**Adults:** Various loading and maintenance doses have been reported in studies or in clinical care. Suggested dose in Emergency Use Authorization (EUA)[1] for hospitalized adults/adolescents ≥50 kg: 800 mg PO one time dose on Day 1, then 400 mg PO once daily for 4-7 days based on clinical evaluation. Per EUA: some experts recommend a dose reduction of 50% for GFR < 10 mL/min, hemodialysis, or peritoneal dialysis; no dose reduction is recommended if GFR > 10 mL/min **Infants, Children, and Adolescents:** 13 mg/kg (maximum: 800 mg) PO followed by 6.5 mg/kg (maximum: 400 mg) PO at 6 hours, 24 and 48 hours after initial dose; could extend up to a total of duration of 5 days. **OR** 6.5 mg/kg/dose (maximum: 400 mg/dose) PO BID on day 1, followed by 3.25 mg/kg/dose (maximum: 200 mg/dose) PO BID for up to a total duration of 5 days **Neonates:** dosing not established	• Prolonged QT interval, Torsades de Pointes, AV block, ventricular arrhythmia • Gastrointestinal effects (e.g., nausea, vomiting, diarrhea, hepatitis) • Hypoglycemia • Myopathy • Anxiety, agitation, hallucinations, psychosis • Allergic reaction/rash	• CBC, hepatic panel, blood glucose, S.Cr., potassium, magnesium • Baseline ECG • Follow-up ECG if given with concomitant QTc prolonging drugs (e.g. azithromycin) or if underlying cardiac diseases	• Additive effect with other drugs that prolong the QT interval (including azithromycin) or cause hypoglycemia • CYP2D6 inhibitor (moderate) • P-gp inhibitor	Insufficient data for the Panel to recommend for or against use of hydroxychloroquine **(AIII)** Panel recommends against use of HCQ + azithromycin except in a clinical trial **(AIII)** Available through Emergency Use Authorization for hospitalized patients who cannot access chloroquine via clinical trials Long elimination half-life (40–55 days) Dose dependent toxicity. For clinical trials, click here: Hydroxychloroquine
Lopinavir/Ritonavir	**Adults:** Lopinavir 400 mg/ritonavir 100 mg PO twice daily for 10–14 days	• Nausea, vomiting, diarrhea	• HIV antigen/antibody testing at baseline	**High Drug Interaction Potential**	Panel recommends against use of lopinavir/ritonavir

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	Neonates ≥14 days and PMA ≥42 weeks to children < 18 years of age: Lopinavir/r 300/75mg/m2 (maximum 400mg/100mg/dose) PO twice daily for a total of 7 days	• Transaminase elevation • QT interval prolongation and Torsades de Pointes have been reported. • PR interval prolongation	• Serum transaminase levels • Consider monitoring ECG when given with other QTc prolonging medications.	*Lopinavir:* • CYP3A4 inhibitor and substrate *Ritonavir:* • CYP3A4 > 2D6 substrate • Potent CYP3A4 and 2D6 inhibitor • Inducer of UGT1A1 and CYPs 1A2, 2C8, 2C9, and 2C19	except in a clinical trial **(AI)** Liquid formulation commercially available. Crushing lopinavir/ritonavir tablets may result in significantly decreased drug exposure (AUC ↓ 45%). Use with caution in patients with hepatic impairment. For clinical trials, click here: LPV/r
Remdesivir (GS-5734) *Investigational drug*	**Adults:** 200 mg IV once on Day 1, followed by 100 mg IV every 24 hours Duration of therapy varies per clinical trial (typically from 5-10 days) **Pediatrics:** <40 Kg: 5 mg/kg IV loading dose on Day 1, followed by 2.5 mg/kg IV every 24 hours ≥40 kg: 200 mg IV loading dose on Day 1, followed by 100 mg IV every 24 hours	• Transient elevations in ALT or AST (Grade 1 or 2), typically after multiple days of therapy • Mild, reversible PT prolongation without INR change or hepatic effects • Potential for SBECD accumulation in moderate to severe renal impairment • Gastrointestinal symptoms (e.g. nausea, vomiting)	• Monitor for infusion reactions. • Renal and hepatic function • Do not administer remdesivir if eGFR < 30 mL/min (or receiving dialysis), or if ALT or AST is > 5 times ULN	• Remdesivir levels are unlikely to be markedly altered by CYP2C8, CYP2D6, or CYP3A4 enzymes, or by P-gp or OATP drug transporters. It may be administered with weak to moderate inducers or with strong inhibitors of CYP450, OATP or P-gp. • **Strong induction** of P-gp is expected to modestly reduce RDV levels. The clinical relevance of lower RDV levels is unknown. The use of RDV with known inducers of P-gp (e.g., rifampin or herbal medications) is not recommended.	Insufficient data for the Panel to recommend for or against remdesivir use **(AIII)** Drug vehicle is SBECD, which has been associated with renal toxicity. Expanded access and compassionate use programs are available to certain patient population. For clinical trials, click here: Remdesivir

Key: AE = adverse effect; ALT = alanine transaminase; AST = aspartate aminotransferase; AUC = area under the curve; AV = atrioventricular; BID = twice daily; CBC = complete blood count; CHF = congestive heart failure; COVID-19 = coronavirus disease 2019; CrCl = creatinine clearance; CRP = C-reactive protein; CYP = cytochrome P; ECG

Commented [KS([11]: https://www.ncbi.nlm.nih.gov/pubmed/21876444

Commented [CP([12]: REF for all 3 adverse effects Remdesivir (GS-5734) Investigator's Brochure. Edition 5 (dated 21 February 2020) Gilead Sciences Inc.

Commented [PA([13]: https://www.gilead.com/purpose/advancing-global-health/covid-19/emergency-access-to-remdesivir-outside-of-clinical-trials

= electrocardiogram; eGFR = estimated glomerular filtration rate; EUA = Emergency Use Authorization; FDA = Food and Drug Administration; IND = Investigational New Drug Application; INR = international normalized ratio; IV = intravenous; P-gp = P-glycoprotein; PMA = postmenstrual age; PO = orally; PT = prothrombin time; RDV = remdesivir; SBECD = sulfobutylether β-cyclodextrin sodium; UGT = uridine diphosphate glucuronyl transferase; ULN = upper limit of normal

[1] The EUA authorizes the use of these drugs from the SNS for treatment of hospitalized adolescent and adult COVID-19 patients who weight 50 kg or more and for whom a clinical trial is not available, or participation is not feasible.

Novel Coronavirus Pneumonia Diagnosis and Treatment Plan (Provisional ~~6th~~ 7th Edition)

Since December 2019, many cases of novel coronavirus pneumonia have been found in Wuhan City, Hubei Province, and with the spread of the epidemic, such cases have also been found in other regions of China and overseas. As an acute respiratory infectious disease, the disease has been listed as a Class B infectious disease as provided by the "Law of the People's Republic of China on Prevention and Control of Infectious Diseases", and is managed as a Class A infectious disease.

Through the adoption of a series of preventive control and medical treatment measures, the rise of the epidemic situation in China has been contained to a certain extent. The epidemic situation has eased in most provinces, but the number of cases outside the country has shown an upward trend. With the deepened understanding of the clinical manifestations and pathological knowledge of the disease and the accumulation of experience in diagnosis and treatment, in order to further strengthen the early diagnosis and early treatment of the disease, improve the cure rate, reduce the mortality rate, and avoid hospital infections, it is also necessary to pay attention to overseas input Transmission and spread due to sexual cases,~~With a deepened understanding of the disease and accumulation of experience in diagnosis and treatment~~, we revised "The Diagnosis and Treatment Plan for COVID-19 (Provisional 5th edition)" to make the "The Diagnosis and Treatment Plan for COVID-19 (Provisional ~~6th~~ 7th edition)".

I. Epidemiological Characteristics

The Novel Coronavirus belonging to the genus of betacoronavirus. The enveloped viral particles may appear spherical or oblong, with a diameter of 60-140nm. The genetic characteristics are distinctively different from SARS-CoV or MERS-CoV. Current research found more than 85% homology between the sequences of 2019-nCoV and bat SARS-like coronavirus (bat-SL-CoVZC4). When cultured in vitro, 2019-nCoV appears after 96 hours in the inoculated human respiratory epithelial cells and after 6 days in VeroE6 or Huh-7 cell lines.

Most of the knowledge on physicochemical properties of coronavirus comes from the research on SARS-CoV and MERS-CoV. 2019-nCoV is sensitive to UV radiation and heat, and can be inactivated by heating (30 minutes at 56-degree celsius), diethyl ether, 75% ethanol, chlorine-containing disinfectants, peracetic acid, and organic solvents including chloroform. Chlorhexidine does not effectively inactivate the virus.

II. Epidemiological Characteristics

(1) Source of infection. At present, the source of infection is mainly patients infected by the novel coronavirus. Those who are asymptomatic but infected may also become a source of infection. As the coronavirus can be isolated in feces and urine, attention should be paid to aerosol or contact transmission caused by fecal and urine pollution to the environment.

(2) Route of transmission. The main route of transmission is respiratory droplets and close contact. There is the possibility of aerosol transmission when exposed to high concentration aerosol for a long time in a relatively closed environment.

(3) Susceptible populations.

The population is generally susceptible.

III. Pathological changes

<This part is not the word-word translation.>

Lung, spleen and hilar lymph nodes, heart and blood vessels, liver and gallbladder, kidney, brain tissue, adrenal glands, esophagus, stomach and intestine, etc. will be described in terms of general and microscopic views. Mainly lung and immune system damage. Other organs are different due to different underlying diseases, and most of them are secondary damage.

~~III~~IV. Clinical Characteristics

(1) Clinical presentation. Based on the current epidemiological investigation, the incubation period is 1-14 days, and most often between 3-7 days.

The primary presentations are fever, dry cough, and fatigue. A minority of patients have symptoms such as nasal congestion, nasal discharge, sore throat, muscle pain, and diarrhea. Severe patients often suffer from dyspnea and/or hypoxemia one week after onset, and severe patients can rapidly progress to acute respiratory distress syndrome, septic shock, difficult to correct metabolic acidosis, coagulation dysfunction and multiple organ failure. It is worth noting that severe and critical patients may have moderate to low fever or even no obvious fever during the course of the disease. Symptoms in some children and newborns may be atypical, manifested as gastrointestinal symptoms such as vomiting and diarrhea, or showing lack of energy and shortness of breath.

Patients with the mild form of the disease present only as low fever, slight fatigue, and so forth, with no lung inflammation.

Judging from the current cases, most patients have a good prognosis and a minority are in critical condition. The prognosis of the elderly and those with chronic underlying diseases is more poor. Pregnant women's clinical process is similar to that of patients of the same age. The symptoms of child cases are relatively mild.

(2) Laboratory examination.

a) General examination

In the early stage of the disease, the total number of peripheral blood leukocytes is normal or decreased, and the lymphocyte count was decreased, and some patients may have increased liver enzyme, lactate dehydrogenase (LDH), myoenzyme and myoglobin, and some critically ill patients may have elevated troponin. C-reactive protein (CRP) and erythrocyte sedimentation rate increased in most patients, and procalcitonin was normal. In severe cases, D- dimer increased and peripheral blood lymphocytes progressively decreased. Inflammatory cytokines often increase in severe and critical patients.

b) Etiology and Serology test

Novel coronavirus nucleic acid can be detected in nasopharyngeal swabs, sputum and other lower respiratory tract secretions, blood, feces and other samples.

Most of the new coronavirus-specific IgM antibodies are positive after 3-5 days of onset, IgG antibody titer recovery period increased by more than 4 times than the acute phase.

In order to improve the positive rate of nucleic acid detection, it is suggested that sputum be collected as much as possible, collecting secretions from the lower respiratory tract of patients undergoing tracheal intubation, and sending samples for examination as soon as possible after collection.

(3) Chest Imaging.

In the early stage, there are multiple small patches and interstitial changes, most notably in the outer lung. It further develops into multiple ground-glass opacity and infiltration shadows in both lungs; and in severe cases, consolidation of the lungs may occur, and pleural effusion is rare.

IV. Diagnostic Standards

(1) Suspected cases.

Comprehensively analyze combinations of the following epidemiological history and clinical presentations:

- Epidemiological history

1) Within 14 days prior to onset, had history of travel or residence in Wuhan or surrounding regions, or other communities reporting cases;
2) Within 14 days before onset had a history of contact with those infected by the novel coronavirus (positive nucleic acid testing);
3) Within 14 days prior to onset, had contact with patients who had a fever or respiratory tract symptoms that had come from Wuhan, its surrounding regions, or other communities reporting cases.
4) Aggregated onset~~.~~: within two weeks, two or more cases of fever and/or respiratory symptoms in a small area such as home, office, school class, etc.

- Clinical symptoms:

1) Fever and/or respiratory tract symptoms;
2) Having the imaging features of novel coronavirus pneumonia discussed above;
3) The white blood cell count is normal or decreased and lymphocyte count was decreased in the early stage of the disease.

Where there are any of the epidemiologic history items, and any 2 of the clinical symptoms are met. Where there is no clear epidemiological history, and at least 3 of the clinical symptoms are met.

(2) Confirmed cases.

Suspected cases have one of the following pathological evidence:

1. Tests positive for real-time fluorescence RT-PCR detection of novel coronavirus nucleic acid;
2. The viral gene sequencing is highly homologous with the known novel coronavirus.
3. ~~2.~~ New coronavirus-specific IgM antibodies and IgG positive, new coronavirus-specific IgG antibodies changed from negative to positive or the recovery period is more than 4 times higher than the acute phase.

VI. Clinical Classification

(1) Mild form.

Clinical symptoms are minor, imaging does not show signs of lung inflammation.

(2) Ordinary form.

Has fever and respiratory tract symptoms, imaging shows visible lung inflammation.

(3) Severe form.

a) Adult:

Meeting any of the following:

1. Shortness of breath, RR above 30 times/min;
2. In resting state, oxygen saturation is less than 93%;
3. Arterial oxygen partial pressure (Pa)/ oxygen concentration (Fio.) greater than 300mmHg (ImmHg=0.133kPa).

For high altitude (altitude over 1000 meters), (Pa0/F10) should be corrected according to the following formula: Pa0/F10 = 2x [atmospheric pressure (mmHg)/760]

Where lung imaging shows that the lesion has progressed significantly more than 50% within 24-48 hours, it should be re-classified as severe form.

b) Children:

Meeting any of the following:

1. Shortness of breath (<2 months of age, RR≥60 beats / min; 2 to 12 months of age, RR≥50 beats / min; 1 to 5 years old, RR≥40 beats / min;> 5 years old, RR≥30 beats / min Points), except for the effects of fever and crying;

2. Oxygen saturation ≤92% at rest;

3. Assisted breathing (groaning, nasal fan movement, triple concave sign), cyanosis, intermittent apnea;

4. lethargy and convulsions;

5. Difficulty or refuse feeding, signs of dehydration

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(4) Critical form.

Meeting any of the following criteria:

1. Respiratory failure occurs and mechanical ventilation is required;
2. Shock;
3. other organ failure requiring ICU monitoring;

VII: Severe and Critical Early Surveillance Indicators

a) Adult:

Meeting any of the following:

1. Progressive decline in peripheral blood lymphocytes
2. Peripheral blood inflammatory factors such as IL-6 and C-reactive protein are increasing
3. Progressive elevation of lactic acid
4. Rapid intrapulmonary pathological progression in the short term

b) Children:

Meeting any of the following:

1. Elevated respiratory rate
2. Poor mental response, lethargy
3. Progressive elevation of lactic acid
4. Imaging showing bilateral or multilobe infiltration, pleural effusion, or rapid progression of lesions in the short term
5. Infants under 3 months of age or with underlying diseases (congenital heart disease, bronchopulmonary dysplasia, respiratory malformations, abnormal hemoglobin, severe malnutrition, etc.), immunodeficiency or immunosuppression (long-term use of immunosuppressive agents)

VIII. Differential diagnosis

(1) COVID-19 cases with mild presentations need to be differentiated from other virus-induced upper respiratory tract infections.

(2) COVID-19 is to be differentiated from pneumonia caused by known viral agents such as influenza, adenovirus, and respiratory syncytial virus, as well as mycoplasma pneumonia. Suspected cases should be tested for common pathogens using methods such as rapid antigen test and multiplex PCR nucleic acid test as much as possible.

(3) Also consider non-infectious diseases such as vasculitis, dermatomyositis, and organizing pneumonia.

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IX~~VII~~. Discovery and Reporting of Cases

When a suspected case is discovered by medical workers at various level or type of medical institution, the patient should receive treatment in isolation immediately. Consultations of specialists or primary care clinicians should consider differential diagnosis and report the case online within 2 hours. Samples should be collected for nCoV-19 nucleic acid testing. The suspected case should then be transferred to designated hospitals under safe transferring conditions immediately. It's recommended that patients who tested positive for other respiratory antigens be tested also for nCoV-19 if they had had close contact with nCoV-19 patients.

Suspected case exclusion criteria: two consecutive new coronavirus nucleic acid tests are negative (sampling time interval of at least 24 hours), and new coronavirus-specific antibodies IgM and IgG are still negative 7 days after onset of disease.

~~VIII~~X. Treatment

(1) Determine the place of treatment based on the patients' conditions.

1. Suspected and confirmed cases should be treated in quarantine, in designated hospitals with effective isolation and disease control capacity. Suspected cases should be treated in individual isolation. Confirmed cases can be treated with multiple patients in the same isolation room.
2. Critical cases shall be put in ICU treatment as soon as possible.

(2) Regular treatment.

1. Treatment for mild cases includes bed rest, supportive treatments, and maintenance of caloric intake. Pay attention to fluid and electrolyte balance and maintain homeostasis. Closely monitor the patient's vitals and oxygen saturation.
2. As indicated by clinical presentations, monitor the hematology panel, routine urinalysis, CRP, biochemistry (liver enzymes, cardiac enzymes, kidney function), coagulation, arterial blood gas analysis, chest radiography, and so on. Cytokines can be tested if possible.
3. Administer effective oxygenation measures promptly, including nasal catheter, oxygen mask, and high flow nasal cannula. If feasible, use mixed oxygen and hydrogen inhalation (H2 / O2: 66.6% / 33.3%)
4. Antiviral therapies: Interferon-alpha (adult: 5 million units or equivalent can be added to 2ml sterile water for injection and delivered with a nebulizer twice daily), lopinavir/ritonavir (adult: 200mg/50mg/tablet, 2 tablets twice daily; the length of treatment should not exceed 10 days), ribavirin (recommended in combination with interferon or lopinavir/ritonavir, adult: 500mg twice or three times daily via IV, the length of treatment should not exceed 10 days), chloroquine phosphate (adult: 500mg twice daily; the length of treatment should not exceed 10 days), umifenovir (adult: 200mg three times daily; the length of treatment should not exceed 10 days). ~~Pay attention to the adverse effects associated with lopinavir/ritonavir, such as diarrhea, nausea, vomiting and liver dysfunction, as well as interactions with other medications.~~ Pay attention to adverse reactions, contraindications, and interactions with other drugs. The efficacy of the current medications in use will be evaluated in clinical application. Using 3 or more antiviral drugs is not recommended. Corresponding medication should be discontinued should intolerable side effects are present. For the treatment of pregnant women, the number of weeks of pregnancy should be considered, and as far as possible, use drugs that have a minimal impact on the fetus, and inform patients whether to terminate of pregnancy before the treatment.
5. Antibiotic therapies: avoid unjustifiable or inappropriate usage of antibiotics, especially combinatory use of broad-spectrum antibiotics.

(3) Treatment of severe and critical cases.

1. Treatment principles: on the basis of symptom management, proactively prevent and manage complications, treat underlying diseases, prevent secondary infections, and prompt organ function support.
2. Respiratory support:
    a. Oxygen therapy: patients with severe symptoms should be receiving oxygenation through nasal cannulas or oxygen masks. Assess the patient timely to determine whether dyspnea and/or hypoxemia have been alleviated.
    b. High flow nasal cannula or non-invasive ventilation: when patients with dyspnea and/or hypoxemia do not respond to regular oxygen therapy, consider using high

flow nasal cannula or non-invasive ventilation. If the symptoms do not improve or worsen within a short period of time (1-2 hours), tracheal intubation and invasive mechanical ventilation should be used.

c. Invasive mechanical ventilation: using lung-protective ventilation strategy (LPVS), i.e. low tidal volume of 4-8ml/kg ideal body weight, and low inspiratory pressure (plateau pressure < 30cm H2O) for mechanical ventilation in order to reduce ventilation-associated lung injury. Patient-ventilator asynchrony is common.There are something about using high PEEP when airway plateau pressure is less than 35cmH2O... According to the airway secretions, choose closed sputum suction, and if necessary, perform bronchoscopy and take appropriate treatment. Sedation and muscle relaxant should be used appropriately.

d. Salvage therapy: for patients with severe ARDS, a recruitment maneuver is recommended. When resources allow, prone ventilation should be carried out for 12 hours per day. If prone ventilation is ineffective, extracorporeal membrane oxygenation (ECMO) should be considered if conditions allow. Related indications: 1) When FiO2> 90%, the oxygenation index is less than 80mmHg for more than 3-4 hours; 2)~~(2)~~Airway plateau pressure ≥35cmH2O. For simple respiratory suffering patients, the preferred method is VV-ECMO model.

3. Circulatory support: starting with sufficient fluid resuscitation and improve microcirculation. Use vasoactive drugs, and monitor hemodynamics when necessary. Perform non-invasive or invasive hemodynamic monitoring, pay attention to fluid balance strategies during treatment (avoiding excessive and insufficient).

~~3.~~4. Renal failure and renal replacement therapy: In addition to finding the cause of renal impairment, continuous renal replacement therapy (CRRT) can be selected for severe patients with renal failure, and treatment indications should be given.

5. Use of convalescent plasma collected from recovered patients: indicated for patients with rapid disease progression, and severe or critical cases For usage and dosage, see "The Diagnosis and Treatment Plan for COVID-19 (Provisional 1st edition)".

6. Blood purification treatment: For cytokine storms in severe and critically ill patients, in order to clear inflammatory factors, block "cytokine storm".

~~4.~~7. Immunotherapy: For those with extensive lung disease and severe patients who have elevated IL-6 levels in the laboratory, Tocilizumab is used for immunotherapy. First dose: 4-8mg/kg, recommended dose is 400mg, 0.9% saline diluted till 100ml, dose time should be longer than 1 hour; for patients who don't improve after the first dose, add a second lose (the same dose amount as the first dose) 12-hour later. Total dose can't be more than two, amount of a single dose can't be more than 800mg. Pay attention to allergic reactions. People with active infection such as tuberculosis are prohibited.

~~5.~~8. Other treatment measures

For patients with progressively deteriorating oxygenation index, rapid imaging progression, and overactive inflammatory responses, short-term (3-5 days) glucocorticoid treatment may be used at the clinician's discretion. It's recommended that the dosage should not exceed the equivalence of methylprednisolone at 1-2mg/kg/day, since the immunosuppressive function of high-dose glucocorticoid may delay the clearance of coronavirus from the system. Xuebijing may be given intravenously at 100ml twice a day. Probiotics can be given to maintain intestinal microbiome balance and to prevent secondary bacterial infection. For severe and critical cases with hyper-inflammation, extracorporeal blood purification techniques such as plasma exchange, plasma absorption, plasma perfusion, and hemofiltration may be considered.

In children with severe or critical cases, intravenous drip of gamma globulin may be considered as appropriate. Patients with severe or critically ill pregnancy should actively terminate the pregnancy, and cesarean delivery is preferred.

Patients often have anxiety and fear, and psychological counseling should be strengthened.

(4) Treatment by Chinese Medicine.

Several pages of Chinese traditional medicine treatment method.

~~IX~~I. ~~Matters for attention after release from isolation or hospital.~~Discharge standard

(1) Criteria for ~~release from isolation and~~ hospital discharge

1) Temperature returned to normal for 3 days or more;
2) Respiratory symptoms have a clear turn for the better;
3) Chest radiology findings show substantial improvement of acute exudative lesions.
4) Two consecutive negative nucleic acid tests using respiratory tract samples (taken at least 24 hours apart).

Those meeting the requirements above may be released from isolation or hospital.

(2) Matters for attention after hospital discharge.

1. Designated hospitals should communicate with primary care facilities at the patient's place of residence and share medical records. Information on the discharged patients should be forwarded to the relevant neighborhood committees and primary care facilities in a timely manner.
2. Discharged patients are at increased risk of acquiring other pathogens due to their reduced immune functions during recovery. It's recommended that the patients: continue quarantine management ~~to~~ and self-monitoring for 14 days, wear masks, live in well-ventilated individual suites if possible, reduce close contact with family members, eat separately, practice good hand hygiene, and avoid going outside.
3. Follow-up visits are recommended at 2 and 4 weeks after discharge.

XII. Implementation Principles

Implement in accordance with the "Work Plan for Transport of Novel Coronavirus Pneumonia Cases (Provisional)" released by our Commission.

XIII. Prevention and Control of Infection in Medical Establishments

Strictly follow this guideline and distribute to all regions.

General Office of the National Health Commission

Released ~~February~~ March ~~18~~3, 2020

COVID-19 BARDA Overview

Date: March 18, 2020

1. BARDA Broad Agency Announcements published 3/9/2020
   - BAA: Dx (Hand-held, point-of-care) Rx (Antiviral, Host-targeted, pre/post exposure prophylaxis), Vx, Advanced Manufacturing
   - EZ-BAA: Dx (FDA cleared platforms, point-of-care), Vx, Advanced Manufacturing, Non-Clinical models and Screening for SARS-CoV-2 virus

2. Diagnostics
   - BARDA has partnered with Hologic, DiaSorin, Qiagen, MesaBioTech to develop diagnostic tests to detect 2019-nCoV
   - Hologic SARS-CoV-2 diagnostic and LabCorp LDT received EUA 03/16/2020
   - LabCorp and Quest Diagnostics are both testing for 2019-nCoV
   - FDA authorized the Roche Cobas SARS-CoV-2 Test
     - FDA allowed pre-positioning; laboratories can immediately run tests

3. Therapeutics
   - Adaptive randomized clinical trial (NIAID-led).
     i. US Patient Enrollment as of 03/13/2020: 11 in US
     ii. 10 US sites activated: (3 in WA, 2 in CA, 1 each in NE, MD, GA, MN, MA)
   - Genentech preparing draft synopsis for α-IL-6R antibody clinical trial for COVID-19
     i. Draft synopsis and pre-IND request sent to FDA on 03/13/2020
   - Regeneron submitted expanded synopsis to FDA using α-IL-6R antibody for COVID-19
     i. FDA sent safe-to-proceed letter on 3/16/2020
     ii. Targeting to enroll first patient by 03/20/2020
   - Regeneron is screening candidate mAbs
     i. Obtained PBMC from Singapore screened for human SARS-CoV-2 antibodies
     ii. TMPRSS2 program deprioritized to favor neutralizing antibodies
   - Janssen has entered assay validation phase for high throughput screening
     i. Targeting to finish validation phase 3/23/2020 at the Rega Institute

4. Vaccines
   - Sanofi Pasteur is pursuing a vaccine construct that is thought to be more stable.
     i. Targeting to enter Phase 1 Sept/Oct 2020
   - NIH lead mRNA-1273 Vaccine clinical trial received a "safe to proceed" from FDA
     i. First normal healthy volunteer vaccinated 03/16/2020
   - Janssen vaccine candidates show immunogenicity in mice 3 weeks after 1 vaccine dose
     i. Plan to identify lead candidate(s) by end of March

1. MCM Task Force
    a. Diagnostics Working Group
        i. 81 PHLs in 50 states and D.C. verified COVID-19 diagnostics and are offering testing
        ii. Confirmatory testing by CDC on positive samples from PH labs no longer required
        iii. FDA posted alternative transport media options on their Diagnostics FAQ website
        iv. LabCorp and Quest Diagnostics are both testing for 2019-nCoV
        v. LabCorp received EUA from FDA on 3/16/2020
    b. Clinical Trials Working Group
        i. WHO posted revised COVID-19 clinical guidelines
        ii. NIAID multi-center, multi-country, multi-arm adaptive RCT with remdesivir
            1. 10 active US sites, 2 active global sites
                a. 11 patients enrolled in US as of 3/13/2020, 3 global patients
                    i. 3 UNMC, 5 Evergreen, 1 Emory, 2 Mass General
        iii. China: two remdesivir clinical trials underway in China
            1. Mild/moderate disease: 74/308 individuals enrolled as of 3/15/2020
            2. Severe disease: 237/453 individuals enrolled as of 3/15/2020
                a. Kaletra exclusion removed because enrollment has stalled
        iv. Remdesivir compassionate use: >100 US and >500 global
            1. NIAID requested remdesivir not be used in patients ineligible for RCT
        v. Gilead SIMPLE studies: 15 sites activated (2 in US)
    c. Therapeutics Working Group
        i. NIAID contractor (Utah State University) has capacity to screen 150 compounds
        ii. USAMRIID has high-throughput screening capacity for compound libraries
    d. Vaccines WG coordinating closely with NIAID (VRC and DMID)
        i. mRNA-1273 vaccine: First normal healthy volunteer vaccinated 03/16/2020
    e. Sample Sharing Working Group engaging to identify PBMCs for product developers
        1. Potential partnership with NYU for sample collection in process – anticipate award week of 3/16/2020
        2. Potential source of convalescent serum from VA patient
2. **BARDA Diagnostics**
    a. [PROCUREMENT SENSITIVE] Cepheid 2019-nCov diagnostic assay
        i. Targeting EUA submission on 3/20/2020 with an estimated ship date of 3/27/2020 for test kits.
        ii. Cepheid reported domestic shortage of Copan NP flocked swabs
            1. Evaluating use of additional sample types in their assay to mitigate.
    b. [PROCUREMENT SENSITIVE] EZ-BAA submissions
        i. Hologic EUA issued on 3/16/2020
        ii. DiaSorin Molecular
            1. Targeting EUA submission by 03/17/2020

a. Met FDA expectations for the limit of detection.

iii. MesaBioTech Point of care (hand-held device)

a. Kick-off call scheduled 03/16/2020

iv. Qiagen

1. Determining what is needed based on FDA pre-sub response to reduce timeline to EUA submission from current 12 week estimate

v. Pending EZ-BAA contract actions

1. Genmark in negotiations, targeting award week of 03/16/2020
   a. SARS-CoV-2 assay has been submitted to FDA for EUA
2. Inbios: In technical review, additional information requested
3. Nanomix: Pending technical review
4. Luminex: Company working on Stage 2 submission.
5. AOI 4.1-C (Diagnostic Assay for detection of COVID-19 disease)
   a. 7 submissions, 5 pending review, 1 acceptable, 1 unacceptable.

c. Other Diagnostics

i. Click Diagnostics: Awaiting their updated proposal as of 03/13/2020

ii. Hound Labs: TechWatch on 2/27, BARDA will follow up on expanded EZ-BAA AOI

iii. Orasure: TechWatch on 3/5, BARDA followed up on 03/13/2020

3. BARDA Therapeutics

a. Regeneron

i. Obtained patient PBMC sample to identify human SARS-CoV-2 neutralizing antibodies

ii. 2019-nCoV specific mAb on track to have leads by end of April and production in August 2020

iii. TMPRSS2 program deprioritized to favor neutralizing antibodies.

1. Antibody against TMPRSS-2 reduced 2019-nCoV entry into cultured cells

b. Antiviral screening

i. Janssen antiviral therapeutics screening

1. Rega Institute is validating screening assay (targeting finish 3/23/2020)

ii. Gilead interested in screening their compound library with NIAID

iii. Roche interested in screening FDA licensed compounds at Rega Institute

4. BARDA Vaccines

a. Janssen Ad26 vaccine

i. Janssen's Vaccine Candidates: immunogenic in mice 3 weeks after prime

ii. Will identify lead candidate(s) by end of March.

iii. Preliminary data on virus challenge in NHP model

1. Virus stock infects animals and replicates (viral load in nose)
2. No obvious clinical disease observed

iv. FDA indicated at Pre-pre-IND meeting it would not be appropriate to use the vaccine under EUA.

1. Clinical disease efficacy trial/interim analysis would be required to support EUA application, according to CBER

b. Sanofi Pasteur
    i. Transfer plasmid being assembled, target completion by 3/14/2020
        1. Re-designing spike protein DNA construct to contain stabilizing mutations (~3 week delay)
    ii. SP indicated to FDA that they expect to enter Phase 1 study Sept/Oct 2020.
    iii. CBER prefers traditional regulatory approval pathway
    iv. Non-clinical studies should include assessing theoretical risk of vaccine induced disease enhancement.
c. Moderna SSA brief scheduled for 3/17/2020 at 5:30 PM
d. Inovio submitted White Paper in response to BAA

5. BARDA Rapidly Deployable Technology
    a. Anticipating 3-4 proposals in next 2 weeks
    b. Market research calls with companies monitoring patients remotely (Emory, Medable, Current Health) and Determination of risk severity (Inflammatix).
6. BARDA Clinical
    a. Genentech IL-6R antibody clinical trial in COVID-19 patients
        i. Draft synopsis and pre-IND submitted to FDA 3/13/2020
        ii. Targeting to enroll patients early April
    b. Regeneron IL-6R antibody clinical trial in COVID-19 patients (Adaptive Phase 2/3 study)
        i. FDA sent safe-to-proceed letter on 3/16/2020
        ii. Expect to enroll first patient by 03/20/2020
7. BARDA Non-clinical
    a. Nonclinical RTOR: TEP held 3/16/2020
        i. Business proposals due 3/17/2020
8. BARDA Manufacturing
    a. Emergent expects agreement with Vaxart to be finalized (3/16)
    b. Fuji Diosynth (College Station) has capacity to perform BSL-2 fill/finish with their VanRx system.

COVID-19 BARDA Overview

Date: April 04, 2020

1. Diagnostics
   - BARDA has partnered with Hologic, DiaSorin, Qiagen, MesaBioTech, GenMark, Cepheid, Luminex (NxTag and Aries), and Vela to develop diagnostic tests to detect 2019-nCoV
   - Qiagen received EUA 03/30/2020 for their respiratory panel including SARS-CoV-2
   - 25 Diagnostics with EUA
     - First serological test received EUA Cellex Inc lateral flow assay

2. Therapeutics
   - Shipments of Chloroquine/Hydroxychloroquine have left SNS for use under EUA
     i. 15 cases (1872 bottles) shipped to 3 sites (US Virgins Islands, CA, NY)
   - Emergent developing a plasma-derived Polyclonal Antibody-based COVID-19 Rx
   - Genentech Tocilizumab (α-IL-6R) clinical trial for COVID-19 targeting start early April
     i. 2 patients enrolled 04/03/2020
   - Regeneron adaptive phase 2/3 study of Sarilumab (α-IL-6R antibody) for COVID-19
     i. 50 sites activated (15 in NY, 5 in NJ, 4 in MA, 2 in CA, FL, GA, IL, PA, TX, VA, WA, 1 each in CO, CT, DC, MI, MN, OK, UT)
     ii. 617 Patients enrolled and dosed as of 04/02/2020
   - Regeneron has identified mAbs that neutralize SARs-CoV-2 virus in vitro
     i. 42 Lead mAbs candidates being further screened for neutralizing activity
     ii. Scaling up manufacturing of leads for additional screening
   - Janssen validation phase on going for high throughput screening
     i. Potential hit identified during validation

3. Vaccines
   - Sanofi Pasteur is pursuing a vaccine construct that is thought to be more stable.
     i. Award in process for development through Phase 1
   - Janssen preliminary non-clinical data in immunogenicity mice and NHP virus challenge model
     i. 3 candidates identified, clinical trials expected early fall 2020

1) **BARDA Diagnostics**
    a) **14 White Papers submitted, reviews in progress.**
    b) **Current Diagnostic EUAs**
        i) 25 Diagnostics with (EUA):
            I. https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations#covid19ivd
    c) **Cepheid**
        i) **Shipped 150,000 tests in the past two weeks**
    d) **Cue**
        i) **Completed LoD study using SARS-CoV-2 genomic RNA spiked into nasal matrix**
    e) **[PROCUREMENT SENSITIVE] EZ-BAA submissions**
        i) **Hologic**
            I. **Shipped 142,000 tests to date**
            II. **Targeting production 95,000 tests/week starting by 04/03/2020**
                (a) **Goal to produce/ship ~600,000 tests in April.**
            III. **Completed testing on lower respiratory tract specimens (to update EUA)**
                (a) **Targeted to be included in 04/13/2020 submission to FDA**
        ii) **DiaSorin Molecular**
            I. **50K tests shipped to US labs as of 04/02/2020**
        iii) **MesaBioTech Point of care (hand-held device)**
            I. **Shipping of cartridges last week was delayed**
                (a) **Aiming to ship by 04/03/2020**
        iv) **Qiagen**
            I. **No update**
        v) **Genmark**
            I. **No Updates**
        vi) **Luminex Corp**
            I. **Luminex NxTAG- A total of 869 kits sent as of 04/02/2020**
            II. **Luminex Aries targeting to submit EUA by 04/03/2020**
        vii) **Vela Diagnostics**
            I. **LOD study completed, verification and validation in progress**
        viii) **Nanomix awarded 04/02/2020**
            I. **Development and testing of viral antigen/antibody assay for COVID-19**
        ix) **OraSure and Nanomix (antigen based Dx) awarded 04/03/2020**
        x) **Pending EZ-BAA contract actions**
            I. **DiaSorin (Antibody) targeting award 04/03/2020**
            II. **Hememics (Antigen/Antibody): Stage 2 negotiations in process**
2) **BARDA Therapeutics**
    a) **Regeneron**
        i) **2019-nCoV specific mAb on track to have leads by end of April and production in August**

1. **42 Lead mAbs candidates being further screened for neutralizing activity**

ii. **Regeneron adaptive phase 2/3 study of Sarilumab (α-IL-6R antibody) for COVID-19**

1. **47 sites activated (15 in NY, 5 in NJ, 3 in MA, 2 in CA, FL, GA, IL, PA, TX, WA, 1 each in CO, CT, DC, MI, MN, OK, UT, VA)**
2. **617 Patients enrolled and dosed as of 04/03/2020**
   a. **Phase II – 215**
   b. **Phase III – 402**
3. **DMC scheduled to meet 04/04/2020**

b) **Genentech IL-6R antibody (Tocilizumab) clinical trial in COVID-19 patients**

i) **2 patients enrolled in Spain as of 04/03/2020**

c) **Antiviral screening**

i) **Discussions on steps to test hits in non-clinicals, expecting JOC by 04/10/2020**

d) **SAb Biotherapeutics – Polyclonal antibody product**

i) **Clinical trial planned for late June/July**

e) **Grifols (HIG)**

i) **SOW being finalized at Grifols for delivery to DoD for execution**

f) **Emergent**

i) **Task Order awarded 04/02/2020 via CIADM Network**

3) **BARDA Vaccines**

a) **Discussion with DoD on their support of Inovio scheduled 4/3/2020**

b) **Janssen Ad26 vaccine**

i) **3 candidates identified, lead in process of being identified**

ii) **Targeting to start clinical trial early September**

c) **Sanofi Pasteur**

i) **SP indicated to FDA that they expect to enter Phase 1 study Sept/Oct 2020**

ii) **Waiting for SSA approval as of 04/02/2020**

d) **Moderna**

i) **Moderna returned draft contract with comments. Review in progress.**

e) **Merck proposals expected 04/03/2020**

f) **Pfizer proposal "days away" according to company**

4) **BARDA Rapidly Deployable Technology**

a) **2 EZ BAA in negotiations/1 EZ BAA awaiting Stage II proposal**

i) **Awards expected 04/06/2020**

b) **Aiming to modify existing ENACT and Sepsis contracts to support COVID-19**

5) Sample Sharing Working Group

i) Serum urgently needed for diagnostic developers

6) **BARDA Clinical**

a) NIAID ACTT Trial

i) Will be a 4 arm study investigating standard of care, remdesivir, baracitinib, combination of remdesivir, and baracitinib

b) **Chloroquine/Hydroxychloroquine EUA**

i) Web link for collection of outcomes data went live 04/01/2020
ii) One million doses of chloroquine donated by Bayer arrived to the SNS
I. ~1.3 millions tablets shipped as of 04/03/2020

7) BARDA Non-clinical
a) 4 non-clinical kick off meetings scheduled for week of 04/06/2020
i) Battelle, MRI Global, Lovelace, Southern Research
ii) BARDA/NIAID nonclinical collaboration meeting scheduled for 04/07/2020

8) BARDA RQA
a) Standing weekly meetings scheduled with CDER and CBER
b) Shipments of Chloroquine/Hydroxychloroquine have left SNS as of 04/03/02020
iii. 15 cases (1872 bottles) shipped to 3 sites (US Virgins Islands, CA, NY)

9) BARDA Manufacturing
a) Janssen plans to tech transfer Drug Substance manufacturing at Emergent and DP (BSL2) fill finish to Catalent
i) Timelines, raw material evaluations, risks and mitigations presented
b) Phlow contract targeting award by 04/03/2020

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CC:	MCM Task Force /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=49010f8ab3ab4aed868a72c707c08d08-MCM Task Fo <MCMTaskForce@hhs.gov>
Subject:	Sunday updates for MCM Task Force: for review
Date:	2020/04/11 19:09:52
Priority:	Normal
Type:	Note

Rick, Gary, Linda,

Tomorrow's updates for the MCM Task Force are shown here. Please let us know if you have any concerns.

- ACTT Clinical trial to test remdesivir for treatment of COVID-19: 704 (+100) new patients at 65 (+1) sites, including 5 military treatment facilities, in last 24 hrs (target = 700)
- Emergency Use Authorizations granted by FDA: 33 (+1) molecular diagnostic tests, 9 (+3) laboratory-developed tests, 1 antibody test, and 2 repurposed treatments (chloroquine, hydroxychloroquine)
- Executed 2 orders to obtain convalescent serum to support serology testing and a contract to develop convalescent plasma treatments
- Expanded partnership to develop blood biomarker test and entered into 3 new agreements to develop SARS-CoV-2 diagnostic tests
- 2099 (+39) market research submissions and 199 (+3) CoronaWatch meetings held
- 19 National Animal Health Laboratory Network (NAHLN) labs are testing animal samples for SARS-CoV-2, and 1 NAHLN lab is testing human samples
    - CDC PCR is used to confirm presumptive positive results

Christy

--
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SARS-CoV-2 Medical Countermeasures Task Force
Date: April 2, 2020
FOR OFFICIAL USE ONLY

Agencies reporting: BARDA, NIAID, DoD, FDA, USDA
Agencies not reporting: CDC, DHS

Talking Points for 1200 SLB and 1230 VTC

Accomplishments

- Clinical trial to test remdesivir for treatment of COVID-19: 334 (+27) new patients in last 24 hrs (target = 700)
- Antibody therapeutic trial: 537 (+76) new patients dosed, 47 (+2) sites in last 24 hrs (target = 400)
- First unit of plasma collected from recovered COVID-19 patient under American Red Cross expanded access protocol

Currently Working

- Continuing to enroll patients in clinical trials to evaluate vaccines and therapeutics for COVID-19
- Providing expertise and strategic planning to support new Serology Project Team

Active USG-sponsored Clinical Trials

	Candidate	Sponsor	Target Enrollment	Number of Sites	Enrollment
Adaptive COVID-19 Treatment Trial (ACTT)	Remdesivir	NIAID, Gilead	700	47 (+1)	334 (+27)
Sarilumab (anti-IL-6R mAb)	Sarilumab	BARDA, Regeneron	400	47 (+2)	537 (+76)
COVACTA: tocilizumab (anti-IL-6R mAb)	Actemra	BARDA, Genentech	330	TBD	TBD
Moderna mRNA-1273 Vaccine Phase I	mRNA-1273	NIAID, Moderna	45	2	30
Epidemiology, Immunology and Clinical Characteristics (EpICC) Study	N/A	DoD	TBD	4	8

- Adaptive COVID-19 Treatment Trial - NIAID
  - Currently remdesivir vs. placebo control (with options to add additional arms as needed)
  - Target enrollment = 440
  - Inclusion criteria – Confirmed SARS-CoV-2 infection (efficacy, but a little gray area PEP too)
  - Primary endpoint:
    - 8pt ordinal scale scored at Day 15, ranging from death to discharged with no limitation on activities and no requirement for home oxygen

- Sarilumab (Anti IL-6R mAb, aka Kevzara), Regeneron/Sanofi
  - Sarilumab high dose vs. Sariluman low dose vs. placebo control
  - Target enrollment = 400
  - Inclusion criteria – Confirmed SARS-CoV-2 infection AND evidence of pneumonia and severe disease (a true efficacy study)
  - Primary endpoints:
    - Time to resolution of fever for at least 48 hours
    - 6pt ordinal scale scored on Day 15, ranging from death to discharged

- mRNA-1273, Moderna
  - Phase I safety/immunogenicity
  - Target enrollment = 45
  - NHV study
  - Cohorts (all n=15, including 4 sentinels):
    - Low dose = 25ug
    - Medium dose = 100ug
    - High dose = 250ug

- EpICC Study, IDCRP
  - Observational natural history study
  - Clinical parameters being evaluated: risk factors, outcomes, virology, immunology

Proposed Clinical Trials

Vaccine / Therapeutic Product	Date / Range for Entry into Clinic
Convalescent plasma	Approx. late April/early May
IVIg	Late Spring 2020
Regeneron SARS-CoV-2 specific mAbs	June-July 2020 for treatment study in COVID-19 patients
Janssen screening leads	Early Summer 2020 or later; highly dependent on leads identified
SAb	June to mid-Summer 2020
Janssen Ad26 Vaccine	Phase 1: Q3-2020
Moderna mRNA Vaccine	Phase 1 enrollment: March 16, 2020 Phase 2: Q2-2020 (likely about June 2020)
Sanofi-Pasteur Vaccine	Phase 1: Q1-2021 (September/October 2020 provided to CBER)

Response to the Coronavirus Led by HHS from Day 1

1. Containment

- Within two weeks of China's notifying WHO about the virus and just 45 cases in China, CDC began screening travelers from Wuhan.
- HHS came up with idea for and drove:
  - Travel suspension from Hubei and China on January 31.
  - Travel suspension from Europe on March 11.
  - Shutdown of cruise line travel on March 13.
- In January, HHS led the safe repatriation and quarantine of hundreds of Americans, the first use of federal quarantine power in more than 50 years.
- In March, HHS came up with idea for and drove the President's unprecedented national social-distancing guidelines.

2. Preparation and Supplies

- Led effort on President Trump's executive order to invoke the Defense Production Act to purchase and allocate needed supplies, if necessary.
- Beginning in January, HHS coordination drove N95 mask production capacity on U.S. soil from ≈250 million to ≈640 million.
- On March 4, ASPR issued procurement for 500 million N95 masks, leading factories to re-open, convert to masks, and run round the clock.
- On March 2, authorized millions of industrial N95s to be used in healthcare settings.
- Partnered with DoD to airlift swabs and test kit supplies to the U.S. from Italy.
- FDA authorized alcohol distillers to help boost supply production of hand sanitizer.
- Examining through FDA a new spray to allow reuse of N95s.
- Worked with Hanes to invent washable cloth surgical mask.
- Purchased 10,000 ventilators for Strategic National Stockpile in late 2019.
- Secured 2,000 portable ventilators from the Department of Defense.
- Procurement pending for up to hundreds of thousands of portable ventilators.
- FDA guidance to expand manufacturing options for ventilators, such as car makers, and allow repurposing of other machines to work as ventilators.
- Created consortium of medical product distributors to allocate the $1 trillion of private medical products to areas of greatest need.

3. Healthcare Capacity

- Prepared 30 field hospitals with capacity for care for 250 patients each.
- Convened hospitals to learn best practices and lessons from Seattle and California.
- Working to waive all restrictions on interstate practice of medicine.
- Expanded Medicare coverage for telehealth, allowed waiver of copays for telehealth in federal programs, and allowed use of everyday technologies like FaceTime for all Americans to talk to doctors.

4. Countermeasures

Commented [BP(1]: Hayes is going to track down when we started this.

- MCM portal has received over 1,000 submissions that are being reviewed by the MCM task force working group. Over 90 face-to-face or telephonic meetings with companies have occurred in the past three weeks with no signs of slowing down moving forward.
- Launched the world's first COVID-19 vaccine trial, reaching human patients in record time – Moderna's mRNA product with clinical support from NIAID
- NIAID established a randomized clinical trial to evaluate remdesivir, a drug made by Gilead. It is an adaptive trial design to allow inclusion of additional therapeutics as they become available.
- NIAID and the VRC are working with industry to evaluate products in non-clinical studies and are making reagents available to product developers
- BARDA and Regeneron have initiated a phase 2/3 clinical trial to evaluate their FDA approved drug Kevzara in severely ill COVID-19 individuals
- BARDA is also working with Genentech to launch a similar study with Genentech's FDA approved IL-6 receptor antagonist drug.
- BARDA is working with additional manufactures of Janssen to develop a vaccine and also screen their library of compounds. The screening capability will be made available to other drug manufactures for screening of their libraries. ~~.~~
- BARDA is partnering with Regeneron to develop novel monoclonal antibodies against the novel coronavirus and the team is moving quickly identifying those monoclonal antibodies with the best binding ~~characterisites~~characteristics.
- NIAID, BARDA and the FDA are working together to develop a plan to evaluate human hyperimmune globulin and potentially convalescent plasma as treatment options for COVID-19 individuals
- BARDA has supported multiple diagnostics companies; Cephied, Hologic, DiaSorin, Qiagen, MesaBioTech and GenMark – almost all have received EUA from the FDA
- FDA continues to work with diagnostics, vaccine and therapeutic companies quickly reviewing submissions and providing quick turnaround times, streamlining the process
- FDA has issued guidance for diagnostics, sample collection and sample extraction that have allowed for maximal flexibility to the industry and labs while maintaining safety for patients.
- FDA has established a 24/7 command room for diagnostics to interact with public health labs, commercial labs, suppliers and other industry partners.
- ASPR is w~~W~~orking to secure millions of donated hydroxychloroquine tablets from Bayer and Novartis.
- CDC and FDA working on guidance on off-label use of hydroxychloroquine.
- ~~Remdesivir being delivered under compassionate use and in NIH clinical trial.~~
- ~~Supported Phase 2/3 clinical trial for Kevzara, a rheumatoid arthritis drug.~~

5. Testing

- Nearly 200,000 tests performed by CDC and labs as of March 20, plus tens of thousands of hospital and lab tests not reported.
- Record-speed authorizations of high-throughput automatic private tests (processing applications in >24 hours).
- Authorized point-of-care diagnostic on March 21 that can provide results in 45 minutes.
- Starting in January, developed accurate test at CDC in two weeks, breaking records.
- No denials of test requests by CDC at any point.

- U.S. testing capacity tracked or outpaced peer nations at comparable points in epidemiological spread.

6. Funding and Administrative Flexibilities

- On January 25, five days before WHO declared a public health emergency of international concern, the Secretary notified Congress to allow use of up to $105 million from the Infectious Disease Rapid Response Reserve Fund.
- On January 31, the Secretary declared a Public Health Emergency, allowing work to begin on new authorities and flexibilities like Medicare coverage for telehealth.
- On February 2, the Secretary transferred $136 million in department funds to support entry screening, preparedness, vaccines, and therapeutics.
- Starting in late January, led work on an emergency request for the first $8.3 billion emergency supplemental appropriation, signed into law March 6.
- Led efforts to have Congress pass liability reforms that further spurred domestic production and expanded the supply of non-health care masks.
- Secured additional critical resources in the second supplemental (Families First Coronavirus Response Act), including $1 billion for coronavirus testing for the uninsured and $250 million for meals for vulnerable seniors.

COVID-19 BARDA Overview

Date: March 23, 2020

1. Diagnostics
   - BARDA has partnered with Hologic, DiaSorin, Qiagen, MesaBioTech, GenMark, Cepheid to develop diagnostic tests to detect 2019-nCoV
   - 13 Diagnostics with EUA
   - Cepheid received EUA for their SARS-CoV-2 diagnostic on 03/20/2020
     - POC test with results in 45 minutes

2. Therapeutics
   - Adaptive randomized clinical trial with remdesivir (NIAID-led).
     i. Enrollment as of 03/20/2020: 36 US Patients, 6 Patients Globally
     ii. 18 US sites activated: (5 in CA, 3 in WA, 2 in TX, 1 each in NE, MD, GA, MN, MA, TX, IL, CO)
   - Genentech protocol for α-IL-6R antibody clinical trial for COVID-19 under FDA review
     i. Draft synopsis and pre-IND request sent to FDA on 03/13/2020
   - Regeneron adaptive phase 2/3 study of Sarilumab (α-IL-6R antibody) for COVID-19
     i. 11 sites activated (6 in NY, 1 each in IL, MI, NJ, PA, TX,)
     ii.30 Patients enrolled as of 03/22/2020
   - Regeneron is screening candidate mAbs for SARs-CoV-2 neutralization
   - Janssen has entered assay validation phase for high throughput screening
     i. Targeting to finish validation phase 3/23/2020 at the Rega Institute

3. Vaccines
   - Sanofi Pasteur is pursuing a vaccine construct that is thought to be more stable.
     i. Targeting to enter Phase 1 Sept/Oct 2020
   - NIH lead mRNA-1273 Vaccine clinical trial received a "safe to proceed" from FDA
     i. 8 healthy volunteers vaccinated as of 03/18/2020
   - Janssen vaccine candidates show immunogenicity in mice 3 weeks after 1 vaccine dose
     i. Plan to identify lead candidate(s) by end of March

1. MCM Task Force
    1. Diagnostics Working Group
        i. 13 Diagnostics with EUA: Cepheid, Primerdesign Ltd, GenMark, **DiaSorin,** Abbott Molecular, Quest Diagnostics, Quidel Corp, LabCorp, **Hologic**, Thermo Fisher, Roche, NYSDOH, CDC
        ii. Cepheid, GenMark, **DiaSorin** systems do not need the extraction reagents that are in short supply: "Sample to Answer" tests
        iii. BioFire: DoD funded SARS-2 assay development for FilmArray platform
            1. Submitting EUA 03/20/2020
    2. Clinical Trials Working Group
        i. WHO posted revised COVID-19 clinical guidelines
        ii. WG does not currently recommend use of chloroquine/hydroxychloroquine for COVID-19 based on available information
            1. Recommend RCTs to evaluate efficacy
            2. WG preparing protocols to evaluate (hydroxyl)chloroquine
            3. WG evaluating potential supply chain issues
        iii. NIAID multi-center, multi-country, multi-arm adaptive RCT with remdesivir
            1. 18 active US sites, 3 active global sites
                a. 42/440 enrolled (36 US, 6 global)
                    i. 3 UNMC, 8 Evergreen, 4 Emory, 4 Mass General, 4 Montefiore, 5 Univ of WA-Harborview, 1 UCLA, 2 UCSF
        iv. China: two remdesivir clinical trials underway in China
            1. Mild/moderate disease: 74/308 individuals enrolled as of 3/15/2020
            2. Severe disease: 237/453 individuals enrolled as of 3/15/2020
        v. Remdesivir compassionate use: >1500 requests approved, 1/3 of requests from US
        vi. Gilead SIMPLE studies: 29 sites activated (2 in US)
            1. 103/400 enrolled in severe disease study, 35/600 enrolled in mild/moderate study
    3. Therapeutics Working Group
        i. Established sub-WG with Therapeutics & Clinical Trials members to develop prioritization strategy for preclinical and clinical therapeutics evaluation
    4. Vaccines WG coordinating closely with NIAID (VRC and DMID)
        i. mRNA-1273 vaccine: 8 healthy volunteers vaccinated as of 03/18/2020
    5. Sample Sharing Working Group engaging to identify PBMCs for product developers
        i. Established mechanism with NYU to access and deliver clinical samples from COVID-19 patients
        ii. Provide 18 samples each of serum, plasma, PBMCs, whole blood, and viral isolates with the ability to increase as needed.
        iii. 10 patients enrolled in sample collection protocol at NYU

2. BARDA Diagnostics
    1. [PROCUREMENT SENSITIVE] Cepheid 2019-nCov diagnostic assay
        i. EUA received on 3/20/2020
            1. POC device with results in 45 minutes
            2. Expecting 90K cartridges by 03/27/2020 to start fulfilling orders.
    2. [PROCUREMENT SENSITIVE] EZ-BAA submissions
        i. Hologic EUA issued on 3/16/2020
            1. Started shipping test kits 03/17/2020
                a. Second lot has ~18,000 tests and has been sent out.
        ii. DiaSorin Molecular
            1. Received EUA 03/19/2020
            2. Preparing to ship the kits by 03/20/2020
        iii. MesaBioTech Point of care (hand-held device)
            1. EUA submitted 03/18/2020
            2. Started building inventory to ship early week of 03/23/2020
        iv. Qiagen
            1. Determining what is needed based on FDA pre-sub response to reduce timeline to EUA submission from current 12 week estimate
            2. Predicting market release 3/23 (pre-EUA)
        v. Genmark
            1. EZ-BAA awarded 03/21/2020
            2. SOW adds SARS-CoV-2 assay to existing respiratory panel covering a range of pathogens in single test.
        vi. Pending EZ-BAA contract actions
            1. Nanomix, Luminex: In Stage 2 negotiations
3. BARDA Therapeutics
    1. Regeneron
        i. OTA modified 03/21/2020 to include Sarulimab (α-IL-6R) clinical study and SARS-CoV-2 neutralizing mAbs.
        ii. 2019-nCoV specific mAb on track to have leads by end of April and production in August 2020
        iii. TMPRSS2 development paused to prioritize development of SARS-CoV-2 mAbs
        ii. Regeneron adaptive phase 2/3 study of Sarilumab (α-IL-6R antibody) for COVID-19
            1. 11 sites activated (6 in NY, 1 each in IL, MI, NJ, PA, TX,)
            2. 30 Patients enrolled as of 03/22/2020
    2. Genentech IL-6R antibody (Tocilizumab) clinical trial in COVID-19 patients
        i. Protocol under FDA review as of 03/19/2020
    3. Antiviral screening
        i. Janssen antiviral therapeutics screening
            1. Rega Institute is validating screening assay (targeting finish 3/23/2020)

ii. Pfizer and AstraZeneca have indicated that they will participate in the screening at Rega Institute

4. SAb Biotherapeutics – Development of a polyclonal antibody product
   i. IAA was approved to transfer funds to DoD
   ii. Targeting transfer of fund week of 3/23; Award to SAb to follow funds transfer

4. BARDA Vaccines
   1. Janssen Ad26 vaccine
      i. Janssen's Vaccine Candidates: immunogenic in mice 3 weeks after prime
      ii. Will identify lead candidate(s) by end of March.
      iii. Preliminary data on virus challenge in NHP model
         1. Virus stock infects animals and replicates
         2. No obvious clinical disease observed
   2. Sanofi Pasteur
      i. Re-designing spike protein DNA construct to contain stabilizing mutations
      ii. SP indicated to FDA that they expect to enter Phase 1 study Sept/Oct 2020.
   3. Moderna Norwood site visit scheduled for 03/20/2020
      i. Site where material for clinical trial will be made
      ii. Looking at transferring technology to additional CMOs to expand capacity
5. BARDA Rapidly Deployable Technology
   1. 2 proposals in EZ-BAA queue
6. BARDA Clinical
7. BARDA Non-clinical
   1. Nonclinical strategy briefed to NIAID to mitigate duplicative efforts.
   2. Nonclinical RTOR recommendation brief for leadership approval being developed
8. BARDA RQA
   1. First CBER/Janssen working group meeting for their COVID-19 vaccine.
      i. Focused on cell line and release package for clinical material
9. BARDA Manufacturing
   1. Working on Raw Material Analysis for 3 vaccines and 3 mAbs to reduce risk of low supply and long lead time
      i. Investigating additional manufacturing and fill finish facilities for these products in case "scaling out" is needed
   2. Reviewing proposal under BAA for advanced manufacturing.
      i. Domestic API manufacturer

SARS-CoV-2 Medical Countermeasures Task Force
Date: April 1, 2020
FOR OFFICIAL USE ONLY

Agencies reporting: BARDA, NIAID, DoD, FDA, USDA
Agencies not reporting: CDC, DHS

Talking Points for 1200 SLB and 1230 VTC

Accomplishments

- Clinical trial to test remdesivir for treatment of COVID-19: 307 (+33) new patients in last 24 hrs (target = 440)
- Antibody therapeutic trial: 377 (+73) new patients dosed, 41 (+2) sites in last 24 hrs (target = 400)
- FDA granted EUA to Bodysphere Inc for its fingerstick test for COVID-19 antibodies that provides results in 2 minutes – for use by healthcare professionals as screening tool [Note: we have not received confirmation from FDA about the Bodysphere test and will NOT report unless FDA confirms before 0900]

Currently Working

- Continuing to enroll patients in clinical trials to evaluate vaccines and therapeutics for COVID-19
- Identifying and prioritizing next therapeutics to be included in clinical trials
- USDA is investigating the stability of SARS-CoV-2 in foods that could become contaminated by food handlers with COVID-19

Updates for 1700 Operations Summary and SLB

Line of Effort: Clinical Trials
Activity: Ongoing and proposed clinical trials to test treatments for COVID-19 and to measure immune responses over time
Limiting Factors: Swabs for sample collection and PPE for healthcare workers

Line of Effort: Vaccines
Activity: Development and manufacturing of mRNA vaccine
Limiting Factors: Reagents (lipids) for vaccine production; vials for packaging of sterile vaccine products

Active USG-sponsored Clinical Trials

	Candidate	Sponsor	Target Enrollment	Number of Sites	Enrollment
Adaptive COVID-19 Treatment Trial (ACTT)	Remdesivir	NIAID, Gilead	440	46 (+2)	307 (+33)
Sarilumab (anti-IL-6R mAb)	Sarilumab	BARDA, Regeneron	400	41 (+2)	377 (+73)
COVACTA: tocilizumab (anti-IL-6R mAb)	Actemra	BARDA, Genentech	330	TBD	TBD
Moderna mRNA-1273 Vaccine Phase I	mRNA-1273	NIAID, Moderna	45	2	30
Epidemiology, Immunology and Clinical Characteristics (EpICC) Study	N/A	DoD	TBD	4	8

- Adaptive COVID-19 Treatment Trial - NIAID
  - Currently remdesivir vs. placebo control (with options to add additional arms as needed)
  - Target enrollment = 440
  - Inclusion criteria – Confirmed SARS-CoV-2 infection (efficacy, but a little gray area PEP too)
  - Primary endpoint:
    - 8pt ordinal scale scored at Day 15, ranging from death to discharged with no limitation on activities and no requirement for home oxygen

- Sarilumab (Anti IL-6R mAb, aka Kevzara), Regeneron/Sanofi
  - Sarilumab high dose vs. Sariluman low dose vs. placebo control
  - Target enrollment = 400
  - Inclusion criteria – Confirmed SARS-CoV-2 infection AND evidence of pneumonia and severe disease (a true efficacy study)
  - Primary endpoints:
    - Time to resolution of fever for at least 48 hours
    - 6pt ordinal scale scored on Day 15, ranging from death to discharged

- mRNA-1273, Moderna
  - Phase I safety/immunogenicity
  - Target enrollment = 45
  - NHV study
  - Cohorts (all n=15, including 4 sentinels):
    - Low dose = 25ug
    - Medium dose = 100ug
    - High dose = 250ug

- EpICC Study, IDCRP
  - Observational natural history study

- Clinical parameters being evaluated: risk factors, outcomes, virology, immunology

Proposed Clinical Trials

Vaccine / Therapeutic Product	Date / Range for Entry into Clinic
Convalescent plasma	Approx. late April/early May
IVIg	Late Spring 2020
Regeneron SARS-CoV-2 specific mAbs	June-July 2020 for treatment study in COVID-19 patients
Janssen screening leads	Early Summer 2020 or later; highly dependent on leads identified
SAb	June to mid-Summer 2020
Janssen Ad26 Vaccine	Phase 1: Q3-2020
Moderna mRNA Vaccine	Phase 1 enrollment: March 16, 2020 Phase 2: Q2-2020 (likely about June 2020)
Sanofi-Pasteur Vaccine	Phase 1: Q1-2021 (September/October 2020 provided to CBER)

From:	Brett Pletcher <Brett.Pletcher@gilead.com>
To:	Bright, Rick (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=53034752f35a4317aa74f46348442d39-Bright, Ric <Rick.Bright@hhs.gov>
CC:	Disbrow, Gary (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0fd5845defda4dc0bb45f8fac629cf09-Disbrow, Ga <Gary.Disbrow@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0851e89240324306b78740a4a60745e2-Johnson, Ro <Robert.Johnson@hhs.gov>
Subject:	Re: [EXTERNAL] Re: Gilead Donation of Remdesivir
Date:	2020/03/04 15:25:47
Priority:	Normal
Type:	Note

My understanding is that she may want to deploy some of it to the outbreak in Washington. We are also looking at whether we can route patients through planned clinical trials instead. My cell is (b)(6) if you need to talk live.

Brett Pletcher
EVP, Corporate Affairs, General Counsel and Corporate Secretary
Gilead Sciences | Office: 1 (650) 522 6219

On 3/4/20, 12:17 PM, "Bright, Rick (OS/ASPR/BARDA)" <Rick.Bright@hhs.gov> wrote:

Dear Brett,

Thanks for letting me know about this request. I will discuss with our team and determine the context of the request. Do you have a specific request from Dr. Birx that you can share with me so I can target my inquiry?

Thank you.

Rick.

> On Mar 4, 2020, at 2:52 PM, Brett Pletcher <Brett.Pletcher@gilead.com> wrote:
>
> Dear Dr. Bright,
>
> It appears that Dr. Birx would like to start drawing down on our donation of 7,500 courses of treatment for remdesivir. We have not yet received a donation letter from HHS and do not know who to contact about it. Can you please let me know who we should contact to accelerate this process?
>

> Thanks
>
> Brett Pletcher
> EVP, Corporate Affairs, General Counsel and Corporate Secretary
> Gilead Sciences | Office: 1 (650) 522 6219
>
> NOTICE: This e-mail and all attachments transmitted with it are intended solely for the use of the addressees and may contain legally privileged, protected or confidential information. If you have received this message in error, please notify the sender immediately by e-mail reply and please delete this e-mail message from your computer and destroy any copies.
>

Sender:	Brett Pletcher <Brett.Pletcher@gilead.com>
Recipient:	Bright, Rick (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=53034752f35a4317aa74f46348442d39-Bright, Ric <Rick.Bright@hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0fd5845defda4dc0bb45f8fac629cf09-Disbrow, Ga <Gary.Disbrow@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0851e89240324306b78740a4a60745e2-Johnson, Ro <Robert.Johnson@hhs.gov>
Sent Date:	2020/03/04 15:25:17
Delivered Date:	2020/03/04 15:25:47