From:	Disbrow, Gary (OS/ASPR/BARDA) </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0FD5845DEFDA4DC0BB45F8FAC629CF09-DISBROW, GA>
To:	Oxner, Julie (OS/ASPR/OEA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f96241c6a5f8401a9a218c259f2e614a-Oxner, Juli <Julie.Oxner@hhs.gov>; Blatner, Gretta (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=623cb123c2324236b1db6fb9153e0bbf-Blatner, Gr <Gretta.Blatner@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>
Subject:	RE: FOUO Follow up
Date:	2020/04/24 05:54:14
Priority:	Normal
Type:	Note

Julie,

You have much more experience working with the previous Director and I know he always did a great job engaging with Congressional members or their staff.

If you have ideas of ways I can improve messaging, always happy to hear that feedback. I don't take it as criticism.

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

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

---

From: Oxner, Julie (OS/ASPR/OEA) <Julie.Oxner@hhs.gov>
Sent: Wednesday, April 22, 2020 1:59 PM
To: Twomey, John K. (HHS/ASL) <John.Twomey@HHS.GOV>; Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>; Rybak, Bailey (OS/ASPR/OEA) <Bailey.Rybak@hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>
Subject: RE: Sen. Carper Request to Speak w/ Dr. Bright

Good for me.

From: Twomey, John K. (HHS/ASL) <John.Twomey@HHS.GOV>
Sent: Wednesday, April 22, 2020 1:58 PM
To: Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>; Rybak, Bailey (OS/ASPR/OEA) <Bailey.Rybak@hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>
Cc: Oxner, Julie (OS/ASPR/OEA) <Julie.Oxner@hhs.gov>
Subject: RE: Sen. Carper Request to Speak w/ Dr. Bright

Dr. Disbrow/Julie – Sen. Carper is running a few minutes behind they have asked that we start the call at 2:10 PM. Please let me know if that works for you all??

From: Twomey, John K. (HHS/ASL)
Sent: Thursday, April 16, 2020 5:57 PM
To: Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>; Rybak, Bailey (OS/ASPR/OEA) <Bailey.Rybak@hhs.gov>
Cc: Oxner, Julie (OS/ASPR/OEA) <Julie.Oxner@hhs.gov>
Subject: RE: Sen. Carper Request to Speak w/ Dr. Bright

Can we confirm Wednesday, April 22nd at 2:00 pm? If so, we can use the line (b)(6) (b)(6)

From: Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>
Sent: Thursday, April 16, 2020 5:27 PM
To: Twomey, John K. (HHS/ASL) <John.Twomey@HHS.GOV>; Rybak, Bailey (OS/ASPR/OEA) <Bailey.Rybak@hhs.gov>

Cc: Oxner, Julie (OS/ASPR/OEA) <Julie.Oxner@hhs.gov>
Subject: RE: Sen. Carper Request to Speak w/ Dr. Bright

Tuesday or Wed from 1-2:30 are both open at the moment.

From: Twomey, John K. (HHS/ASL) <John.Twomey@HHS.GOV>
Sent: Thursday, April 16, 2020 5:24 PM
To: Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>; Rybak, Bailey (OS/ASPR/OEA) <Bailey.Rybak@hhs.gov>
Cc: Oxner, Julie (OS/ASPR/OEA) <Julie.Oxner@hhs.gov>
Subject: RE: Sen. Carper Request to Speak w/ Dr. Bright

They asked for any times that Dr. Bright as next week. So please let me know if there are some good windows and we can try to lock this in and clear the slate.

From: Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>
Sent: Thursday, April 16, 2020 4:43 PM
To: Twomey, John K. (HHS/ASL) <John.Twomey@HHS.GOV>; Rybak, Bailey (OS/ASPR/OEA) <Bailey.Rybak@hhs.gov>
Cc: Oxner, Julie (OS/ASPR/OEA) <Julie.Oxner@hhs.gov>
Subject: RE: Sen. Carper Request to Speak w/ Dr. Bright

Hi John,

Rick has now been invited to a meeting with the Secretary and has a call with Senator Blunt at noon, so if possible 11 or 11:15 would be best.

Thanks
g

From: Twomey, John K. (HHS/ASL) <John.Twomey@HHS.GOV>
Sent: Thursday, April 16, 2020 4:40 PM
To: Rybak, Bailey (OS/ASPR/OEA) <Bailey.Rybak@hhs.gov>
Cc: Oxner, Julie (OS/ASPR/OEA) <Julie.Oxner@hhs.gov>; Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>
Subject: RE: Sen. Carper Request to Speak w/ Dr. Bright

I have asked about this time for Sen. Carper.

From: Rybak, Bailey (OS/ASPR/OEA) <Bailey.Rybak@hhs.gov>
Sent: Wednesday, April 15, 2020 3:52 PM
To: Twomey, John K. (HHS/ASL) <John.Twomey@HHS.GOV>
Cc: Oxner, Julie (OS/ASPR/OEA) <Julie.Oxner@hhs.gov>; Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>
Subject: FW: Sen. Carper Request to Speak w/ Dr. Bright

Hi John,

Following up on this request. Dr. Bright can be available to speak with Senator Carper between 10:30 and 12 on Friday if that will work for the Senator.

Very Respectfully,
Bailey

Bailey I Rybak
Division of Congressional Affairs

U.S. Department of Health and Human Services | Assistant Secretary for Preparedness and Response
Office of External Affairs
Thomas P. O'Neill Jr. Federal Building 4430C | 200 C St. SW | Washington, DC 20024
Office: 202.692.4799 | Email: Bailey.Rybak@hhs.gov

From: Twomey, John K. (HHS/ASL) <John.Twomey@HHS.GOV>
Sent: Monday, April 13, 2020 4:05 PM
To: Oxner, Julie (OS/ASPR/OEA) <Julie.Oxner@hhs.gov>
Cc: Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>
Subject: RE: Sen. Carper Request to Speak w/ Dr. Bright

Carper is now not available tomorrow. They have circled back and ask for other times that Dr. Bright is available this week or next. Obviously this is not an urgent request but I am sure all parties included would like to close this out. If there are some windows that work well for Dr. Bright I will let Carper staff know.

From: Oxner, Julie (OS/ASPR/OEA) <Julie.Oxner@hhs.gov>
Sent: Monday, April 13, 2020 2:29 PM
To: Twomey, John K. (HHS/ASL) <John.Twomey@HHS.GOV>
Cc: Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>
Subject: RE: Sen. Carper Request to Speak w/ Dr. Bright

Hi John,

Are we set for a call with Carper tomorrow?

Julie

From: Twomey, John K. (HHS/ASL) <John.Twomey@HHS.GOV>
Sent: Friday, April 10, 2020 2:40 PM
To: Oxner, Julie (OS/ASPR/OEA) <Julie.Oxner@hhs.gov>
Cc: Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>
Subject: RE: Sen. Carper Request to Speak w/ Dr. Bright

I will share the link, the ask is still an overview of investment I think Dr. Bright is a victim of his success on the call he had w/ Sen. Alexander because the Senator keeps suggesting folks talk with Dr. Bright. If there is another SME from BARDA to speak with Carper that works here, his folks are very accommodating.

For the staff call we will certainly provide more parameters this was more of a flag/heads up that it is a direction we are trying to go.

From: Oxner, Julie (OS/ASPR/OEA) <Julie.Oxner@hhs.gov>
Sent: Friday, April 10, 2020 2:30 PM
To: Twomey, John K. (HHS/ASL) <John.Twomey@HHS.GOV>
Cc: Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>
Subject: RE: Sen. Carper Request to Speak w/ Dr. Bright

Hi John,

For starters, could you please share the following link with Senator Carper's staff? https://www.medicalcountermeasures.gov/app/barda/coronavirus/COVID19.aspx It includes all of the BARDA investments, to date, for COVID medical countermeasures and should give them a good overview of work done to date. Is Carper still wanting an overview of investments or is there something more specific they are hoping to discuss? We really like to get a focused/identified ask so we can have the appropriate briefer and the appropriate level of information.

Second, on the staff call with Committees of Jurisdictions, different from supply chain, each agency could use an hour to describe efforts and activities. Will ASL provide more parameters on what we should specifically highlight?

Sorry for the questions, again, we just want to make sure we have the correct POC and appropriate level of information.

Thanks,

Julie

From: Twomey, John K. (HHS/ASL) <John.Twomey@HHS.GOV>
Sent: Friday, April 10, 2020 2:18 PM
To: Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>
Cc: Oxner, Julie (OS/ASPR/OEA) <Julie.Oxner@hhs.gov>
Subject: RE: Sen. Carper Request to Speak w/ Dr. Bright

Gretta – Carper's office just go back to me on the request for speak with Dr. Bright. Times below:

-Monday, April 13th at 1 pm
-Tuesday, April 14th at 3 pm
- Wednesday, April 15th at 1:30 pm - 2:30 pm

I also wanted to flag that this week ASL hosted two calls with staff from HHS Committees of Jurisdiction to discuss 1) supply chain 2) testing work.

Next week we plan to host another call and we would like to discuss countermeasures and vaccine developments. We will have SMEs from NIH, FDA, and we will also include BARDA. I will circle back on times.

From: Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>
Sent: Monday, April 6, 2020 8:45 PM
To: Twomey, John K. (HHS/ASL) <John.Twomey@HHS.GOV>
Cc: Oxner, Julie (OS/ASPR/OEA) <Julie.Oxner@hhs.gov>
Subject: RE: Sen. Carper Request to Speak w/ Dr. Bright

Hi John,

Sorry about not replying about timing. Rick wanted to see what the Senator had available.

For Remdesivir, BARDA is not directly working on the clinical trials or emergency INDs. NIAID is sponsoring one of the clinical trials.

Thanks
g

From: Twomey, John K. (HHS/ASL) <John.Twomey@HHS.GOV>
Sent: Monday, April 6, 2020 8:04 PM
To: Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>

Cc: Oxner, Julie (OS/ASPR/OEA) <Julie.Oxner@hhs.gov>
Subject: RE: Sen. Carper Request to Speak w/ Dr. Bright

Gretta – wanted to follow up on timing and had one other unrelated question.

I know that that currently the SNS (b)(3):42 U.S.C. § 247d-6b(d) but that the FDA has allowed for it to be utilized by providers in a clinical setting with COVID-19 positive patients.

Does BARDA play a role in directing Gilead to send its stocks of remdesivir anywhere or is it the discretion of the company?

Thanks,
John

From: Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>
Sent: Sunday, April 5, 2020 9:56 PM
To: Twomey, John K. (HHS/ASL) <John.Twomey@HHS.GOV>
Cc: Oxner, Julie (OS/ASPR/OEA) <Julie.Oxner@hhs.gov>
Subject: RE: Sen. Carper Request to Speak w/ Dr. Bright

I'll talk to Rick in the morning and see what's available. If you hear from the Senator, please let me know.

Thanks
g

From: Twomey, John K. (HHS/ASL) <John.Twomey@HHS.GOV>
Sent: Sunday, April 5, 2020 7:30 PM
To: Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>
Cc: Oxner, Julie (OS/ASPR/OEA) <Julie.Oxner@hhs.gov>
Subject: RE: Sen. Carper Request to Speak w/ Dr. Bright

They said tomorrow will not work, please let me know if there are additional times later in the week. I have asked the same of them as well.

Best,
John

From: Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>
Sent: Sunday, April 5, 2020 3:29 PM
To: Twomey, John K. (HHS/ASL) <John.Twomey@HHS.GOV>

Cc: Oxner, Julie (OS/ASPR/OEA) <Julie.Oxner@hhs.gov>
Subject: RE: Sen. Carper Request to Speak w/ Dr. Bright

Hi John,

Dr. Bright could do tomorrow anytime between 3-4. Please let us know if that will work for the Senator.

Thank you

Gretta

From: Twomey, John K. (HHS/ASL) <John.Twomey@HHS.GOV>
Sent: Saturday, April 4, 2020 6:07 PM
To: Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>
Cc: Oxner, Julie (OS/ASPR/OEA) <Julie.Oxner@hhs.gov>
Subject: RE: Sen. Carper Request to Speak w/ Dr. Bright

I have that request back to his staff. Knowing him and his office I think he will be curious as to know what is the in pipeline, does BARDA have the resources it needs, how is BARDA planning ahead to be ready when a vaccine or therapeutic can become mass procudced.

From: Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>
Sent: Saturday, April 4, 2020 6:03 PM
To: Twomey, John K. (HHS/ASL) <John.Twomey@HHS.GOV>
Cc: Oxner, Julie (OS/ASPR/OEA) <Julie.Oxner@hhs.gov>
Subject: RE: Sen. Carper Request to Speak w/ Dr. Bright

HI John,

Do you know what areas of MCM development the Sen would like to discuss? We can definitely find a time, I just need to talk to Dr. Bright as he sometimes has meetings that are not yet on his calendar.

Thanks
Gretta

From: Twomey, John K. (HHS/ASL) <John.Twomey@HHS.GOV>
Sent: Saturday, April 4, 2020 4:55 PM
To: Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>

Cc: Oxner, Julie (OS/ASPR/OEA) <Julie.Oxner@hhs.gov>
Subject: Sen. Carper Request to Speak w/ Dr. Bright

Gretta/Julie – Sen. Carper had a call with members of the supply chain task force yesterday and he started asking questions about the medical countermeasure side of the response. As a result the Senator is requesting a call with Dr. Bright or one of his deputies to discuss the work of BARDA. Are there some times that Dr. Bright is available or is there another BARDA SME we could work with to connect Sen. Caprer with?

Best,

John Twomey

Chief of Staff
Office of the Assistant Secretary for Legislation
U.S. Department of Health & Human Services
Cell: (b)(6)
Desk: (202) 690-6578

Sender:	Disbrow, Gary (OS/ASPR/BARDA) </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0FD5845DEFDA4DC0BB45F8FAC629CF09-DISBROW, GA>
Recipient:	Oxner, Julie (OS/ASPR/OEA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f96241c6a5f8401a9a218c259f2e614a-Oxner, Juli <Julie.Oxner@hhs.gov>; Blatner, Gretta (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=623cb123c2324236b1db6fb9153e0bbf-Blatner, Gr <Gretta.Blatner@hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0fd5845defda4dc0bb45f8fac629cf09-Disbrow, Ga <Gary.Disbrow@hhs.gov>
Sent Date:	2020/04/24 05:54:13
Delivered Date:	2020/04/24 05:54:14

Pre-Decisional/FOUO
June 2, 2020

USG Early Outbreak Support for SARS-CoV-2 Therapeutics

Basic Timeline

The federal government has been working from very early on, prior to, and continuing after the HHS Secretary declared a public health emergency on January 31, 2020, to develop therapeutics that are critical for the response. Below are some of the high-level interagency efforts and specific actions the Biomedical Advanced Research and Development Authority (BARDA) took to support development of the therapeutics for various mechanism of actions utilizing funding mechanisms across Other Transaction Authorization (OTA), Indefinite Delivery (Indefinite Quantity) (IDIQ), Broad Agency Announcement (BAA), and EZ-BAA. The timing of the immediate actions were as followed:

- **January 11, 2020: BARDA Program** emailed sequence information to Regeneron which ordered sequence:
    - January 20, 2020: JOC meeting was conducted
    - January 31, 2020: Contract modification was executed for lead selection; and in vivo testing was awarded
    - February 4, 2020: Mice were immunized

- **January 20, 2020: BARDA Program** emailed to inquire if Janssen was interested in screening compounds against the SARS-CoV-2

- **January 23, 2020: Interagency** Therapeutics WG stood up and met (BARDA, CDC, DoD/DARPA, DoD/OCET, FDA/Antivirals, FDA/OCET, NIH)

- **January 25, 2020 Medical Countermeasures Task Force Established** – Jan 25, 2020: ASPR Requests BARDA establish the Medical Countermeasures Task force to lead USG medical countermeasure development in response to the outbreak
    - Initial meeting of the task force Jan. 29, 2020
    - Six interagency partners: ASPR, BARDA, CDC, DoD, FDA, NIAID.
    - Four Working Groups: Clinical, Diagnostics, Therapeutics, Vaccines.
    - Three Sub-working Groups: NIAID RCT, Sample Sharing, Therapeutics Prioritization

- **January 26, 2020: BARDA Market Research** BARDA initiated market research calls with industry leading pharmaceutical companies to gauge their interest in developing SARS-CoV-2 therapeutics and to encourage their initiation of engagement through the currently active OTA contracts. A list of companies for the initial engagement:
    - Roche, QPEX, GSK, Pfizer, Janssen and Genentech
    - To date BARDA and the interagency MCM Task Force Portal has received over 1043 Market Research submissions for Therapeutics out of our total 2725 submissions

- **January 28, 2020: Interagency** MCM Therapeutics WG's first expansion of the membership (BARDA, CDC, DoD/DARPA, DoD/HA, DoD/DTRA, DoD/JPEO, FDA/DAV, FDA/OAP, FDA/OCET, FDA/ONDP, NIH)

- **February 3, 2020: Interagency** MCM Therapeutics WG conducted first regularly scheduled Monday afternoon meetings.

- **February 11-12, 2020: WHO and GLOPID-R Research Meeting:** BARDA staff participated in the 2019 Novel Coronavirus Global Research and Innovation Forum: Towards a research roadmap.

- **March 4, 2020: BARDA's Broad agency announcement (BAA)** Amendment 13 has been implemented to include funding opportunities for COVID-19 Therapeutics as the following:
  - AOI 9.2 COVID-19 Therapeutics,
  - AOI 9.3 Immunomodulators or therapeutics targeting lung repair, and
  - AOI 9.5 Pre-exposure and Post-exposure Prophylaxis,
  - As of June 1, 2020, 106 submissions have been received to BARDA's BAA (66 for AOI 9.2; 33 for AOI 9.3; and 7 for AOI 9.5) for SARS-CoV-2 therapeutics; awards are expected in the near future

- **March 12, 2020: BARDA First Application** First Therapeutics White Paper application (BAA) received, which was from (b)(3):42 U.S.C. § for the BAA
  - There are 2 Full Proposals being awarded as SARS-CoV-2 Therapeutics to date. There are several additional candidates being funded through the OTA contractual mechanism (Please refer to Table)

- **March 19, 2020: FDA Guidance** has been issued on "Postmarketing Adverse Event Reporting for Medical Products and Dietary Supplements During a Pandemic"
  - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/postmarketing-adverse-event-reporting-medical-products-and-dietary-supplements-during-pandemic

- **March 28, 2020: FDA** issued an EUA to allow hydroxychloroquine sulfate and chloroquine phosphate products donated to the Strategic National Stockpile (SNS) to be distributed and used for certain hospitalized patients with COVID-19.
  - https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#covidtherapeutics
  - **FDA** has accelerated the development and use of therapies product, Chloroquine phosphate and hydroxychloroquine sulfate for treatment of COVID-19, sponsored by the Assistant Secretary of Preparedness and Response (ASPR).

- **April 2, 2020: BARDA's Broad agency announcement (BAA)** Amendment 15 has been implemented to include funding opportunities for COVID-19 Therapeutics as the following:
  - BARDA will accept full proposal submissions for rolling reviews to accelerate the research and development of only medical countermeasures to fight the 2019 novel coronavirus disease (COVID-19) or the SARS-CoV-2 virus. The submission must highlight how your product address SARS-CoV-2 and if not directly acting on the virus, provide documentation of how your product can address COVID-19 disease.
  - All reviews will be continuous (i.e., the "soft" submission deadline indicated in "Table 1: Submission Deadlines and Government Response Time" will not apply) as they are received in the BARDA-BAA@hhs.gov mailbox,
  - All reviews and responses are anticipated to be expedited,
  - All awards are anticipated to be expedited and made in FY2020.

- **April 3, 2020: FDA** has accelerated the development and use of therapies product, Hyperimmune Globulin, sponsored by the Collaboration between industry, academic and government partners, where National Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health is the Lead Institution

- **April 5, 2020: BARDA First Funded Full Proposal** First funded Therapeutics Full Proposal application received, which was from Alchem Laboratories Corp. through the BAA
    - The final award date is April 14, 2020 indicating 9 days turnaround from FP to Award.

- **April 9, 2020: FDA** has accelerated the development and use of therapies product, Convalescent Plasma, sponsored by the Collaboration between industry, academic and government partners, where Mayo Clinic is the Lead Institution.

- **April 13, 2020: FDA Guidance** has been issued on "Product-Specific Guidances for Chloroquine Phosphate and Hydroxychloroquine Sulfate"
    - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/product-specific-guidances-chloroquine-phosphate-and-hydroxychloroquine-sulfate

- **April 16, 2020: FDA Guidance** has been issued on "Temporary Policy for Compounding of Certain Drugs for Hospitalized Patients by Outsourcing Facilities During the COVID-19 Public Health Emergency"
    - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/temporary-policy-compounding-certain-drugs-hospitalized-patients-outsourcing-facilities-during-covid

- **April 16, 2020: FDA Guidance** has been issued on "FDA Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Public Health Emergency"
    - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/fda-guidance-conduct-clinical-trials-medical-products-during-covid-19-public-health-emergency

- **April 20, 2020: FDA Guidance** has been issued on "Temporary Policy for Compounding of Certain Drugs for Hospitalized Patients by Pharmacy Compounders not Registered as Outsourcing Facilities During the COVID-19 Public Health Emergency Guidance for Industry"
    - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/temporary-policy-compounding-certain-drugs-hospitalized-patients-pharmacy-compounders-not-registered

- **April 22, 2020: FDA Guidance** has been issued on "Temporary Policy on Repackaging or Combining Propofol Drug Products During the COVID-19 Public Health Emergency"
    - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/temporary-policy-repackaging-or-combining-propofol-drug-products-during-covid-19-public-health

- **April 24, 2020: BARDA's Broad agency announcement (BAA)** Amendment 16 has been implemented to include funding opportunities for COVID-19 Therapeutics as the following:

  - Rolling review means an offeror can submit a completed Technical Proposal and Attachment section of its Full Proposal for review by BARDA, rather than submitting the Full Proposal package (Technical and Cost) prior to technical review.
  - Clarification of manufacturing of products in the United States are in a 21 CFR 210, 211 current Good Manufacturing Practices compliant facility.
  - White papers and proposals should address any ongoing clinical trials of their candidate therapeutic, and how a proposed study is different than the ongoing studies.

- **May 1, 2020: FDA** issued an EUA to allow remdesivir to be distributed and used by licensed health care providers to treat adults and children hospitalized with severe COVID-19.
  - **FDA** has accelerated the development and use of therapies product, Remdesivir, sponsored by Gilead Sciences, Inc.

- **May 1, 2020: BARDA's Broad agency announcement (BAA)** Awarded a contract to Mayo Clinic for the Nationwide Expanded Access Program (EAP) to facilitate the use of human convalescent plasma. This is part of a larger effort for the collection of convalescent plasma. BARDA is supporting the American Red Cross and American Blood Centers to collect plasma for the EAP.

- **May 15, 2020: White House: Operation Warp Speed Framework and Leadership Announced.** The Trump Administration announces the appointment of Moncef Slaoui as chief advisor and General Gustave F. Perna as chief operating officer of Operation Warp Speed (OWS), the administration's national program to accelerate the development, manufacturing, and distribution of COVID-19 medical countermeasures. BARDA is a part of this whole-of-government effort. Janet Woodcock appointed as therapeutics lead.

- **May 18, 2020: BARDA Phlow Corp award:** BARDA formed a strategic partnership in May 2020 with Phlow to foster and expand Pharmaceutical Manufacturing in America by increasing U.S.-based manufacturing capacity to produce active pharmaceutical ingredients and generic medicines needed during the COVID-19 response, , and also during future public health emergencies

Pre-Decisional/FOUO
June 2, 2020

Table of all BARDA Therapeutics Awards for COVID-19

Project Name	Organization Name	Funding Mechanism	Date Submitted/ JOC Date	Date of BARDA Award
Novel Therapeutic Efforts for COVID-19	Regeneron Pharmaceuticals, Inc	OTA	01/20/2020	02/03/2020
(b)(3):42 U.S.C. § 247d-6b(d)				02/14/2020
Drug Screening Efforts	Janssen Research & Development, LLC	OTA		02/14/2020
SARS-CoV-2 mAb	Regeneron Pharmaceuticals, Inc	OTA	03/12/2020	03/20/2020
Sarilumab (Anti IL-6) Phase 2/3	Regeneron Pharmaceuticals, Inc	OTA	03/15/2020	03/20/2020
#1 Hit from antiviral screening post hit through Phase 2b (therapeutic)	Janssen Research & Development, LLC	OTA	03/20/2020	03/20/2020
Expanded Access Treatment Protocol for Hydrochloroquine and Chloroquine	PPD Development LP	FFP		03/24/2020
Actemra COVID-19 Therapeutic	Genentech USA, Inc.	OTA	03/17/2020	03/27/2020
Convalescent Plasma Collection and Distribution	American National Red Cross, The	Letter Contract		3/27/2020
SAb Therapeutics Hyperimmune plasma	SAB BIOTHERAPEUTICS, INC.	IAA		03/30/2020
Grifols Hyperimmune Globulin	Grifols Pharmaceutical	IAA		04/01/2020
Emergent Hyperimmune Globulin	Emergent Biosolutions	IDIQ		04/02/2020
Investigator initiated clinical Trial - hydroxychloroquine	Alchem Laboratories Corp	BAA	04/04/2020	04/14/2020
Dev't of systems for Convalescent Plasma Collection	America's Blood Centers	FFP		4/17/2020
Emerging Pathogen Readiness - Year 2	Cerus Corporation	Option on Existing Contract		04/18/2020
SARS-CoV-2 mAb	Regeneron Pharmaceuticals, Inc*	OTA	04/22/2020	04/29/2020

Nationwide Expanded Access Program (EAP) to facilitate the use of human convalescent plasma	Mayo Clinic	BAA	04/15/2020	05/01/2020
Nationwide Expanded Access Program (EAP) to facilitate the use of human convalescent plasma	Mayo Clinic	Modification to Existing Contract		5/11/2020
10 Liters of COVID-19 Convalescent Serum	Blood Centers of America	FFP		5/14/2020
Dev't of systems for Convalescent Plasma Collection	America's Blood Centers	FFP		5/20/2020
Dev't of systems for Convalescent Plasma Collection	America's Blood Centers	FFP		5/21/2020
COVASTIL - Phase II Study for Safety/Efficacy of MSTT1041A and UTTR1147A for Patients with Severe COVID-19 Pneumonia	Genentech, Inc.	OTA	5/5/2020	5/27/2020
Additional Manufacturing Capacity				
US-Based Advanced Manufacturing for COVID-19 Essential Medicines and Future Threats	Phlow Corp.	FFP	3/18/2020	4/23/2020
US-Based Advanced Manufacturing for COVID-19 Essential Medicines and Future Threats	Phlow Corp.	C Type Contract		5/18/2020

*Note: this is the same project as line 1 & 4. Additional funding was provided in stages as R&D was advancing

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

-----Original Message-----
From: Kadlec, Robert (OS/ASPR/IO) <Robert.Kadlec@hhs.gov>
Sent: Wednesday, March 25, 2020 9:35 PM
To: Townsend, Frances <FTownsend@MAFGRP.COM>
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>; Houchens, Christopher (OS/ASPR/BARDA) <Christopher.Houchens@hhs.gov>
Subject: RE: Remdesivir
Importance: High

Fran will pursue possible alternatives. Thanks for sharing be back to you soon. Best Bob

-----Original Message-----
From: Townsend, Frances <FTownsend@MAFGRP.COM>
Sent: Wednesday, March 25, 2020 9:31 PM
To: Kadlec, Robert (OS/ASPR/IO) <Robert.Kadlec@hhs.gov>
Cc: Shuy, Bryan (OS/ASPR/IO) <Bryan.Shuy@hhs.gov>
Subject: Remdesivir

Bob - i am sorry to bother you guys so please direct me elsewhere to the right place.

46 year old Dr in Overlook Hospital in NJ with COVID-19 was in otherwise good health. Is deteriorating having tried the Zpack/malaria drug protocol on him to no effect and they now are looking to try remdesivir. But given the recent Gilead public announcement that they have stopped compassionate use cases the family asked me where and to who they go in government to plead their case.

Again I am sorry to ask but this is a young Dr. Not asking you or Bryan to take this on please just point me in the right direction and i will do the rest.

God bless you both for the job you are doing! 🙏

Fran

Sender:	Disbrow, Gary (OS/ASPR/BARDA) </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0FD5845DEFDA4DC0BB45F8FAC629CF09-DISBROW, GA>
Recipient:	Beigel, John (NIH) [E] <jbeigel@niaid.nih.gov>; Marston, Hilary (NIH/NIAID) [E] /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=93be476c17024bbcbc5b44add01fe6a8-hilary.mars <hilary.marston@nih.gov>; Johnson, Robert (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0851e89240324306b78740a4a60745e2-Johnson, Ro <Robert.Johnson@hhs.gov>; Houchens, Christopher (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7ac94a574bd04528b7c91bbd61893975-Houchens, C <Christopher.Houchens@hhs.gov>
Sent Date:	2020/03/26 07:21:14
Delivered Date:	2020/03/26 07:21:00

From:	Disbrow, Gary (OS/ASPR/BARDA) </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0FD5845DEFDA4DC0BB45F8FAC629CF09-DISBROW, GA>
To:	Walker, Robert (OS/ASPR/BARDA) (Robert.Walker@hhs.gov) <Robert.Walker@hhs.gov>; Benford, Joffrey (OS/ASPR/AMCG) (Joffrey.Benford@hhs.gov) <Joffrey.Benford@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>; Lambert, Linda (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ce6824b6a92a4a4e893ea7b54e17eb3c-Lambert, Li <Linda.Lambert@hhs.gov>
Subject:	This may have also come through the BAA
Date:	2020/04/06 04:23:00
Priority:	Normal
Type:	Note

Team,

This effort has been identified as an activity that the ASPR wants supported. He wrote a letter of intent to the company on March 20th. I will send that, although I believe Bob and Linda already have it. Please move forward with the quickest way to provide funds. BARDA is not the sponsor, does not have to provide a CRO, and they will be responsible for compliance with the FDA. They want to start enrolling this week. There will be others like this coming so we need to identify a mechanism. Happy to get on a phone to discuss.

Gary

Sender:	Disbrow, Gary (OS/ASPR/BARDA) </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0FD5845DEFDA4DC0BB45F8FAC629CF09-DISBROW, GA>
Recipient:	Walker, Robert (OS/ASPR/BARDA) (Robert.Walker@hhs.gov) <Robert.Walker@hhs.gov>; Benford, Joffrey (OS/ASPR/AMCG) (Joffrey.Benford@hhs.gov) <Joffrey.Benford@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>
Sent Date:	2020/04/06 04:24:13
Delivered Date:	2020/04/06 04:23:00
From:	<jtalton@alchem.com>
To:	BARDA-BAA (OS/ASPR) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f5820d6842574b75b95a4bc020f2ac5b-BARDA-BAA <BARDA-BAA@hhs.gov>
CC:	<rmalone@alchem.com>; 'Conigliaro, Joseph' <Jconigliaro@northwell.edu>; Disbrow, Gary (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0fd5845defda4dc0bb45f8fac629cf09-Disbrow, Ga <Gary.Disbrow@hhs.gov>
Subject:	RE: Submission of Full Proposal under BAA-18-100-SOL-00003 Amendment 15

Date: 2020/04/05 19:35:41
Priority: Normal
Type: Note

Please find attached a revised Volume 1 Technical Proposal Attachments document, a page at the end was left off.

Thanks,

Jim

From: jtalton@alchem.com <jtalton@alchem.com>
Sent: Sunday, April 05, 2020 7:09 PM
To: BARDA-BAA@hhs.gov
Cc: rmalone@alchem.com; 'Conigliaro, Joseph' <Jconigliaro@northwell.edu>; 'Disbrow, Gary (OS/ASPR/BARDA)' <Gary.Disbrow@hhs.gov>
Subject: Submission of Full Proposal under BAA-18-100-SOL-00003 Amendment 15

Please find attached Alchem and Northwell's submission of our Full Proposal under BAA-18-100-SOL-00003 Amendment 15 entitled "A Multi-site, Randomized, Double-Blind, Multi-Arm Historical Control, Comparative Trial of the Safety and Efficacy of Hydroxychloroquine, and the Combination of Hydroxychloroquine and Famotidine for the Treatment of COVID-19 in Hospitalized Adults".

The FDA designated Northwell's study Exempt on Friday. Since this clinical study is expected to start tomorrow, we requested expedited review for the proposal.

Please contact me if you require any additional information. Please confirm receipt of this submission.

Thanks,

Jim

James Talton, Ph.D.
President &CEO

Alchem Laboratories Corp.
13305 Rachael Blvd
Alachua, FL 32615
(386) 418-1650
(386) 401-6304 Direct

Sender: <jtalton@alchem.com>

Recipient:	BARDA-BAA (OS/ASPR) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f5820d6842574b75b95a4bc020f2ac5b-BARDA-BAA <BARDA-BAA@hhs.gov>; <rmalone@alchem.com>; 'Conigliaro, Joseph' <Jconigliaro@northwell.edu>; Disbrow, Gary (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0fd5845defda4dc0bb45f8fac629cf09-Disbrow, Ga <Gary.Disbrow@hhs.gov>
Sent Date:	2020/04/05 19:34:45
Delivered Date:	2020/04/05 19:35:41
From:	<jtalton@alchem.com>
To:	BARDA-BAA (OS/ASPR) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f5820d6842574b75b95a4bc020f2ac5b-BARDA-BAA <BARDA-BAA@hhs.gov>
CC:	<rmalone@alchem.com>; 'Conigliaro, Joseph' <Jconigliaro@northwell.edu>; Disbrow, Gary (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0fd5845defda4dc0bb45f8fac629cf09-Disbrow, Ga <Gary.Disbrow@hhs.gov>
Subject:	Submission of Full Proposal under BAA-18-100-SOL-00003 Amendment 15
Date:	2020/04/05 19:11:23
Priority:	Normal
Type:	Note

Please find attached Alchem and Northwell's submission of our Full Proposal under BAA-18-100-SOL-00003 Amendment 15 entitled "A Multi-site, Randomized, Double-Blind, Multi-Arm Historical Control, Comparative Trial of the Safety and Efficacy of Hydroxychloroquine, and the Combination of Hydroxychloroquine and Famotidine for the Treatment of COVID-19 in Hospitalized Adults".

The FDA designated Northwell's study Exempt on Friday. Since this clinical study is expected to start tomorrow, we requested expedited review for the proposal.

Please contact me if you require any additional information. Please confirm receipt of this submission.

Thanks,

Jim

James Talton, Ph.D.
President &CEO

Alchem Laboratories Corp.
13305 Rachael Blvd
Alachua, FL 32615
(386) 418-1650
(386) 401-6304 Direct

Sender:	<jtalton@alchem.com>
Recipient:	BARDA-BAA (OS/ASPR) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f5820d6842574b75b95a4bc020f2ac5b-BARDA-BAA <BARDA-BAA@hhs.gov>; <rmalone@alchem.com>; 'Conigliaro, Joseph' <Jconigliaro@northwell.edu>; Disbrow, Gary (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0fd5845defda4dc0bb45f8fac629cf09-Disbrow, Ga <Gary.Disbrow@hhs.gov>
Sent Date:	2020/04/05 19:08:42
Delivered Date:	2020/04/05 19:11:23

From:	Disbrow, Gary (OS/ASPR/BARDA) </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0FD5845DEFDA4DC0BB45F8FAC629CF09-DISBROW, GA>
To:	Billet, Courtney (NIH/NIAID) [E] <billetc@niaid.nih.gov>; Kane, Elleen (OS/ASPR/OEA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=user25dbd6c7 <Elleen.Kane@hhs.gov>; Oakley, Caitlin B. (OS/ASPA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e5ee4c35534c4af9bdac46789c034790-Oakley, Cai <Caitlin.Oakley@HHS.GOV>; Michael, Gretchen (OS/ASPR/OEA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0632b4526d6447b5af26552afde05c33-Michael, Gr <Gretchen.Michael@hhs.gov>; Waters, Cicely (OS/ASPR/OEA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=00e638c4ddf64006bcc009e8032dd700-Waters, Cic <Cicely.Waters@hhs.gov>; Shuy, Bryan (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fdeb5ca04b6b4ed19fec2209b5f571e7-Shuy, Bryan <Bryan.Shuy@hhs.gov>; Hayes, Jonathan (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8cdfb7232de4428794f2901218bc1360-Hayes, Jona <Jonathan.Hayes@hhs.gov>; Sellman, Suzanne (OS/ASPR/OEA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5bfe40dc98b54fc7989a00075a9c8ab7-Sellman, Su <Suzanne.Sellman@hhs.gov>; Bialek, Stephanie M. (ASPR/SNS) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a7d77e22d4bd40b6a0b205df4d8a2f58-stephanie.b <ilq8@cdc.gov>; Routh, Jennifer (NIH/NIAID) [E] /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2dd951edf9be461f93276b338e2b0b08-jennifer.ro <jennifer.routh@nih.gov>; Stover, Kathy (NIH/NIAID) [E] /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d2241aa54aa341ceb7ff993d88eba4df-kathy.stove <kathy.stover@nih.gov>
CC:	McKeogh, Katherine (OS/ASPA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c652f2c415b44dff8369dd7f4596f030-McKeogh, Ka <Katherine.McKeogh@hhs.gov>; Murphy, Ryan (OS/ASPA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=314e69c69a844b47bdd9f74bc60a8d44-Murphy, Rya <Ryan.Murphy1@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>
Subject:	RE: For ASPR Review--more info: price of remdesivir
Date:	2020/04/07 18:44:00
Priority:	Normal
Type:	Note

Please remove me from this email train

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

From: Billet, Courtney (NIH/NIAID) [E] <billetc@niaid.nih.gov>
Sent: Tuesday, April 7, 2020 6:42 PM
To: Kane, Elleen (OS/ASPR/OEA) <Elleen.Kane@hhs.gov>; Oakley, Caitlin B. (OS/ASPA) <Caitlin.Oakley@HHS.GOV>; Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Michael, Gretchen (OS/ASPR/OEA) <Gretchen.Michael@hhs.gov>; Waters, Cicely (OS/ASPR/OEA) <Cicely.Waters@hhs.gov>; Shuy, Bryan (OS/ASPR/IO) <Bryan.Shuy@hhs.gov>; Hayes, Jonathan (OS/ASPR/IO) <Jonathan.Hayes@hhs.gov>; Sellman, Suzanne (OS/ASPR/OEA) <Suzanne.Sellman@hhs.gov>; Bialek, Stephanie M. (ASPR/SNS) <ilq8@cdc.gov>; Routh, Jennifer (NIH/NIAID) [E] <jennifer.routh@nih.gov>; Stover, Kathy (NIH/NIAID) [E] <kathy.stover@nih.gov>
Cc: McKeogh, Katherine (OS/ASPA) <Katherine.McKeogh@hhs.gov>; Murphy, Ryan (OS/ASPA) <Ryan.Murphy1@hhs.gov>; Stimson, Brian (HHS/OGC) <Brian.Stimson@hhs.gov>; Barry, Daniel J (HHS/OGC) <daniel.barry@hhs.gov>
Subject: RE: For ASPR Review--more info: price of remdesivir

Checking...

From: Kane, Elleen (OS/ASPR/OEA) <Elleen.Kane@hhs.gov>
Sent: Tuesday, April 7, 2020 6:34 PM
To: Oakley, Caitlin B. (OS/ASPA) <Caitlin.Oakley@HHS.GOV>; Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Michael, Gretchen (OS/ASPR/OEA) <Gretchen.Michael@hhs.gov>; Waters, Cicely (OS/ASPR/OEA) <Cicely.Waters@hhs.gov>; Shuy, Bryan (OS/ASPR/IO) <Bryan.Shuy@hhs.gov>; Hayes, Jonathan (OS/ASPR/IO) <Jonathan.Hayes@hhs.gov>; Sellman, Suzanne (OS/ASPR/OEA) <Suzanne.Sellman@hhs.gov>; Bialek, Stephanie M. (ASPR/SNS) <ilq8@cdc.gov>; Billet, Courtney (NIH/NIAID) [E] <billetc@niaid.nih.gov>; Routh, Jennifer (NIH/NIAID) [E] <jennifer.routh@nih.gov>; Stover, Kathy (NIH/NIAID) [E] <kathy.stover@nih.gov>
Cc: McKeogh, Katherine (OS/ASPA) <Katherine.McKeogh@hhs.gov>; Murphy, Ryan (OS/ASPA) <Ryan.Murphy1@hhs.gov>; Stimson, Brian (HHS/OGC) <Brian.Stimson@hhs.gov>; Barry, Daniel J (HHS/OGC) <Daniel.Barry@HHS.GOV>
Subject: RE: For ASPR Review--more info: price of remdesivir

NIH is doing a clinical trial of remdesivir with Gilead. Adding colleagues for possible insight.

https://www.nih.gov/news-events/news-releases/nih-clinical-trial-remdesivir-treat-covid-19-begins

---

From: Oakley, Caitlin B. (OS/ASPA) <Caitlin.Oakley@HHS.GOV>
Sent: Tuesday, April 7, 2020 6:32 PM
To: Kane, Elleen (OS/ASPR/OEA) <Elleen.Kane@hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Michael, Gretchen (OS/ASPR/OEA) <Gretchen.Michael@hhs.gov>; Waters, Cicely (OS/ASPR/OEA) <Cicely.Waters@hhs.gov>; Shuy, Bryan (OS/ASPR/IO) <Bryan.Shuy@hhs.gov>; Hayes, Jonathan (OS/ASPR/IO) <Jonathan.Hayes@hhs.gov>; Sellman, Suzanne (OS/ASPR/OEA) <Suzanne.Sellman@hhs.gov>; Bialek, Stephanie M. (ASPR/SNS) <ilq8@cdc.gov>
Cc: McKeogh, Katherine (OS/ASPA) <Katherine.McKeogh@hhs.gov>; Murphy, Ryan (OS/ASPA) <Ryan.Murphy1@hhs.gov>; Stimson, Brian (HHS/OGC) <Brian.Stimson@hhs.gov>; Barry, Daniel J (HHS/OGC) <daniel.barry@hhs.gov>
Subject: RE: For ASPR Review--more info: price of remdesivir

Ok. Can ASPR please draft a reactive statement for NY Times?

Need this group to clear it. Thank you.

Caitlin B. Oakley
Deputy Assistant Secretary, National Spokesperson
Office of the Assistant Secretary for Public Affairs
U.S. Department of Health and Human Services
caitlin.oakley@hhs.gov

From: Kane, Elleen (OS/ASPR/OEA) <Elleen.Kane@hhs.gov>
Sent: Tuesday, April 7, 2020 6:31 PM
To: Oakley, Caitlin B. (OS/ASPA) <Caitlin.Oakley@HHS.GOV>; Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Michael, Gretchen (OS/ASPR/OEA) <Gretchen.Michael@hhs.gov>; Waters, Cicely (OS/ASPR/OEA) <Cicely.Waters@hhs.gov>; Shuy, Bryan (OS/ASPR/IO) <Bryan.Shuy@hhs.gov>; Hayes, Jonathan (OS/ASPR/IO) <Jonathan.Hayes@hhs.gov>; Sellman, Suzanne (OS/ASPR/OEA) <Suzanne.Sellman@hhs.gov>; Bialek, Stephanie M. (ASPR/SNS) <ilq8@cdc.gov>
Cc: McKeogh, Katherine (OS/ASPA) <Katherine.McKeogh@hhs.gov>; Murphy, Ryan (OS/ASPA) <Ryan.Murphy1@hhs.gov>; Stimson, Brian (HHS/OGC) <Brian.Stimson@hhs.gov>; Barry, Daniel J (HHS/OGC) <daniel.barry@hhs.gov>
Subject: RE: For ASPR Review--more info: price of remdesivir

No.

From: Oakley, Caitlin B. (OS/ASPA) <Caitlin.Oakley@HHS.GOV>
Sent: Tuesday, April 7, 2020 6:30 PM
To: Kane, Elleen (OS/ASPR/OEA) <Elleen.Kane@hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Michael, Gretchen (OS/ASPR/OEA) <Gretchen.Michael@hhs.gov>; Waters, Cicely (OS/ASPR/OEA) <Cicely.Waters@hhs.gov>; Shuy, Bryan (OS/ASPR/IO) <Bryan.Shuy@hhs.gov>; Hayes, Jonathan (OS/ASPR/IO) <Jonathan.Hayes@hhs.gov>; Sellman, Suzanne (OS/ASPR/OEA) <Suzanne.Sellman@hhs.gov>; Bialek, Stephanie M. (ASPR/SNS) <ilq8@cdc.gov>
Cc: McKeogh, Katherine (OS/ASPA) <Katherine.McKeogh@hhs.gov>; Murphy, Ryan (OS/ASPA) <Ryan.Murphy1@hhs.gov>; Stimson, Brian (HHS/OGC) <Brian.Stimson@hhs.gov>; Barry, Daniel J

(HHS/OGC) <daniel.barry@hhs.gov>
Subject: RE: For ASPR Review--more info: price of remdesivir

Did they receive donations?

From: Kane, Elleen (OS/ASPR/OEA) <Elleen.Kane@hhs.gov>
Sent: Tuesday, April 7, 2020 6:30 PM
To: Oakley, Caitlin B. (OS/ASPA) <Caitlin.Oakley@HHS.GOV>; Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Michael, Gretchen (OS/ASPR/OEA) <Gretchen.Michael@hhs.gov>; Waters, Cicely (OS/ASPR/OEA) <Cicely.Waters@hhs.gov>; Shuy, Bryan (OS/ASPR/IO) <Bryan.Shuy@hhs.gov>; Hayes, Jonathan (OS/ASPR/IO) <Jonathan.Hayes@hhs.gov>; Sellman, Suzanne (OS/ASPR/OEA) <Suzanne.Sellman@hhs.gov>; Bialek, Stephanie M. (ASPR/SNS) <ilq8@cdc.gov>
Cc: McKeogh, Katherine (OS/ASPA) <Katherine.McKeogh@hhs.gov>; Murphy, Ryan (OS/ASPA) <Ryan.Murphy1@hhs.gov>; Stimson, Brian (HHS/OGC) <Brian.Stimson@hhs.gov>; Barry, Daniel J (HHS/OGC) <daniel.barry@hhs.gov>
Subject: RE: For ASPR Review--more info: price of remdesivir

Neither the SNS nor BARDA has purchased remdesivir from Gilead.

From: Oakley, Caitlin B. (OS/ASPA) <Caitlin.Oakley@HHS.GOV>
Sent: Tuesday, April 7, 2020 6:26 PM
To: Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Michael, Gretchen (OS/ASPR/OEA) <Gretchen.Michael@hhs.gov>; Kane, Elleen (OS/ASPR/OEA) <Elleen.Kane@hhs.gov>; Waters, Cicely (OS/ASPR/OEA) <Cicely.Waters@hhs.gov>; Shuy, Bryan (OS/ASPR/IO) <Bryan.Shuy@hhs.gov>; Hayes, Jonathan (OS/ASPR/IO) <Jonathan.Hayes@hhs.gov>; Sellman, Suzanne (OS/ASPR/OEA) <Suzanne.Sellman@hhs.gov>; Bialek, Stephanie M. (ASPR/SNS) <ilq8@cdc.gov>
Cc: McKeogh, Katherine (OS/ASPA) <Katherine.McKeogh@hhs.gov>; Murphy, Ryan (OS/ASPA) <Ryan.Murphy1@hhs.gov>; Stimson, Brian (HHS/OGC) <Brian.Stimson@hhs.gov>; Barry, Daniel J (HHS/OGC) <daniel.barry@hhs.gov>
Subject: For ASPR Review--more info: price of remdesivir

Team ASPR—See below. More info from the reporter…

Any guidance on what happened with this?

Happy to chat on this. I'm at (b)(6)

Thanks.

DRAFT PRE-DECISIONAL DELIBERATIVE

From: Thomas, Katie <katie.thomas@nytimes.com>
Sent: Tuesday, April 7, 2020 6:03 PM
To: Oakley, Caitlin B. (OS/ASPA) <Caitlin.Oakley@HHS.GOV>
Subject: Re: Deadline q: price of remdesivir

Hi,

Gilead gave me a response, which unfortunately only confuses matters a bit more. Wondering if you can tell me what the story is with regards to procuring remdesivir doses, whether they were actually acquired, etc? And I have until tomorrow now as I try to sort this out.

This is what they told me:

It appears as if two distinct discussions around procuring remdesivir may have been conflated. In February and March 2020, Gilead and HHS discussed making certain amounts of our very limited supply available to HHS for use by the government for various purposes, including supplying military needs. HHS's desire was to purchase quantities of between 2,000 and 7,500 patient courses. Instead of charging the government for these amounts, Gilead committed to donating them. At no time has Gilead sold remdesivir to the government. Under the remdesivir clinical supply agreement entered into several years ago during the Ebola breakout, the government had the ability to purchase remdesivir for use to treat Ebola outside of clinical trials. It did not do so. Gilead has had no discussion with the government about remuneration to Gilead for supplying remdesivir to treat patients infected with COVID-19.

By the way, I noticed that Navarro has mentioned this price point and doses another time, in late February:
https://protect2.fireeye.com/url?k=e814ffe8-b440e694-e814ced7-0cc47adc5fa2-776f6a4db7b07790&u=https://protect2.fireeye.com/url?k=3b195864-674d4118-3b19695b-0cc47adc5fa2-bac7302cd6980ca9&u=https://www.hughhewitt.com/white-house-trade-advisor-peter-navarro-on-the-admins-coronavirus-response/

"If somebody gets Corona, and they're moderately to severely infected, there's, first of all, there's a drug called Remdesivir. It's made by Gilead. What we've done there are a number of things. First of all, we've secured the 4,500 doses that they have. In addition, as a cost of almost $200 million, we're moving to secure the other 90,000 doses they have in involved material."

(if you do the math there, it's about $2,200 a dose)

Katie Thomas
Staff Writer, New York Times
(b)(6)
Twitter: @katie_thomas

On Tue, Apr 7, 2020 at 3:56 PM Thomas, Katie <katie.thomas@nytimes.com>wrote:
thanks!

Katie Thomas
Staff Writer, New York Times
(b)(6)
Twitter: @katie_thomas

On Tue, Apr 7, 2020 at 3:55 PM Oakley, Caitlin B. (OS/ASPA) <Caitlin.Oakley@hhs.gov>wrote:
Hi Katie—Checking on this!

Caitlin B. Oakley
Deputy Assistant Secretary, National Spokesperson
Office of the Assistant Secretary for Public Affairs
U.S. Department of Health and Human Services
caitlin.oakley@hhs.gov

From: Thomas, Katie <katie.thomas@nytimes.com>
Sent: Tuesday, April 7, 2020 4:46 PM
To: Oakley, Caitlin B. (OS/ASPA) <Caitlin.Oakley@HHS.GOV>
Subject: Deadline q: price of remdesivir

Hi Caitlin,

I'm working on a deadline story (ASAP) about the price of remdesivir

In the leaked memo from Navarro:
https://www.axios.com/exclusive-navarro-deaths-coronavirus-memos-january-da3f08fb-dce1-4f69-89b5-ea048f8382a9.html

It says that HHS paid Gilead $2,200 per dose for 4,500 doses of remdesivir, and that it was imperative that they secure 90,000 more doses for a total cost of $198 million

Wondering if HHS can comment on what it has paid for remdesivir, and if that additional order for 90,000 additional doses was placed. If not, what is the total amount of remdesivir that has been ordered and at what price?

I'm sorry for the quick turnaround but just got the story and we are trying to put it out quickly. If my timing changes I'll try to give you as much of a heads up as I can.

Katie

Katie Thomas
Staff Writer, New York Times
(b)(6)
Twitter: @katie_thomas

Sender:	Disbrow, Gary (OS/ASPR/BARDA) </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0FD5845DEFDA4DC0BB45F8FAC629CF09-DISBROW, GA>
Recipient:	Billet, Courtney (NIH/NIAID) [E] <billetc@niaid.nih.gov>; Kane, Elleen (OS/ASPR/OEA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=user25dbd6c7 <Elleen.Kane@hhs.gov>; Oakley, Caitlin B. (OS/ASPA) /o=ExchangeLabs/ou=Exchange Administrative Group

	(FYDIBOHF23SPDLT)/cn=Recipients/cn=e5ee4c35534c4af9bdac46789c034790-Oakley, Cai <Caitlin.Oakley@HHS.GOV>; Michael, Gretchen (OS/ASPR/OEA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0632b4526d6447b5af26552afde05c33-Michael, Gr <Gretchen.Michael@hhs.gov>; Waters, Cicely (OS/ASPR/OEA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=00e638c4ddf64006bcc009e8032dd700-Waters, Cic <Cicely.Waters@hhs.gov>; Shuy, Bryan (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fdeb5ca04b6b4ed19fec2209b5f571e7-Shuy, Bryan <Bryan.Shuy@hhs.gov>; Hayes, Jonathan (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8cdfb7232de4428794f2901218bc1360-Hayes, Jona <Jonathan.Hayes@hhs.gov>; Sellman, Suzanne (OS/ASPR/OEA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5bfe40dc98b54fc7989a00075a9c8ab7-Sellman, Su <Suzanne.Sellman@hhs.gov>; Bialek, Stephanie M. (ASPR/SNS) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a7d77e22d4bd40b6a0b205df4d8a2f58-stephanie.b <ilq8@cdc.gov>; Routh, Jennifer (NIH/NIAID) [E] /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2dd951edf9be461f93276b338e2b0b08-jennifer.ro <jennifer.routh@nih.gov>; Stover, Kathy (NIH/NIAID) [E] /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d2241aa54aa341ceb7ff993d88eba4df-kathy.stove <kathy.stover@nih.gov>; McKeogh, Katherine (OS/ASPA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c652f2c415b44dff8369dd7f4596f030-McKeogh, Ka <Katherine.McKeogh@hhs.gov>; Murphy, Ryan (OS/ASPA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=314e69c69a844b47bdd9f74bc60a8d44-Murphy, Rya <Ryan.Murphy1@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>
Sent Date:	2020/04/07 18:44:08
Delivered Date:	2020/04/07 18:44:00

From:	Disbrow, Gary (OS/ASPR/BARDA) </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0FD5845DEFDA4DC0BB45F8FAC629CF09-DISBROW, GA>
To:	Kadlec, Robert (OS/ASPR/IO) (Robert.Kadlec@hhs.gov) <Robert.Kadlec@hhs.gov>; Shuy, Bryan (OS/ASPR/IO) (Bryan.Shuy@hhs.gov) <Bryan.Shuy@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:	FW: FLASH CLEARANCE: COVID-19 -- Remdesivir Options Paper
Date:	2020/03/07 21:02:00
Priority:	Normal
Type:	Note

Bob,

I have no comments. I saw your clearance and did not know I was supposed to respond.

My apologies.

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

From: Kadlec, Robert (OS/ASPR/IO) <Robert.Kadlec@hhs.gov>
Sent: Saturday, March 7, 2020 7:42 PM
To: Franco, Celinda (OS/IOS) <Celinda.Franco@hhs.gov>; Shuy, Bryan (OS/ASPR/IO) <Bryan.Shuy@hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Hahn, Stephen <SH1@fda.hhs.gov>; Lenihan, Keagan (FDA/OC) <Keagan.Lenihan@fda.hhs.gov>; Charrow, Robert (HHS/OGC) <Robert.Charrow@hhs.gov>; Amin, Stacy (FDA/OC) <Stacy.Amin@fda.hhs.gov>; Chang, William (HHS/OGC) <William.Chang@hhs.gov>; Stannard, Paula (HHS/IOS) <Paula.Stannard@hhs.gov>
Cc: Mango, Paul (HHS/IOS) <Paul.Mango@hhs.gov>; Agnew, Ann (HHS/IOS) <Ann.Agnew@hhs.gov>; Robinson, Wilma (HHS/IOS) <Wilma.Robinson@hhs.gov>; Horska, Katerina (HHS/IOS) <Katerina.Horska@hhs.gov>; Hawkins, Jamar (HHS/OS) <jamar.hawkins@hhs.gov>; Johnson, Ciara (OS/IOS) <Ciara.Johnson@hhs.gov>; Stimson, Brian (HHS/OGC) <Brian.Stimson@hhs.gov>
Subject: RE: FLASH CLEARANCE: COVID-19 -- Remdesivir Options Paper

KADLEC ASPR CLEARS

From: Franco, Celinda (OS/IOS) <Celinda.Franco@hhs.gov>
Sent: Saturday, March 7, 2020 7:01 PM
To: Kadlec, Robert (OS/ASPR/IO) <Robert.Kadlec@hhs.gov>; Shuy, Bryan (OS/ASPR/IO) <Bryan.Shuy@hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Hahn, Stephen <SH1@fda.hhs.gov>; Lenihan, Keagan (FDA/OC) <Keagan.Lenihan@fda.hhs.gov>; Charrow, Robert (HHS/OGC) <Robert.Charrow@hhs.gov>; Amin, Stacy (FDA/OC) <Stacy.Amin@fda.hhs.gov>; Chang, William (HHS/OGC) <William.Chang@hhs.gov>; Stannard, Paula (HHS/IOS) <Paula.Stannard@hhs.gov>
Cc: Mango, Paul (HHS/IOS) <Paul.Mango@hhs.gov>; Agnew, Ann (HHS/IOS) <Ann.Agnew@hhs.gov>; Robinson, Wilma (HHS/IOS) <Wilma.Robinson@hhs.gov>; Horska, Katerina (HHS/IOS) <Katerina.Horska@hhs.gov>; Hawkins, Jamar (HHS/OS) <jamar.hawkins@hhs.gov>; Johnson, Ciara (OS/IOS) <Ciara.Johnson@hhs.gov>; Stimson, Brian (HHS/OGC) <Brian.Stimson@hhs.gov>
Subject: FLASH CLEARANCE: COVID-19 -- Remdesivir Options Paper
Importance: High

All,

Please review and clear this document by 9:00 pm and submit comments to Celinda Franco.

Thank you,
Celinda
202.400.1924

From: Johnson, Ciara (OS/IOS) <Ciara.Johnson@hhs.gov>
Sent: Saturday, March 7, 2020 6:52 PM
To: Franco, Celinda (OS/IOS) <Celinda.Franco@hhs.gov>
Subject: FW: COVID-19 -- Remdesivir Options Paper -- FLASH CLEARANCE
Importance: High

FYI

Response to the Coronavirus Led by HHS from Day 1

(b)(5)

(b)(5)

Page 032

Withheld pursuant to exemption

(b)(5)

of the Freedom of Information Act

From:	Disbrow, Gary (OS/ASPR/BARDA) </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0FD5845DEFDA4DC0BB45F8FAC629CF09-DISBROW, GA>
To:	Blatner, Gretta (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=623cb123c2324236b1db6fb9153e0bbf-Blatner, Gr <Gretta.Blatner@hhs.gov>; Oxner, Julie (OS/ASPR/OEA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f96241c6a5f8401a9a218c259f2e614a-Oxner, Juli <Julie.Oxner@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>; Disbrow, Gary (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0fd5845defda4dc0bb45f8fac629cf09-Disbrow, Ga <Gary.Disbrow@hhs.gov>; Homer, Mary (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a240b043664f400699e586236781dfec-Homer, Mary <Mary.Homer@hhs.gov>
Subject:	RE: Slides for Tuesday
Date:	2020/05/05 08:56:13
Priority:	Normal
Type:	Note

Gretta,

On the slides for the discussion with HELP Staffers, we have slide 23 that shows therapeutic and vaccine efforts. I though convalescent plasma was being evaluated in an expanded access program?

Mary, are ARC and BCA not collecting for clinical trials? Or they are not sponsoring?

Also, PPD expanded access protocol, for HCQ is in people, should be blue. Same thing for ALCHEM ongoing clinical trial.

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.

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 far direction

---

From: Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>
Sent: Monday, May 4, 2020 2:03 PM
To: Oxner, Julie (OS/ASPR/OEA) <Julie.Oxner@hhs.gov>
Cc: Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>
Subject: Slides for Tuesday

Hi Julie,

Here are the slides that Gary will use on Tuesday with the HELP Committee Staff. These are the same slides we have used before but with landscape and submissions data updated.

Please let us know if you have any concerns. << File: 20200504 BARDA COVID Strategy-Portfolio Congressional Briefs.pptx >>

Thanks
g

Gretta Blatner, MS MPH
Special Assistant to the Director, BARDA
Office Telephone: 202-401-9386
Cell: (b)(6)

Sender:	Disbrow, Gary (OS/ASPR/BARDA) </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0FD5845DEFDA4DC0BB45F8FAC629CF09-DISBROW, GA>
Recipient:	Blatner, Gretta (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=623cb123c2324236b1db6fb9153e0bbf-Blatner, Gr <Gretta.Blatner@hhs.gov>; Oxner, Julie (OS/ASPR/OEA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f96241c6a5f8401a9a218c259f2e614a-Oxner, Juli <Julie.Oxner@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>; Disbrow, Gary (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0fd5845defda4dc0bb45f8fac629cf09-Disbrow, Ga <Gary.Disbrow@hhs.gov>; Homer, Mary (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a240b043664f400699e586236781dfec-Homer, Mary <Mary.Homer@hhs.gov>
Sent Date:	2020/05/05 08:56:12
Delivered Date:	2020/05/05 08:56:13

COVID-19 MEDICAL COUNTERMEASURE UPDATE

May 5, 2020

Presented to HELP Committee Staff

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.

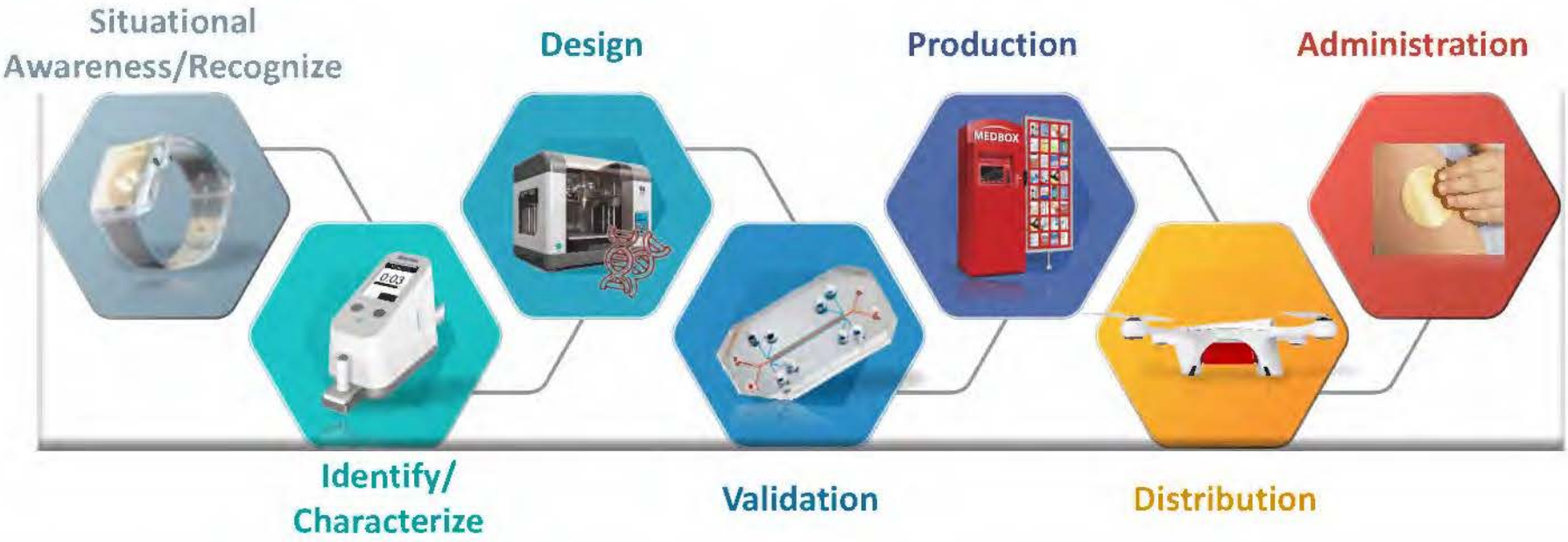
Our Industry Partners

Our Government Partners

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

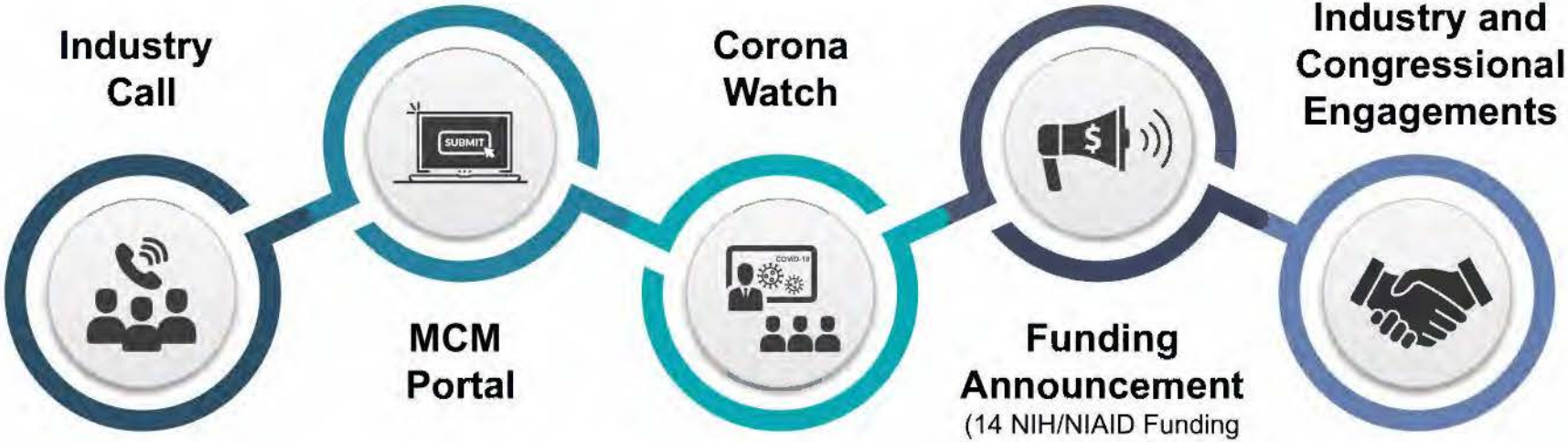
3rd Coronavirus Outbreak

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

COVID-19 MEDICAL COUNTERMEASURE DEVELOPMENT STRATEGY

ACCELERATE DEVELOPMENT

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

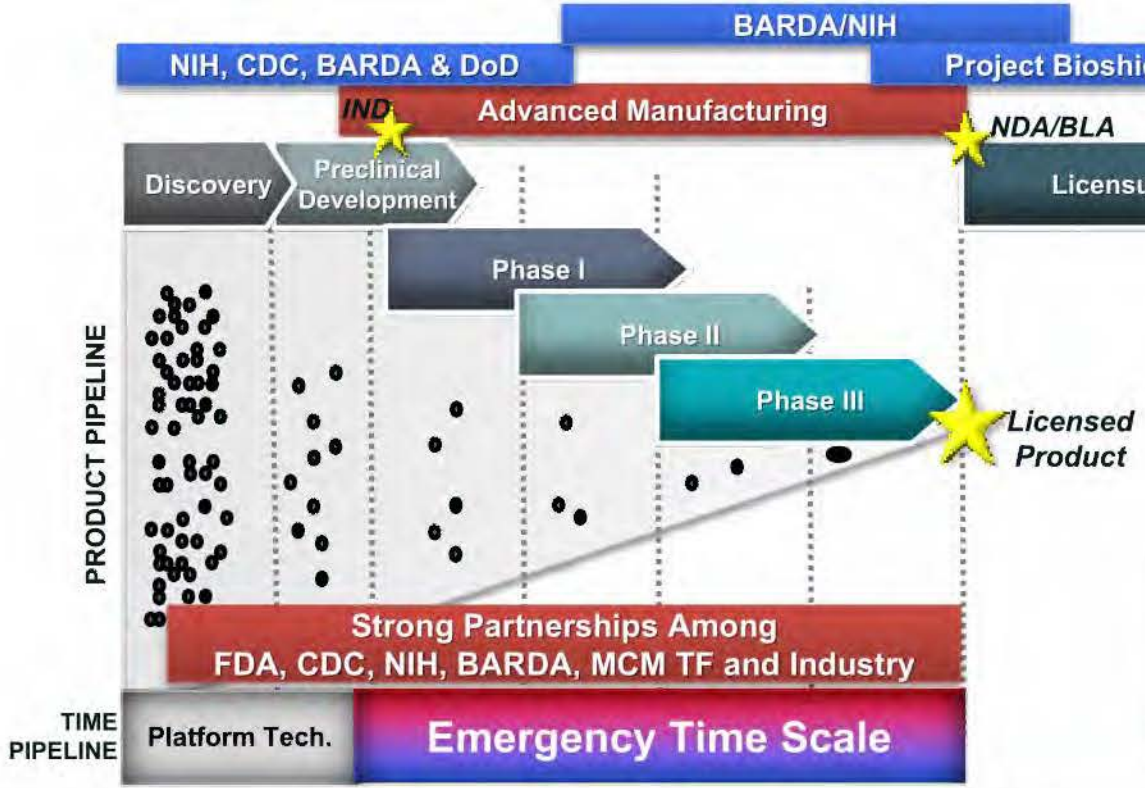
MITIGAGE RISK

- Multiple technologies
- Multiple targets
- Redundancy

DOMESTIC MANUFACTURING

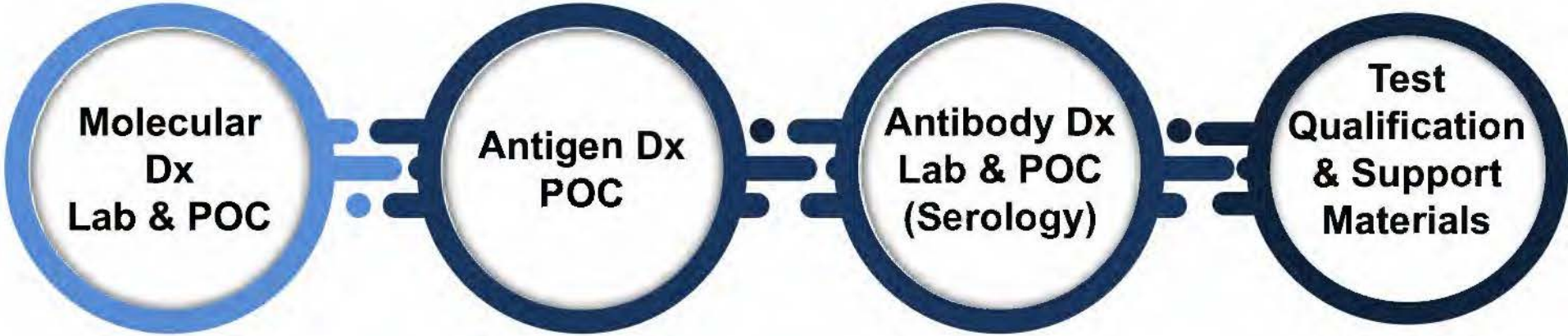
- Scale Up & Scale Out
- Raw materials and supply chains
- Leverage existing facilities

Emergency Vaccine & Drug Development



All of Government and Private Sector Approach

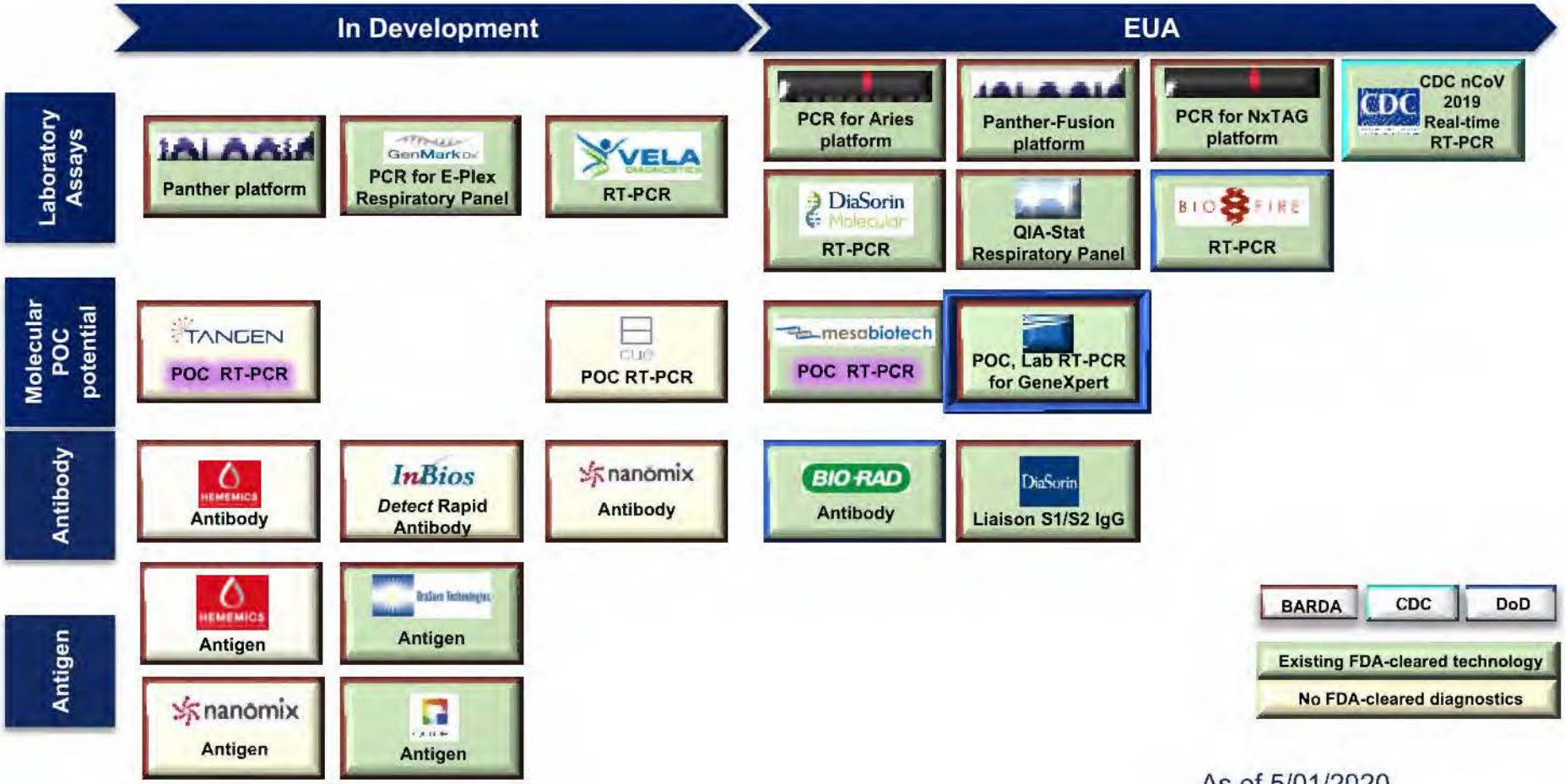
Diagnostics Development: Four-Pronged Approach



Leverage existing Laboratory Infrastructure & Equipment
Leverage Existing & Complete In-Development POC Equipment

04/02/20

USG-Supported SARS-CoV-2 Diagnostic Tests



As of 5/01/2020

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

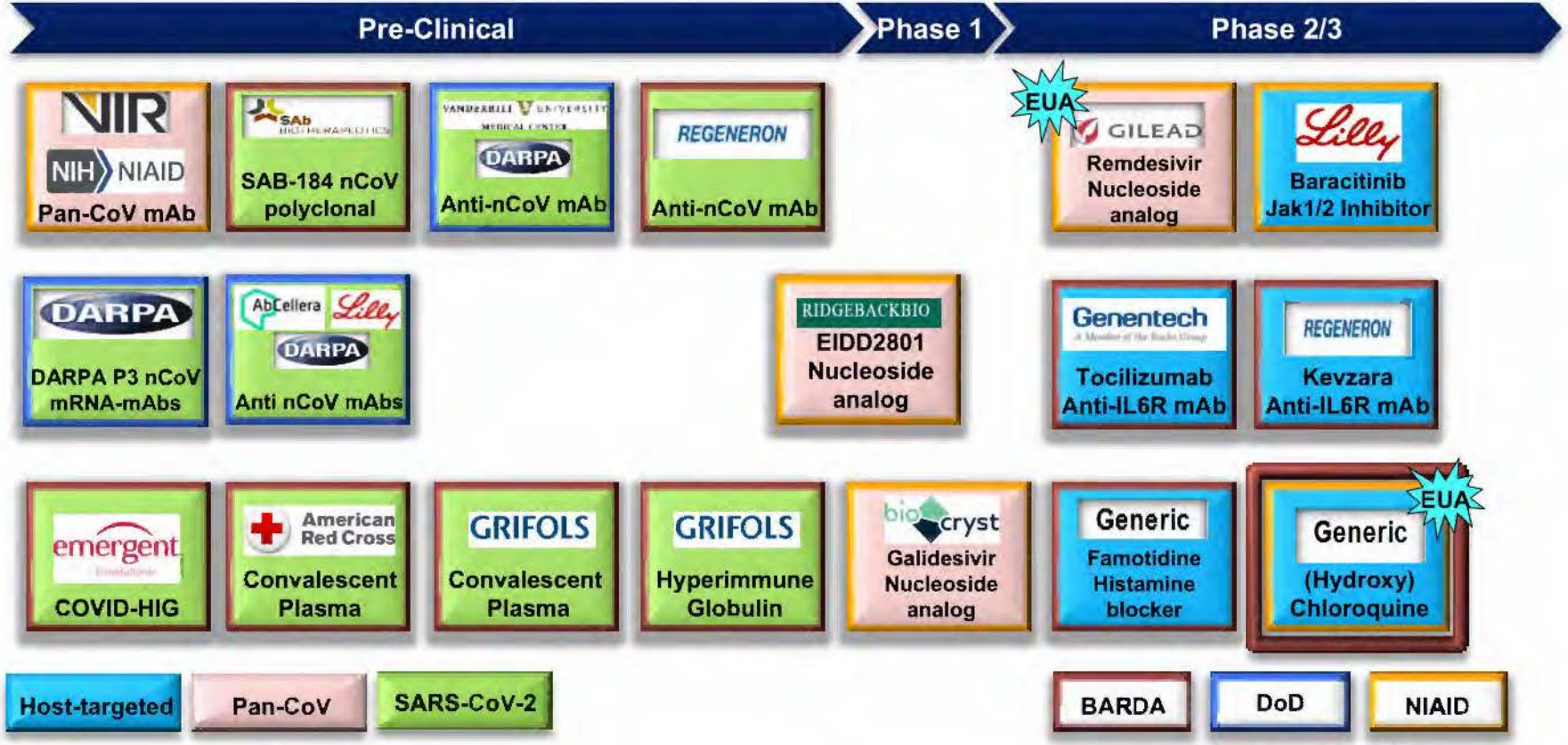
Thousands of compounds currently being screened-low cost/high impact
Many candidates identified and undergoing clinical evaluation

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

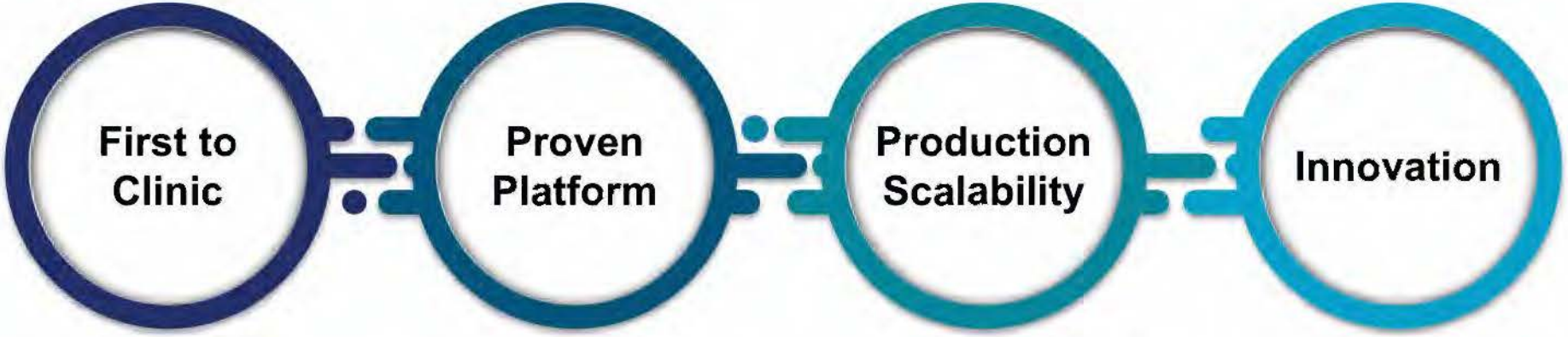
BARDA seeking to leverage existing infrastructure for rapid clinical trial initiation

USG-Supported SARS-CoV-2 Therapeutics



As of 5/01/2020

Vaccine Development



e.g., mRNA based vaccines that allow rapid early development

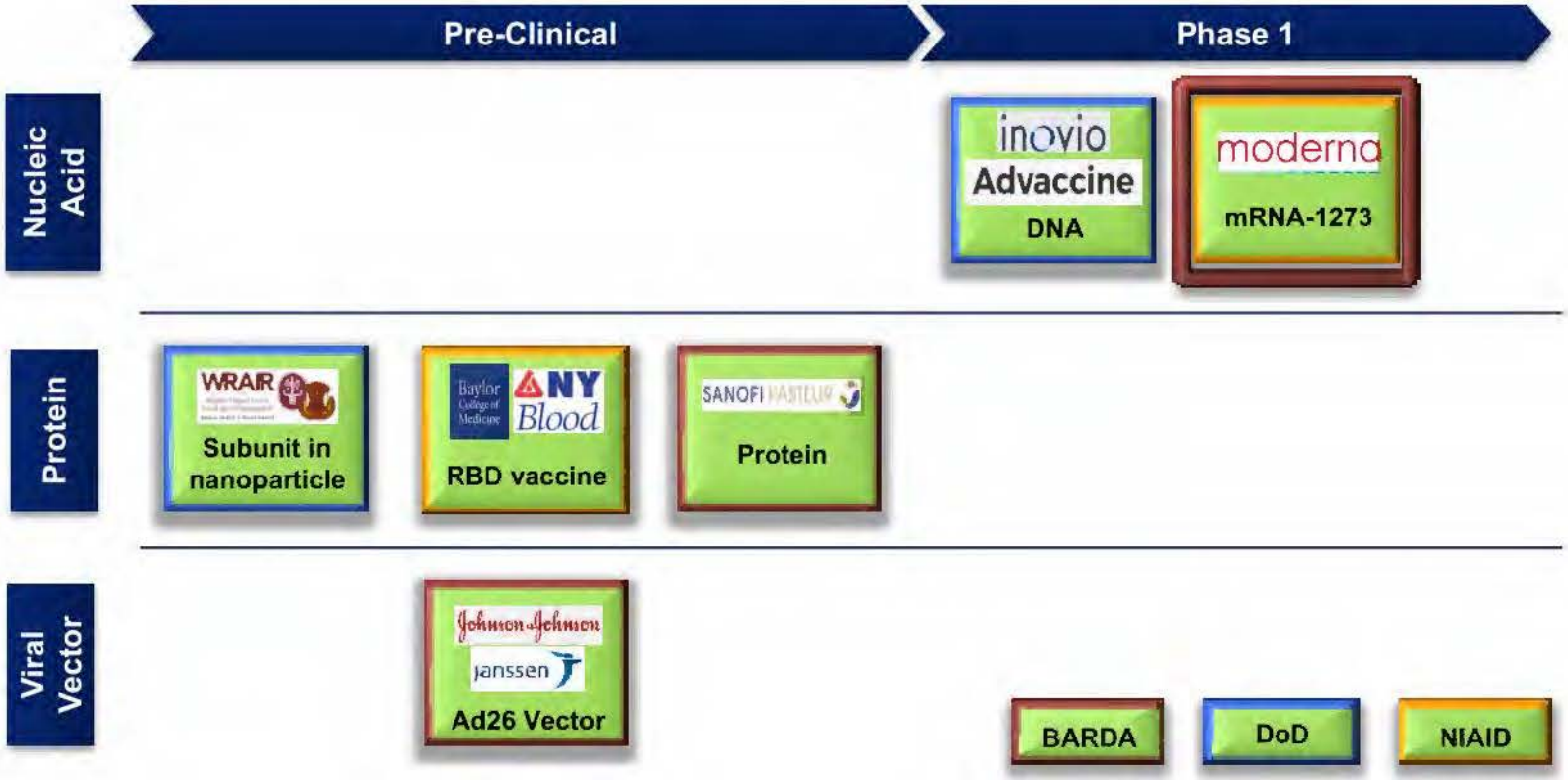
e.g., viral vectors with demonstrated safety and efficacy

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



As of 5/01/2020

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

Portfolio

Therapeutics

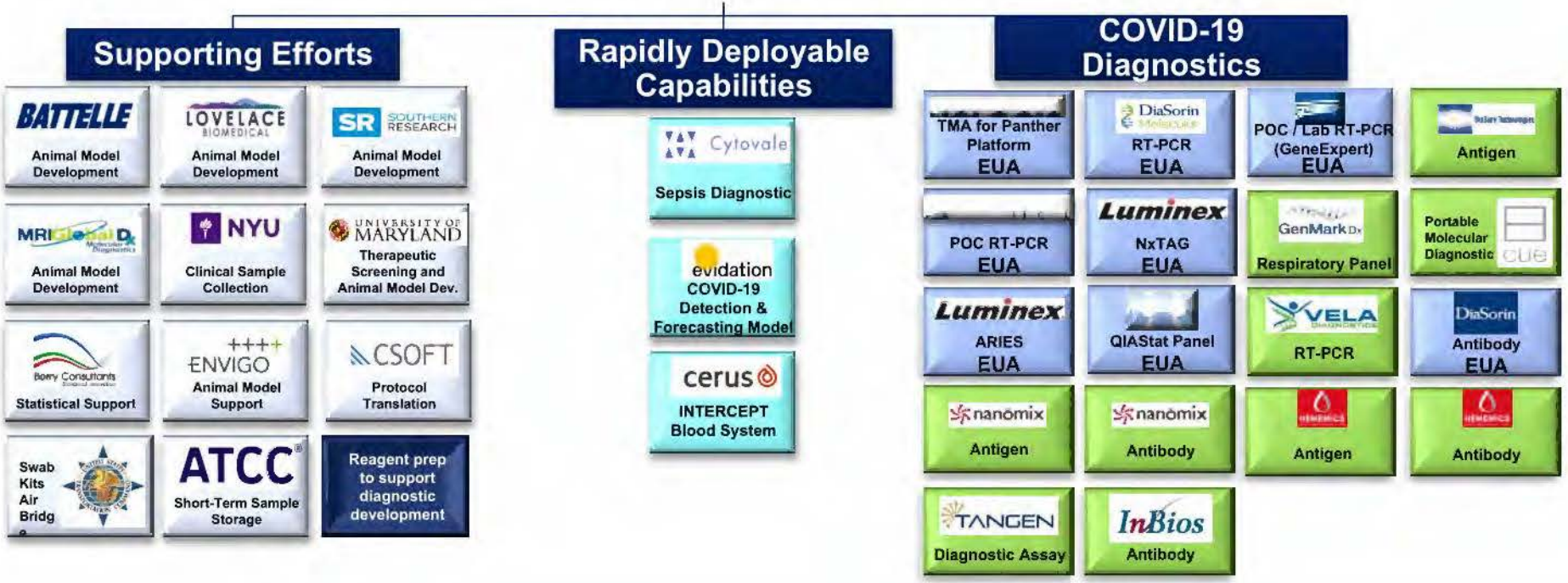
- Anti-viral Library Screening (Johnson & Johnson / Janssen)
- Anti-SARS-CoV-2 mAb (Regeneron)
- Polyclonal Ab (SAb Biotherapeutics)
- Hyperimmune Globulin, Convalescent Plasma (Grifols)
- Anti-IL6R mAb (Kevzara®) (Regeneron)
- Anti-IL6R mAb (Actemra®) (Roche / Genentech)
- Hyperimmune Globulin (emergent)
- Convalescent Plasma Collection (American Red Cross)
- Convalescent Serum Collection (Cantor BioConnect)
- Convalescent Serum Collection (ICON)
- Expanded Access Treatment Protocol - HCQ & CQ (PPD)
- HCQ Clinical Trial (Alchem)
- Whole Blood Samples (Veterans Medical Research Foundation)
- Convalescent Plasma Collection Systems (DCA Blood Centers of America)

Vaccines

- Ad26 Vector (Johnson & Johnson / Janssen)
- Recombinant Protein (Sanofi Pasteur)
- mRNA-1273 (moderna)

= *In Clinical Trials*

BARDA Medical Countermeasures Response Portfolio



Department of Health and Human Services

HHS and our federal partners are working together with state, local, tribal and territorial governments, public health officials, health care providers, researchers, private sector organizations and the public to execute a whole-of-America response.

(b)(5)

(b)(5)

Page 062

Withheld pursuant to exemption

(b)(5)

of the Freedom of Information Act

Page 063

Withheld pursuant to exemption

(b)(5)

of the Freedom of Information Act

From:	Disbrow, Gary (OS/ASPR/BARDA) </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0FD5845DEFDA4DC0BB45F8FAC629CF09-DISBROW, GA>
To:	Marston, Hilary (NIH/NIAID) [E] (hilary.marston@nih.gov) <hilary.marston@nih.gov>; Beigel, John (NIH) [E] /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=45af28983cfa4300b0217b591151861c-john.beigel <jbeigel@niaid.nih.gov>
Subject:	FW: Avaialbility of REMDESIVIR in San Fran
Date:	2020/03/08 11:51:00
Priority:	Normal
Type:	Note

Forwarding to both so you have visibility.

Thanks for the response, John. Much appreciated.

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

From: Anderson, Michael <Michael.Anderson@ucsf.edu>
Sent: Sunday, March 8, 2020 11:35 AM
To: Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Kadlec, Robert (OS/ASPR/IO) <Robert.Kadlec@hhs.gov>
Cc: Bright, Rick (OS/ASPR/BARDA) <Rick.Bright@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) <Robert.Johnson@hhs.gov>; Shuy, Bryan (OS/ASPR/IO) <Bryan.Shuy@hhs.gov>; Merdad Parsey

<merdad.parsey@gilead.com>; Walker, Robert (OS/ASPR/BARDA) <Robert.Walker@hhs.gov>; Mair, Michael (FDA/OC) <Michael.Mair@fda.hhs.gov>
Subject: Re: Avaialbility of REMDESIVIR in San Fran

Will do

Dr Parsey...can I call you?

==========

Michael Anderson, MD, MBA, FAAP, FCCM, FAARC
President, UCSF Benioff Children's Hospitals
Professor and Vice Chair for Children's Health, UCSF
Cell: (b)(6)
O: 415-476-6744

Assistant: joseph.genser@ucsf.edu OR (510) 428-3051

From: "Disbrow, Gary (OS/ASPR/BARDA)" <Gary.Disbrow@hhs.gov>
Date: Sunday, March 8, 2020 at 8:21 AM
To: Michael R Anderson <Michael.Anderson@ucsf.edu>, "Kadlec, Robert (OS/ASPR/IO)" <Robert.Kadlec@hhs.gov>
Cc: "Bright, Rick (OS/ASPR/BARDA)" <Rick.Bright@hhs.gov>, "Johnson, Robert (OS/ASPR/BARDA)" <Robert.Johnson@hhs.gov>, "Shuy, Bryan (OS/ASPR/IO)" <Bryan.Shuy@hhs.gov>, Merdad Parsey <merdad.parsey@gilead.com>, "Walker, Robert (OS/ASPR/BARDA)" <Robert.Walker@hhs.gov>, "Mair, Michael (FDA/OC)" <Michael.Mair@fda.hhs.gov>
Subject: RE: Avaialbility of REMDESIVIR in San Fran

Michael,

RCT is for adults only. Would need to discuss with Gilead if they have any data from treatment of pediatric patients with Ebola to potentially identify a pediatric dose of other than weight based.

Please call Dr. Parsey to obtain additional information on potential use of drug in pediatric patients.

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

From: Anderson, Michael <Michael.Anderson@ucsf.edu>
Sent: Sunday, March 8, 2020 10:52 AM
To: Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Kadlec, Robert (OS/ASPR/IO) <Robert.Kadlec@hhs.gov>
Cc: Bright, Rick (OS/ASPR/BARDA) <Rick.Bright@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) <Robert.Johnson@hhs.gov>; Shuy, Bryan (OS/ASPR/IO) <Bryan.Shuy@hhs.gov>; Merdad Parsey <merdad.parsey@gilead.com>; Walker, Robert (OS/ASPR/BARDA) <Robert.Walker@hhs.gov>; Mair, Michael (FDA/OC) <Michael.Mair@fda.hhs.gov>; Anderson, Michael <Michael.Anderson@ucsf.edu>
Subject: Re: Avaialbility of REMDESIVIR in San Fran

Thanks team.

My plans for the next 24 hrs

1) Make sure my onc team is in the loop
2) Our command center is open and awaiting more data on the 9 make-a-wish children. We have two children's campuses in SF and Oakland. Likewise other peds beds exist in the Bay...
3) Dr Parsey—please feel free to contact me w questions. Once we have a more clear picture on the clinical issues, will decide if enrollment is appropriate
4) Awaiting other input/counsel

Mike
Cell: (b)(6)

==========

Michael Anderson, MD, MBA, FAAP, FCCM, FAARC
President, UCSF Benioff Children's Hospitals
Professor and Vice Chair for Children's Health, UCSF
Cell: (b)(6)
O: 415-476-6744

Assistant: joseph.genser@ucsf.edu OR (510) 428-3051

From: "Disbrow, Gary (OS/ASPR/BARDA)" <Gary.Disbrow@hhs.gov>
Date: Sunday, March 8, 2020 at 7:42 AM
To: Michael R Anderson <Michael.Anderson@ucsf.edu>, "Kadlec, Robert (OS/ASPR/IO)" <Robert.Kadlec@hhs.gov>
Cc: "Bright, Rick (OS/ASPR/BARDA)" <Rick.Bright@hhs.gov>, "Johnson, Robert (OS/ASPR/BARDA)" <Robert.Johnson@hhs.gov>, "Shuy, Bryan (OS/ASPR/IO)" <Bryan.Shuy@hhs.gov>, Merdad Parsey <merdad.parsey@gilead.com>, "Walker, Robert (OS/ASPR/BARDA)" <Robert.Walker@hhs.gov>, "Mair, Michael (FDA/OC)" <Michael.Mair@fda.hhs.gov>
Subject: RE: Avaialbility of REMDESIVIR in San Fran

Michael,

Thanks for the quick call and discussion. Providing information for Chief Medical Officer for Gilead, Dr. Merdad Parsey. I will also check with NIAID to determine if RCT is established in Oakland, if not and if it takes too much time to expand, a treating clinician could request product under an investigator initiated emergency IND.

Merdad Parsey, MD PhD
Chief Medical Officer
Gilead Sciences, Inc.
(M (b)(6)

Also, the company is allowed to preposition drug in advance, if needed.

Providing an FDA contact who could assist if there are questions about eIND paperwork. Michael Mair in the email above could help connect to the review division.

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

From: Anderson, Michael <Michael.Anderson@ucsf.edu>
Sent: Sunday, March 8, 2020 10:18 AM
To: Kadlec, Robert (OS/ASPR/IO) <Robert.Kadlec@hhs.gov>
Cc: Bright, Rick (OS/ASPR/BARDA) <Rick.Bright@hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) <Robert.Johnson@hhs.gov>; Shuy, Bryan (OS/ASPR/IO) <Bryan.Shuy@hhs.gov>
Subject: Re: Avaialbility of REMDESIVIR in San Fran

Ready to help any way we can

Michael R Anderson MD MBA FAAP FCCM
President, UCSF Benioff Children's Hospitals
Professor of Pediatrics
Cell (b)(6)

Sent from my iPhone

On Mar 8, 2020, at 7:17 AM, Kadlec, Robert (OS/ASPR/IO) <Robert.Kadlec@hhs.gov>wrote:

BARDA Team please note there are 9 high risk children (Make a Wish Foundation) with advanced stage cancer. Please request from GILEAD 10 courses for compassionate use to be available immediately. These children have high potential mortality rates if exposed/infected to this virus. Please

advise and keep me informed on any and all developments If you need a POC I have copied Mike Anderson at UCSF Peds hospital.

Sender:	Disbrow, Gary (OS/ASPR/BARDA) </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0FD5845DEFDA4DC0BB45F8FAC629CF09-DISBROW, GA>
Recipient:	Marston, Hilary (NIH/NIAID) [E] (hilary.marston@nih.gov) <hilary.marston@nih.gov>; Beigel, John (NIH) [E] /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=45af28983cfa4300b0217b591151861c-john.beigel <jbeigel@niaid.nih.gov>
Sent Date:	2020/03/08 11:51:04
Delivered Date:	2020/03/08 11:51:00

From:	Disbrow, Gary (OS/ASPR/BARDA) </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0FD5845DEFDA4DC0BB45F8FAC629CF09-DISBROW, GA>
To:	Kadlec, Robert (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a182eda693d040d3832bae6efcf7a255-Kadlec, Rob <Robert.Kadlec@hhs.gov>; Shuy, Bryan (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fdeb5ca04b6b4ed19fec2209b5f571e7-Shuy, Bryan <Bryan.Shuy@hhs.gov>; Stimson, Brian (HHS/OGC) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=338aa495176d4c92bb314f8f3f51d118-Stimson, Br <Brian.Stimson@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>
Subject:	RE: Call with OMB on Remdesivir
Date:	2020/03/11 14:26:00
Priority:	Normal
Type:	Note

I can be available for a call when needed.

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: [redacted]
Fax: 202-205-0873
email: Gary.Disbrow@HHS.gov

From: Kadlec, Robert (OS/ASPR/IO) <Robert.Kadlec@hhs.gov>
Sent: Wednesday, March 11, 2020 1:52 PM
To: Shuy, Bryan (OS/ASPR/IO) <Bryan.Shuy@hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA)

From:	Disbrow, Gary (OS/ASPR/BARDA) </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0FD5845DEFDA4DC0BB45F8FAC629CF09-DISBROW, GA>
To:	Mantoan, Patricia (HHS/OGC) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=user0ebe3257 <Patricia.Mantoan@HHS.GOV>
CC:	Sherman, Susan (HHS/OGC) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=user161a2a33 <Susan.Sherman@HHS.GOV>; Shuy, Bryan (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fdeb5ca04b6b4ed19fec2209b5f571e7-Shuy, Bryan <Bryan.Shuy@hhs.gov>; Kadlec, Robert (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a182eda693d040d3832bae6efcf7a255-Kadlec, Rob <Robert.Kadlec@hhs.gov>; Angelastro, Michael (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=583e910528e7473d9dcdfce9d1a80b83-Angelastro, <Michael.Angelastro@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0851e89240324306b78740a4a60745e2-Johnson, Ro <Robert.Johnson@hhs.gov>; Harper, Victor (OS/ASPR/ORM) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=user0bdee7e8 <Victor.Harper@hhs.gov>; Adams, Steven A. (ASPR/SNS) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f98462fe8d124743a437c7a80b3f60dd-Adams, Stev <saa1@cdc.gov>
Subject:	RE: IRPG: Review donation- Gilead- remdesivir
Date:	2020/04/29 15:21:09
Priority:	Normal
Type:	Note

Patricia,

Comments from BARDA based on conversation today. I am including SNS colleagues for review.

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.

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

---

From: Mantoan, Patricia (HHS/OGC) <Patricia.Mantoan@HHS.GOV>
Sent: Wednesday, April 29, 2020 11:49 AM
To: Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>
Cc: Sherman, Susan (HHS/OGC) <Susan.Sherman@HHS.GOV>; Shuy, Bryan (OS/ASPR/IO) <Bryan.Shuy@hhs.gov>; Kadlec, Robert (OS/ASPR/IO) <Robert.Kadlec@hhs.gov>; Angelastro, Michael (OS/ASPR/BARDA) <Michael.Angelastro@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) <Robert.Johnson@hhs.gov>
Subject: RE: IRPG: Review donation- Gilead- remdesivir

Gary: I need input from BARDA or SNS on certain provisions in the attached draft donation agreement with Gilead. In particular, I need to know if BARDA or SNS are comfortable with terms 1.2 and 1.3 as they are currently drafted in the agreement. I've copied them below for ease of reference:

(b)(5)

<< File: Gilead--Donation Agreement for remdesivir (Gilead draft 4.14.2020) HHS Response.DOCX >>

From: Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>
Sent: Wednesday, April 29, 2020 11:43 AM
To: Mantoan, Patricia (HHS/OGC) <Patricia.Mantoan@HHS.GOV>
Cc: Sherman, Susan (HHS/OGC) <Susan.Sherman@HHS.GOV>; Shuy, Bryan (OS/ASPR/IO) <Bryan.Shuy@hhs.gov>; Kadlec, Robert (OS/ASPR/IO) <Robert.Kadlec@hhs.gov>; Angelastro, Michael (OS/ASPR/BARDA) <Michael.Angelastro@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) <Robert.Johnson@hhs.gov>
Subject: RE: IRPG: Review donation- Gilead- remdesivir

Patricia,

Bob, please advise if other than below.

There is positive data from the clinical trials. Please work with OGC and ASPR IO to get the donation agreement signed. The updated number is 78K TC so please reach out to Gilead and verify that number. Please leave options in the document for the product to be distributed by Gilead OR accepted into the SNS.

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

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

---

From: Mantoan, Patricia (HHS/OGC) <Patricia.Mantoan@HHS.GOV>
Sent: Friday, April 17, 2020 2:57 PM
To: Chandrasekera, Ruvani (OS/ASPR/SPPR) <Ruvani.Chandrasekera@hhs.gov>; Albrecht, Mark (OS/ASPR/BARDA) <Mark.Albrecht@hhs.gov>; Ford, Kenya S. (CDC/OCOO/OGC) <kdf6@cdc.gov>; Godin, Jacquelyn (NIH/OD) [E] <jacquelyn.godin@nih.gov>; Sherman, Susan (HHS/OGC) <Susan.Sherman@HHS.GOV>; Ray Gorrie, Jennifer (HHS/OGC) <Jennifer.Ray-Gorrie@hhs.gov>; CDC IMS 2019 NCOV Response International Task Force <eocevent223@cdc.gov>; Kerr, Lawrence (HHS/OS/OGA) <Lawrence.Kerr@hhs.gov>; Sadove, Elizabeth (FDA/OC) <Elizabeth.Sadove@fda.hhs.gov>; Courtney, Brooke (FDA/OC) <Brooke.Courtney@fda.hhs.gov>; Mair, Michael (FDA/OC) <Michael.Mair@fda.hhs.gov>; AvilesMendoza, Guillermo (OS/OASH) <Guillermo.Aviles-Mendoza@hhs.gov>; Barry, Daniel J (HHS/OGC) <daniel.barry@hhs.gov>; Vinter, Serena (CDC/DDPHSIS/CGH/OD) <uvv3@cdc.gov>; Weir, Charles (OS/ASPR/IO) <Charles.Weir@hhs.gov>; Peerbolte, Stacy (OS/ASPR/EMMO) <Stacy.Peerbolte@hhs.gov>; Phung, Hai Lien (ASPR/SNS) <vvt3@cdc.gov>; Christl, Thomas (OS/ASPR/SIIM) <Thomas.Christl@hhs.gov>; Hamel, Joseph (OS/ASPR/IO) <Joseph.Hamel@hhs.gov>; Lamana, Joseph (OS/ASPR/EMMO) <Joseph.Lamana@hhs.gov>; Moudy, Robin (OS/ASPR/SPPR) <Robin.Moudy@hhs.gov>; Ayala, Ana (OS/OGA) <Ana.Ayala@hhs.gov>; Tewell, Adam (OS/ASPR/SPPR) <Adam.Tewell@hhs.gov>; Fitzgerald, Denis (OS/ASPR/EMMO) <Denis.Fitzgerald@hhs.gov>; Horahan, Kevin (OS/ASPR/EMMO) <Kevin.Horahan@hhs.gov>; Harper, Victor (OS/ASPR/ORM) <Victor.Harper@hhs.gov>; Ashton, Dustun (OS/ASPR/EMMO) <Dustun.Ashton@hhs.gov>; Evans, Pamela (OS/ASPR/EMMO) <Pamela.Evans@hhs.gov>; Vincent, Erik (OS/ASPR/IO) <Erik.Vincent@hhs.gov>; Adams, Steven A. (ASPR/SNS) <saa1@cdc.gov>; Gorman, Susan (ASPR/SNS) <spg4@cdc.gov>; Carpenter, Robert (ASPR/SNS) <dpn4@cdc.gov>; Dillard, Lisa (ASPR/SNS) <lsw9@cdc.gov>; Dolinsky, David (OS/ASPR/MFHC) <David.Dolinsky@hhs.gov>; Arthur, Ray (CDC/DDPHSIS/CGH/DGHP) <rca8@cdc.gov>; Degrange, Elizabeth (HHS/OASH) <Elizabeth.Degrange@hhs.gov>; Walker, Robert (OS/ASPR/BARDA) <Robert.Walker@hhs.gov>; Lambert, Linda (OS/ASPR/BARDA) <Linda.Lambert@hhs.gov>; Weinberger, Collin (OS/OGA) <Collin.Weinberger@hhs.gov>; eocevent209@cdc.gov; Lawrence, Theresa (OS/ASPR/SPPR) <Theresa.Lawrence@HHS.GOV>; Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Dodgen, Daniel (OS/ASPR/SPPR) <Daniel.Dodgen@HHS.GOV>; George, Kysa <Kysa.George@fema.dhs.gov>; Schwartz, Benjamin J CAPT USN NAVHOSP BREMERTON WA (USA) <(b)(6)>; Moniz, Charles R Lt Col USAF DLA LOGISTICS OPERATIONS (USA) <(b)(6)>; Abbott, Christopher J. EOP/WHO <(b)(6)>; Neuhauser, Melinda (CDC/DDID/NCEZID/DHQP) <ikf5@cdc.gov>
Cc: Thomas, Jason (CDC/DDPHSS/CSELS/DHIS) <dvz5@cdc.gov>; Imbriale, Samuel (OS/ASPR/SIIM) <Samuel.Imbriale@hhs.gov>; Greene, Jonathan (OS/ASPR/EMMO) <Jonathan.Greene@hhs.gov>; DLGDESK (HHS/ASPR/OPP) <DLGDESK@hhs.gov>; Smith, Timothy D. (fema.dhs.os) <Timothy.Smith5@fema.dhs.gov>
Subject: RE: IRPG: Review donation- Gilead- remdesivir

Thanks to everyone who participated in the call with Gilead. Gilead shared the attached confidential and privileged slide deck to address your questions. Please note that the data in the attached slide deck is evolving. Also, please note slides 11 and 12 are hypothetical, because there is no current FDA EUA for remdesivir. The draft donation agreement, as revised by Gilead, limits the donated drug to IND or EUA use. Gilead explained during the call that it is interested in PREP Act immunity. I believe Gilead has filed for an EUA with FDA, and that matter is pending.

Patty

<< File: Gilead Government Presentation on Distribution and Allocation (Apr 17 2020).pptx >>

From: Mantoan, Patricia (HHS/OGC)
Sent: Thursday, April 16, 2020 5:30 PM
To: Chandrasekera, Ruvani (OS/ASPR/SPPR) <Ruvani.Chandrasekera@hhs.gov>; Albrecht, Mark (OS/ASPR/BARDA) <Mark.Albrecht@hhs.gov>; Ford, Kenya S. (CDC/OCOO/OGC) <kdf6@cdc.gov>; Godin, Jacquelyn (NIH/OD) [E] <jacquelyn.godin@nih.gov>; Sherman, Susan (HHS/OGC) <Susan.Sherman@HHS.GOV>; Ray Gorrie, Jennifer (HHS/OGC) <Jennifer.Ray-Gorrie@hhs.gov>; CDC IMS 2019 NCOV Response International Task Force <eocevent223@cdc.gov>; Kerr, Lawrence (HHS/OS/OGA) <Lawrence.Kerr@hhs.gov>; Sadove, Elizabeth (FDA/OC) <Elizabeth.Sadove@fda.hhs.gov>; Courtney, Brooke (FDA/OC) <Brooke.Courtney@fda.hhs.gov>; Mair, Michael (FDA/OC) <Michael.Mair@fda.hhs.gov>; AvilesMendoza, Guillermo (OS/OASH) <Guillermo.Aviles-Mendoza@hhs.gov>; Barry, Daniel J (HHS/OGC) <daniel.barry@hhs.gov>; Vinter, Serena (CDC/DDPHSIS/CGH/OD) <uvv3@cdc.gov>; Weir, Charles (OS/ASPR/IO) <Charles.Weir@hhs.gov>; Peerbolte, Stacy (OS/ASPR/EMMO) <Stacy.Peerbolte@hhs.gov>; Phung, Hai Lien (ASPR/SNS) <vvt3@cdc.gov>; Christl, Thomas (OS/ASPR/SIIM) <Thomas.Christl@hhs.gov>; Hamel, Joseph (OS/ASPR/IO) <Joseph.Hamel@hhs.gov>; Lamana, Joseph (OS/ASPR/EMMO) <Joseph.Lamana@hhs.gov>; Moudy, Robin (OS/ASPR/SPPR) <Robin.Moudy@hhs.gov>; Ayala, Ana (OS/OGA) <Ana.Ayala@hhs.gov>; Tewell, Adam (OS/ASPR/SPPR) <Adam.Tewell@hhs.gov>; Fitzgerald, Denis (OS/ASPR/EMMO) <Denis.Fitzgerald@hhs.gov>; Horahan, Kevin (OS/ASPR/EMMO) <Kevin.Horahan@hhs.gov>; Harper, Victor (OS/ASPR/ORM) <Victor.Harper@hhs.gov>; Ashton, Dustun (OS/ASPR/EMMO) <Dustun.Ashton@hhs.gov>; Evans, Pamela (OS/ASPR/EMMO) <Pamela.Evans@hhs.gov>; Vincent, Erik (OS/ASPR/IO) <Erik.Vincent@hhs.gov>; Adams, Steven A. (ASPR/SNS) <saa1@cdc.gov>; Gorman, Susan (ASPR/SNS) <spg4@cdc.gov>; Carpenter, Robert (ASPR/SNS) <dpn4@cdc.gov>; Dillard, Lisa (ASPR/SNS) <lsw9@cdc.gov>; Dolinsky, David (OS/ASPR/MFHC) <David.Dolinsky@hhs.gov>; Arthur, Ray (CDC/DDPHSIS/CGH/DGHP) <rca8@cdc.gov>; Degrange, Elizabeth (HHS/OASH) <Elizabeth.Degrange@hhs.gov>; Walker, Robert (OS/ASPR/BARDA) <Robert.Walker@hhs.gov>; Lambert, Linda (OS/ASPR/BARDA) <Linda.Lambert@hhs.gov>; Weinberger, Collin (OS/OGA) <Collin.Weinberger@hhs.gov>; eocevent209@cdc.gov; Lawrence, Theresa (OS/ASPR/SPPR) <Theresa.Lawrence@HHS.GOV>; Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Dodgen, Daniel (OS/ASPR/SPPR) <Daniel.Dodgen@HHS.GOV>; George, Kysa <Kysa.George@fema.dhs.gov>; Schwartz, Benjamin J CAPT USN NAVHOSP BREMERTON WA (USA) <(b)(6)>; Moniz, Charles R Lt Col USAF DLA LOGISTICS OPERATIONS (USA) <(b)(6)>; Abbott, Christopher J. EOP/WHO <(b)(6)>; Neuhauser, Melinda (CDC/DDID/NCEZID/DHQP) <ikf5@cdc.gov>
Cc: Thomas, Jason (CDC/DDPHSS/CSELS/DHIS) <dvz5@cdc.gov>; Imbriale, Samuel (OS/ASPR/SIIM) <Samuel.Imbriale@hhs.gov>; Greene, Jonathan (OS/ASPR/EMMO) <Jonathan.Greene@hhs.gov>; DLGDESK (HHS/ASPR/OPP) <DLGDESK@hhs.gov>; Smith, Timothy D. (fema.dhs.os)

<Timothy.Smith5@fema.dhs.gov>
Subject: RE: IRPG: Review donation- Gilead- remdesivir

I will share the questions with Gilead and ask them to provide a call-in number, and I will share the call-in information with those listed in Ruvani's most recent email. Many thanks.

From: Chandrasekera, Ruvani (OS/ASPR/SPPR) <Ruvani.Chandrasekera@hhs.gov>
Sent: Thursday, April 16, 2020 5:27 PM
To: Mantoan, Patricia (HHS/OGC) <Patricia.Mantoan@HHS.GOV>; Albrecht, Mark (OS/ASPR/BARDA) <Mark.Albrecht@hhs.gov>; Ford, Kenya S. (CDC/OCOO/OGC) <kdf6@cdc.gov>; Godin, Jacquelyn (NIH/OD) [E] <jacquelyn.godin@nih.gov>; Sherman, Susan (HHS/OGC) <Susan.Sherman@HHS.GOV>; Ray Gorrie, Jennifer (HHS/OGC) <Jennifer.Ray-Gorrie@hhs.gov>; CDC IMS 2019 NCOV Response International Task Force <eocevent223@cdc.gov>; Kerr, Lawrence (HHS/OS/OGA) <Lawrence.Kerr@hhs.gov>; Sadove, Elizabeth (FDA/OC) <Elizabeth.Sadove@fda.hhs.gov>; Courtney, Brooke (FDA/OC) <Brooke.Courtney@fda.hhs.gov>; Mair, Michael (FDA/OC) <Michael.Mair@fda.hhs.gov>; AvilesMendoza, Guillermo (OS/OASH) <Guillermo.Aviles-Mendoza@hhs.gov>; Barry, Daniel J (HHS/OGC) <daniel.barry@hhs.gov>; Vinter, Serena (CDC/DDPHSIS/CGH/OD) <uvv3@cdc.gov>; Weir, Charles (OS/ASPR/IO) <Charles.Weir@hhs.gov>; Peerbolte, Stacy (OS/ASPR/EMMO) <Stacy.Peerbolte@hhs.gov>; Phung, Hai Lien (ASPR/SNS) <vvt3@cdc.gov>; Christl, Thomas (OS/ASPR/SIIM) <Thomas.Christl@hhs.gov>; Hamel, Joseph (OS/ASPR/IO) <Joseph.Hamel@hhs.gov>; Lamana, Joseph (OS/ASPR/EMMO) <Joseph.Lamana@hhs.gov>; Moudy, Robin (OS/ASPR/SPPR) <Robin.Moudy@hhs.gov>; Ayala, Ana (OS/OGA) <Ana.Ayala@hhs.gov>; Tewell, Adam (OS/ASPR/SPPR) <Adam.Tewell@hhs.gov>; Fitzgerald, Denis (OS/ASPR/EMMO) <Denis.Fitzgerald@hhs.gov>; Horahan, Kevin (OS/ASPR/EMMO) <Kevin.Horahan@hhs.gov>; Harper, Victor (OS/ASPR/ORM) <Victor.Harper@hhs.gov>; Ashton, Dustun (OS/ASPR/EMMO) <Dustun.Ashton@hhs.gov>; Evans, Pamela (OS/ASPR/EMMO) <Pamela.Evans@hhs.gov>; Vincent, Erik (OS/ASPR/IO) <Erik.Vincent@hhs.gov>; Adams, Steven A. (ASPR/SNS) <saa1@cdc.gov>; Gorman, Susan (ASPR/SNS) <spg4@cdc.gov>; Carpenter, Robert (ASPR/SNS) <dpn4@cdc.gov>; Dillard, Lisa (ASPR/SNS) <lsw9@cdc.gov>; Dolinsky, David (OS/ASPR/MFHC) <David.Dolinsky@hhs.gov>; Arthur, Ray (CDC/DDPHSIS/CGH/DGHP) <rca8@cdc.gov>; Degrange, Elizabeth (HHS/OASH) <Elizabeth.Degrange@hhs.gov>; Walker, Robert (OS/ASPR/BARDA) <Robert.Walker@hhs.gov>; Lambert, Linda (OS/ASPR/BARDA) <Linda.Lambert@hhs.gov>; Weinberger, Collin (OS/OGA) <Collin.Weinberger@hhs.gov>; eocevent209@cdc.gov; Lawrence, Theresa (OS/ASPR/SPPR) <Theresa.Lawrence@HHS.GOV>; Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Dodgen, Daniel (OS/ASPR/SPPR) <Daniel.Dodgen@HHS.GOV>; George, Kysa <Kysa.George@fema.dhs.gov>; Schwartz, Benjamin J CAPT USN NAVHOSP BREMERTON WA (USA) <(b)(6)>; Moniz, Charles R Lt Col USAF DLA LOGISTICS OPERATIONS (USA) <(b)(6)>; Abbott, Christopher J. EOP/WHO <(b)(6)>; Neuhauser, Melinda (CDC/DDID/NCEZID/DHQP) <ikf5@cdc.gov>
Cc: Thomas, Jason (CDC/DDPHSS/CSELS/DHIS) <dvz5@cdc.gov>; Imbriale, Samuel (OS/ASPR/SIIM) <Samuel.Imbriale@hhs.gov>; Greene, Jonathan (OS/ASPR/EMMO) <Jonathan.Greene@hhs.gov>; DLGDESK (HHS/ASPR/OPP) <DLGDESK@hhs.gov>; Smith, Timothy D. (fema.dhs.os) <Timothy.Smith5@fema.dhs.gov>
Subject: RE: IRPG: Review donation- Gilead- remdesivir

For awareness:

Participants for Gilead call at 1pm tomorrow:
OGC: Patty Mantoan; Susan Sherman
ASPR/IO: Joe Hamel
SNS: Ottem, Ronald (Ron) (ASPR/SNS) <rco9@cdc.gov>; Mabry, Shirley (ASPR/SNS) <aiq8@cdc.gov>; Adams, Steven A. (ASPR/SNS) <saa1@cdc.gov>; Carpenter, Robert (ASPR/SNS) <dpn4@cdc.gov>; Gorman, Susan (ASPR/SNS) spg4@cdc.gov
BARDA: Disbrow, Gary (OS/ASPR/BARDA) Gary.Disbrow@hhs.gov
FDA: Mair, Michael (FDA/OC) Michael.Mair@fda.hhs.gov; Courtney, Brooke (FDA/OC) <Brooke.Courtney@fda.hhs.gov>
FEMA SCTF: Neuhauser, Melinda (CDC/DDID/NCEZID/DHQP) ikf5@cdc.gov; Schwartz, Benjamin J CAPT USN NAVHOSP BREMERTON WA (USA) (b)(6) Moniz, Charles R Lt Col USAF DLA LOGISTICS OPERATIONS (USA) (b)(6)
OGA: Kerr, Lawrence (HHS/OS/OGA) <Larry.Kerr@hhs.gov>; Moudy, Robin (OS/ASPR/OPP) <Robin.Moudy@hhs.gov>; Ayala, Ana (OS/ASPR/SPPR) <Ana.Ayala@hhs.gov>; Chandrasekera, Ruvani (OS/ASPR/ICC/SPPR) <Ruvani.Chandrasekera@hhs.gov>
White House: (b)(6)

Questions for Gilead:

- What is the number of doses being offered and is Gilead making similar donations to other governments?
    - If HHS wants only a portion of the product, how would Gilead handle the remaining portion (i.e. will it be available for expanded access, available to other countries)?
- When can this donation be made available to us (e.g. as soon as the agreement is signed or will it be in batches)?
- What efficacy data does Gilead have that supports remdesivir's use in the treatment of COVID-19 and when is Gilead expecting top-line data from their ongoing Phase 3 clinical studies?
- Has Gilead explored any liability protection mechanisms?

Ruvani Chandrasekera
HHS/OGA/Pandemic and Emerging Threats
Office: 202-260-0512| Cell: (b)(6)

From: Mantoan, Patricia (HHS/OGC) <Patricia.Mantoan@HHS.GOV>
Sent: Thursday, April 16, 2020 5:18 PM
To: Albrecht, Mark (OS/ASPR/BARDA) <Mark.Albrecht@hhs.gov>; Chandrasekera, Ruvani (OS/ASPR/SPPR) <Ruvani.Chandrasekera@hhs.gov>; Ford, Kenya S. (CDC/OCOO/OGC) <kdf6@cdc.gov>; Godin, Jacquelyn (NIH/OD) [E] <jacquelyn.godin@nih.gov>; Sherman, Susan (HHS/OGC) <Susan.Sherman@HHS.GOV>; Ray Gorrie, Jennifer (HHS/OGC) <Jennifer.Ray-Gorrie@hhs.gov>; CDC IMS

2019 NCOV Response International Task Force <eocevent223@cdc.gov>; Ganim, Alexandra M. (CDC/DDID/NCEZID/DPEI) <hrt8@cdc.gov>; Kerr, Lawrence (HHS/OS/OGA) <Lawrence.Kerr@hhs.gov>; Sadove, Elizabeth (FDA/OC) <Elizabeth.Sadove@fda.hhs.gov>; Courtney, Brooke (FDA/OC) <Brooke.Courtney@fda.hhs.gov>; Mair, Michael (FDA/OC) <Michael.Mair@fda.hhs.gov>; AvilesMendoza, Guillermo (OS/OASH) <Guillermo.Aviles-Mendoza@hhs.gov>; Barry, Daniel J (HHS/OGC) <daniel.barry@hhs.gov>; Vinter, Serena (CDC/DDPHSIS/CGH/OD) <uvv3@cdc.gov>; Weir, Charles (OS/ASPR/IO) <Charles.Weir@hhs.gov>; Peerbolte, Stacy (OS/ASPR/EMMO) <Stacy.Peerbolte@hhs.gov>; Phung, Hai Lien (ASPR/SNS) <vvt3@cdc.gov>; Christl, Thomas (OS/ASPR/SIIM) <Thomas.Christl@hhs.gov>; Hamel, Joseph (OS/ASPR/IO) <Joseph.Hamel@hhs.gov>; Lamana, Joseph (OS/ASPR/EMMO) <Joseph.Lamana@hhs.gov>; Moudy, Robin (OS/ASPR/SPPR) <Robin.Moudy@hhs.gov>; Ayala, Ana (OS/OGA) <Ana.Ayala@hhs.gov>; Tewell, Adam (OS/ASPR/SPPR) <Adam.Tewell@hhs.gov>; Fitzgerald, Denis (OS/ASPR/EMMO) <Denis.Fitzgerald@hhs.gov>; Horahan, Kevin (OS/ASPR/EMMO) <Kevin.Horahan@hhs.gov>; Harper, Victor (OS/ASPR/ORM) <Victor.Harper@hhs.gov>; Ashton, Dustun (OS/ASPR/EMMO) <Dustun.Ashton@hhs.gov>; Evans, Pamela (OS/ASPR/EMMO) <Pamela.Evans@hhs.gov>; Vincent, Erik (OS/ASPR/IO) <Erik.Vincent@hhs.gov>; Adams, Steven A. (ASPR/SNS) <saa1@cdc.gov>; Gorman, Susan (ASPR/SNS) <spg4@cdc.gov>; Carpenter, Robert (ASPR/SNS) <dpn4@cdc.gov>; Dillard, Lisa (ASPR/SNS) <lsw9@cdc.gov>; Dolinsky, David (OS/ASPR/MFHC) <David.Dolinsky@hhs.gov>; Arthur, Ray (CDC/DDPHSIS/CGH/DGHP) <rca8@cdc.gov>; Degrange, Elizabeth (HHS/OASH) <Elizabeth.Degrange@hhs.gov>; Walker, Robert (OS/ASPR/BARDA) <Robert.Walker@hhs.gov>; Lambert, Linda (OS/ASPR/BARDA) <Linda.Lambert@hhs.gov>; Weinberger, Collin (OS/OGA) <Collin.Weinberger@hhs.gov>; eocevent209@cdc.gov; Lawrence, Theresa (OS/ASPR/SPPR) <Theresa.Lawrence@HHS.GOV>; Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Dodgen, Daniel (OS/ASPR/SPPR) <Daniel.Dodgen@HHS.GOV>; George, Kysa <Kysa.George@fema.dhs.gov>; Schwartz, Benjamin J CAPT USN NAVHOSP BREMERTON WA (USA) (b)(6) >; Moniz, Charles R Lt Col USAF DLA LOGISTICS OPERATIONS (USA) <(b)(6) >; Abbott, Christopher J. EOP/WHO <(b)(6) >; Neuhauser, Melinda (CDC/DDID/NCEZID/DHQP) <ikf5@cdc.gov>

Cc: Thomas, Jason (CDC/DDPHSS/CSELS/DHIS) <dvz5@cdc.gov>; Imbriale, Samuel (OS/ASPR/SIIM) <Samuel.Imbriale@hhs.gov>; Greene, Jonathan (OS/ASPR/EMMO) <Jonathan.Greene@hhs.gov>; DLGDESK (HHS/ASPR/OPP) <DLGDESK@hhs.gov>; Smith, Timothy D. (fema.dhs.os) <Timothy.Smith5@fema.dhs.gov>

Subject: RE: IRPG: Review donation- Gilead- remdesivir

Gilead has indicated that they are all available on Friday at 1 p.m. for a discussion. I would give them our questions ahead so they can answer them during the call. So far, I have the following questions. Thanks.

- What is the number of doses being offered and is Gilead making similar donations to other governments?
- If HHS wants only a portion of the product, how would Gilead handle the remaining portion (i.e. will it be available for expanded access, available to other countries)?
- When can this donation be made available to us (e.g. as soon as the agreement is signed or will it be in batches)?
- What efficacy data does Gilead have that supports remdesivir's use in the treatment of COVID-19 and when is Gilead expecting top-line data from their ongoing Phase 3 clinical

From: Albrecht, Mark (OS/ASPR/BARDA) <Mark.Albrecht@hhs.gov>
Sent: Thursday, April 16, 2020 4:43 PM
To: Chandrasekera, Ruvani (OS/ASPR/SPPR) <Ruvani.Chandrasekera@hhs.gov>; Ford, Kenya S. (CDC/OCOO/OGC) <kdf6@cdc.gov>; Godin, Jacquelyn (NIH/OD) [E] <jacquelyn.godin@nih.gov>; Sherman, Susan (HHS/OGC) <Susan.Sherman@HHS.GOV>; Ray Gorrie, Jennifer (HHS/OGC) <Jennifer.Ray-Gorrie@hhs.gov>; CDC IMS 2019 NCOV Response International Task Force <eocevent223@cdc.gov>; Ganim, Alexandra M. (CDC/DDID/NCEZID/DPEI) <hrt8@cdc.gov>; Kerr, Lawrence (HHS/OS/OGA) <Lawrence.Kerr@hhs.gov>; Sadove, Elizabeth (FDA/OC) <Elizabeth.Sadove@fda.hhs.gov>; Courtney, Brooke (FDA/OC) <Brooke.Courtney@fda.hhs.gov>; Mair, Michael (FDA/OC) <Michael.Mair@fda.hhs.gov>; AvilesMendoza, Guillermo (OS/OASH) <Guillermo.Aviles-Mendoza@hhs.gov>; Barry, Daniel J (HHS/OGC) <daniel.barry@hhs.gov>; Vinter, Serena (CDC/DDPHSIS/CGH/OD) <uvv3@cdc.gov>; Weir, Charles (OS/ASPR/IO) <Charles.Weir@hhs.gov>; Peerbolte, Stacy (OS/ASPR/EMMO) <Stacy.Peerbolte@hhs.gov>; Phung, Hai Lien (ASPR/SNS) <vvt3@cdc.gov>; Christl, Thomas (OS/ASPR/SIIM) <Thomas.Christl@hhs.gov>; Hamel, Joseph (OS/ASPR/IO) <Joseph.Hamel@hhs.gov>; Lamana, Joseph (OS/ASPR/EMMO) <Joseph.Lamana@hhs.gov>; Moudy, Robin (OS/ASPR/SPPR) <Robin.Moudy@hhs.gov>; Ayala, Ana (OS/OGA) <Ana.Ayala@hhs.gov>; Tewell, Adam (OS/ASPR/SPPR) <Adam.Tewell@hhs.gov>; Fitzgerald, Denis (OS/ASPR/EMMO) <Denis.Fitzgerald@hhs.gov>; Horahan, Kevin (OS/ASPR/EMMO) <Kevin.Horahan@hhs.gov>; Harper, Victor (OS/ASPR/ORM) <Victor.Harper@hhs.gov>; Ashton, Dustun (OS/ASPR/EMMO) <Dustun.Ashton@hhs.gov>; Evans, Pamela (OS/ASPR/EMMO) <Pamela.Evans@hhs.gov>; Vincent, Erik (OS/ASPR/IO) <Erik.Vincent@hhs.gov>; Adams, Steven A. (ASPR/SNS) <saa1@cdc.gov>; Gorman, Susan (ASPR/SNS) <spg4@cdc.gov>; Carpenter, Robert (ASPR/SNS) <dpn4@cdc.gov>; Dillard, Lisa (ASPR/SNS) <lsw9@cdc.gov>; Dolinsky, David (OS/ASPR/MFHC) <David.Dolinsky@hhs.gov>; Arthur, Ray (CDC/DDPHSIS/CGH/DGHP) <rca8@cdc.gov>; Degrange, Elizabeth (HHS/OASH) <Elizabeth.Degrange@hhs.gov>; Mantoan, Patricia (HHS/OGC) <Patricia.Mantoan@HHS.GOV>; Walker, Robert (OS/ASPR/BARDA) <Robert.Walker@hhs.gov>; Lambert, Linda (OS/ASPR/BARDA) <Linda.Lambert@hhs.gov>; Weinberger, Collin (OS/OGA) <Collin.Weinberger@hhs.gov>; eocevent209@cdc.gov; Lawrence, Theresa (OS/ASPR/SPPR) <Theresa.Lawrence@HHS.GOV>; Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Dodgen, Daniel (OS/ASPR/SPPR) <Daniel.Dodgen@HHS.GOV>; George, Kysa <Kysa.George@fema.dhs.gov>; Schwartz, Benjamin J CAPT USN NAVHOSP BREMERTON WA (USA) <(b)(6)>; Moniz, Charles R Lt Col USAF DLA LOGISTICS OPERATIONS (USA) <(b)(6)>; Abbott, Christopher J. EOP/WHO <(b)(6)>; Neuhauser, Melinda (CDC/DDID/NCEZID/DHQP) <ikf5@cdc.gov>
Cc: Thomas, Jason (CDC/DDPHSS/CSELS/DHIS) <dvz5@cdc.gov>; Imbriale, Samuel (OS/ASPR/SIIM) <Samuel.Imbriale@hhs.gov>; Greene, Jonathan (OS/ASPR/EMMO) <Jonathan.Greene@hhs.gov>; DLGDESK (HHS/ASPR/OPP) <DLGDESK@hhs.gov>; Smith, Timothy D. (fema.dhs.os) <Timothy.Smith5@fema.dhs.gov>
Subject: RE: IRPG: Review donation- Gilead- remdesivir

Ruvani,

I suggest augmenting the last question to Gilead to the following:

- What efficacy data does Gilead have that supports remdesivir's use in the treatment of COVID-19 and when is Gilead expecting top-line data from their ongoing Phase 3 clinical studies?

This information would address the technical concerns raised on the call.

Mark

Mark Albrecht, Ph.D.
Branch Chief
Anti-Bacterial (AB) Program
Division of CBRN Countermeasures
Biomedical Advanced Research and Development Authority (BARDA)
Office of the Assistant Secretary for Preparedness and Response (ASPR)
Department of Health and Human Services (DHHS)
Office: 202-691-2015
BB: (b)(6)

From: Chandrasekera, Ruvani (OS/ASPR/SPPR) <Ruvani.Chandrasekera@hhs.gov>
Sent: Thursday, April 16, 2020 4:13 PM
To: Ford, Kenya S. (CDC/OCOO/OGC) <kdf6@cdc.gov>; Godin, Jacquelyn (NIH/OD) [E] <jacquelyn.godin@nih.gov>; Sherman, Susan (HHS/OGC) <Susan.Sherman@HHS.GOV>; Ray Gorrie, Jennifer (HHS/OGC) <Jennifer.Ray-Gorrie@hhs.gov>; CDC IMS 2019 NCOV Response International Task Force <eocevent223@cdc.gov>; Ganim, Alexandra M. (CDC/DDID/NCEZID/DPEI) <hrt8@cdc.gov>; Kerr, Lawrence (HHS/OS/OGA) <Lawrence.Kerr@hhs.gov>; Sadove, Elizabeth (FDA/OC) <Elizabeth.Sadove@fda.hhs.gov>; Courtney, Brooke (FDA/OC) <Brooke.Courtney@fda.hhs.gov>; Mair, Michael (FDA/OC) <Michael.Mair@fda.hhs.gov>; AvilesMendoza, Guillermo (OS/OASH) <Guillermo.Aviles-Mendoza@hhs.gov>; Barry, Daniel J (HHS/OGC) <daniel.barry@hhs.gov>; Vinter, Serena (CDC/DDPHSIS/CGH/OD) <uvv3@cdc.gov>; Weir, Charles (OS/ASPR/IO) <Charles.Weir@hhs.gov>; Peerbolte, Stacy (OS/ASPR/EMMO) <Stacy.Peerbolte@hhs.gov>; Phung, Hai Lien (ASPR/SNS) <vvt3@cdc.gov>; Christl, Thomas (OS/ASPR/SIIM) <Thomas.Christl@hhs.gov>; Hamel, Joseph (OS/ASPR/IO) <Joseph.Hamel@hhs.gov>; Lamana, Joseph (OS/ASPR/EMMO) <Joseph.Lamana@hhs.gov>; Moudy, Robin (OS/ASPR/SPPR) <Robin.Moudy@hhs.gov>; Ayala, Ana (OS/OGA) <Ana.Ayala@hhs.gov>; Tewell, Adam (OS/ASPR/SPPR) <Adam.Tewell@hhs.gov>; Fitzgerald, Denis (OS/ASPR/EMMO) <Denis.Fitzgerald@hhs.gov>; Horahan, Kevin (OS/ASPR/EMMO)

<Kevin.Horahan@hhs.gov>; Harper, Victor (OS/ASPR/ORM) <Victor.Harper@hhs.gov>; Ashton, Dustun (OS/ASPR/EMMO) <Dustun.Ashton@hhs.gov>; Evans, Pamela (OS/ASPR/EMMO) <Pamela.Evans@hhs.gov>; Vincent, Erik (OS/ASPR/IO) <Erik.Vincent@hhs.gov>; Adams, Steven A. (ASPR/SNS) <saa1@cdc.gov>; Gorman, Susan (ASPR/SNS) <spg4@cdc.gov>; Carpenter, Robert (ASPR/SNS) <dpn4@cdc.gov>; Dillard, Lisa (ASPR/SNS) <lsw9@cdc.gov>; Dolinsky, David (OS/ASPR/MFHC) <David.Dolinsky@hhs.gov>; Arthur, Ray (CDC/DDPHSIS/CGH/DGHP) <rca8@cdc.gov>; Degrange, Elizabeth (HHS/OASH) <Elizabeth.Degrange@hhs.gov>; Mantoan, Patricia (HHS/OGC) <Patricia.Mantoan@HHS.GOV>; Walker, Robert (OS/ASPR/BARDA) <Robert.Walker@hhs.gov>; Lambert, Linda (OS/ASPR/BARDA) <Linda.Lambert@hhs.gov>; Weinberger, Collin (OS/OGA) <Collin.Weinberger@hhs.gov>; eocevent209@cdc.gov; Lawrence, Theresa (OS/ASPR/SPPR) <Theresa.Lawrence@HHS.GOV>; Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Dodgen, Daniel (OS/ASPR/SPPR) <Daniel.Dodgen@HHS.GOV>; George, Kysa <Kysa.George@fema.dhs.gov>; Albrecht, Mark (OS/ASPR/BARDA) <Mark.Albrecht@hhs.gov>; Schwartz, Benjamin J CAPT USN NAVHOSP BREMERTON WA (USA) <(b)(6) >; Moniz, Charles R Lt Col USAF DLA LOGISTICS OPERATIONS (USA) <(b)(6) >; Abbott, Christopher J. EOP/WHO <(b)(6) >; Neuhauser, Melinda (CDC/DDID/NCEZID/DHQP) <ikf5@cdc.gov>

Cc: Thomas, Jason (CDC/DDPHSS/CSELS/DHIS) <dvz5@cdc.gov>; Imbriale, Samuel (OS/ASPR/SIIM) <Samuel.Imbriale@hhs.gov>; Greene, Jonathan (OS/ASPR/EMMO) <Jonathan.Greene@hhs.gov>; DLGDESK (HHS/ASPR/OPP) <DLGDESK@hhs.gov>; Smith, Timothy D. (fema.dhs.os) <Timothy.Smith5@fema.dhs.gov>

Subject: RE: IRPG: Review donation- Gilead- remdesivir

Hi All,

I've attempted to capture high-level notes based on what we discussed- if anything is incorrect, please let me know. Please see the questions for Gilead below and let me know if there are other questions to add. I've already heard from a number of you who would like to participate in the call with Gilead tomorrow.

- In short, HHS is open to talking more to Gilead about what a donation could look like, but there are several concerns that would need to be addressed ahead of accepting the donation:
    - Legal and regulatory issues- there are certain limitations under which remdesivir can be used (e.g. under IND and EUA), but how would this affect how the U.S. can share the product with others (e.g., other governments for diplomatic or other reasons)
    - If HHS accepts the donation, and the donation is the entirety of Gilead's remdesivir treatment courses, how will HHS manage the numerous requests from state/local entities (which would come through the FEMA allocation process) for remdesivir? HHS (SNS and others) and FEMA don't have administrative and logistical processes in place to handle the large number of ad hoc requests for small volumes of remdesivir and this could be a major challenge that could prevent effective use of the product and take up more resources.
        - HHS could accept a smaller volume (e.g. ¾) of what Gilead is offering, but the above issue would still need to be worked out.
    - It may be premature to accept the donation when we still don't know how effective the product is. However, we also recognize that such an offer might not be available to the USG in a couple of weeks/months.

- Logistical issues- we need to work out who will hold and distribute the product.
- Christopher Abbott (White House) expressed interest in the U.S. accepting this donation.
- If needed, this can be elevated to the ASPR-led Disaster Leadership Group (DLG) for HHS Senior Leadership to weigh in
- Next Steps:
  - Talk to Gilead on Friday (let Ruvani know if you should be included in the discussion)
  - Everyone discuss with their leadership if there are immediate concerns
  - Reconvene by email or phone to determine next steps in process

Questions for Gilead:

- What is the number of doses being offered and is Gilead making similar donations to other governments?
  - If HHS wants only a portion of the product, how would Gilead handle the remaining portion (i.e. will it be available for expanded access, available to other countries)?
- When can this donation be made available to us (e.g. as soon as the agreement is signed or will it be in batches)?
- Does Gilead have any clinical efficacy data?

Thanks,
Ruvani

Ruvani Chandrasekera
HHS/OGA/Pandemic and Emerging Threats
Office: 202-260-0512| Cell (b)(6)

-----Original Appointment-----
From: Chandrasekera, Ruvani (OS/ASPR/SPPR)
Sent: Thursday, April 16, 2020 9:37 AM
To: Chandrasekera, Ruvani (OS/ASPR/SPPR); Ford, Kenya S. (CDC/OCOO/OGC); Godin, Jacquelyn (NIH/OD) [E]; Sherman, Susan (HHS/OGC); Ray Gorrie, Jennifer (HHS/OGC); CDC IMS 2019 NCOV Response International Task Force; Ganim, Alexandra M. (CDC/DDID/NCEZID/DPEI); Kerr, Lawrence (HHS/OS/OGA); Sadove, Elizabeth (FDA/OC); Courtney, Brooke (FDA/OC); Mair, Michael (FDA/OC); AvilesMendoza, Guillermo (OS/OASH); Barry, Daniel J (HHS/OGC); Vinter, Serena (CDC/DDPHSIS/CGH/OD); Weir, Charles (OS/ASPR/IO); Peerbolte, Stacy (OS/ASPR/EMMO); Phung, Hai Lien (ASPR/SNS); Christl, Thomas (OS/ASPR/SIIM); Hamel, Joseph (OS/ASPR/IO); Lamana, Joseph (OS/ASPR/EMMO); Moudy, Robin (OS/ASPR/SPPR); Ayala, Ana (OS/ASPR/SPPR); Tewell, Adam (OS/ASPR/SPPR); Fitzgerald, Denis (OS/ASPR/EMMO); Horahan, Kevin (OS/ASPR/EMMO); Harper, Victor (OS/ASPR/ORM); Ashton, Dustun (OS/ASPR/EMMO); Evans, Pamela (OS/ASPR/EMMO); Vincent, Erik (OS/ASPR/IO); Adams, Steven A. (ASPR/SNS); Gorman, Susan (ASPR/SNS); Carpenter, Robert (ASPR/SNS); Dillard, Lisa (ASPR/SNS); Dolinsky, David (OS/ASPR/MFHC); Arthur, Ray (CDC/DDPHSIS/CGH/DGHP); Degrange, Elizabeth (HHS/OASH); Mantoan, Patricia (HHS/OGC); Walker, Robert (OS/ASPR/BARDA); Lambert, Linda (OS/ASPR/BARDA); Weinberger, Collin (OS/OGA); eocevent209@cdc.gov; Lawrence, Theresa (OS/ASPR/SPPR); Disbrow, Gary (OS/ASPR/BARDA); Dodgen, Daniel (OS/ASPR/OPP); George, Kysa; Albrecht, Mark (OS/ASPR/BARDA); Schwartz, Benjamin J CAPT USN NAVHOSP BREMERTON WA (USA); Moniz, Charles R Lt Col USAF DLA LOGISTICS OPERATIONS (USA); Abbott, Christopher J.

EOP/WHO; Neuhauser, Melinda (CDC/DDID/NCEZID/DHQP)
Cc: Thomas, Jason (CDC/DDPHSS/CSELS/DHIS); Imbriale, Samuel (OS/ASPR/SIIM); Greene, Jonathan (OS/ASPR/EMMO); DLGDESK (HHS/ASPR/OPP); Smith, Timothy D. (fema.dhs.os)
Subject: IRPG: Review donation- Gilead- remdesivir
When: Thursday, April 16, 2020 1:00 PM-2:00 PM (UTC-05:00) Eastern Time (US & Canada).
Where: 3019455500; 81773807#

Colleagues,

There is a potential donation of remdesivir to HHS from Gilead. Attached is the draft donation agreement between HHS and Gilead that we would like to discuss with the group. Calendar invite for 1pm today to follow.

<< File: HHS Handling and Considerations for MCM donations_20200415.docx >> << File: Gilead--Donation Agreement for remdesivir (Gilead draft 4.14.2020).DOCX >>
Thanks,
Ruvani

Sender:	Disbrow, Gary (OS/ASPR/BARDA) </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0FD5845DEFDA4DC0BB45F8FAC629CF09-DISBROW, GA>
Recipient:	Mantoan, Patricia (HHS/OGC) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=user0ebe3257 <Patricia.Mantoan@HHS.GOV>; Sherman, Susan (HHS/OGC) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=user161a2a33 <Susan.Sherman@HHS.GOV>; Shuy, Bryan (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fdeb5ca04b6b4ed19fec2209b5f571e7-Shuy, Bryan <Bryan.Shuy@hhs.gov>; Kadlec, Robert (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a182eda693d040d3832bae6efcf7a255-Kadlec, Rob <Robert.Kadlec@hhs.gov>; Angelastro, Michael (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=583e910528e7473d9dcdfce9d1a80b83-Angelastro, <Michael.Angelastro@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0851e89240324306b78740a4a60745e2-Johnson, Ro <Robert.Johnson@hhs.gov>; Harper, Victor (OS/ASPR/ORM) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=user0bdee7e8 <Victor.Harper@hhs.gov>; Adams, Steven A. (ASPR/SNS) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f98462fe8d124743a437c7a80b3f60dd-Adams, Stev <saa1@cdc.gov>
Sent Date:	2020/04/29 15:21:09

DONATION AGREEMENT ("Agreement")

between

The U.S. Department of Health & Human Services ("**HHS**")

With offices at 200 Independence Avenue, S.W.
Washington, D.C. 20201

and

Gilead Sciences, Inc. ("**Gilead**")

With offices at 333 Lakeside Drive
Foster City, CA 94404

(b)(5)

(b)(5)

(b)(5)

SIGNATURE PAGE

IN WITNESS WHEREOF, the parties hereto have executed this **Agreement** by their respective duly authorized officers, who have affixed their signatures hereunto, on the day and year hereinafter written. Each individual signing below represents that he or she has authority to bind the party that he or she represents.

For **HHS**:

_____ _____
Signature of Authorized Official Date

Robert Kadlec, M.D., MTM&H, M.S.
Printed Name

Assistant Secretary for Preparedness and Response
Title

For **Gilead**:

_____ _____
Signature of Authorized Official Date

_____
Printed Name

_____
Title

From:	Disbrow, Gary (OS/ASPR/BARDA) </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0FD5845DEFDA4DC0BB45F8FAC629CF09-DISBROW, GA>
To:	Brett Pletcher <Brett.Pletcher@gilead.com>
CC:	Stimson, Brian (HHS/OGC) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=338aa495176d4c92bb314f8f3f51d118-Stimson, Br <Brian.Stimson@hhs.gov>; Chuck Clapton <Chuck.Clapton@gilead.com>
Subject:	RE: Gilead / Remdesivir
Date:	2020/03/28 11:10:00
Priority:	Normal
Type:	Note

Brett,

Still trying to get SNS folks. As you know, they are overwhelmed with shipping critical supplies out to states. Hoping they can get on a call today. I will send out an invite if I can get them on a call.

Thank you for your patients.

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

-----Original Message-----

From: Brett Pletcher <Brett.Pletcher@gilead.com>
Sent: Saturday, March 28, 2020 11:04 AM
To: Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>
Cc: Stimson, Brian (HHS/OGC) <Brian.Stimson@hhs.gov>; Chuck Clapton <Chuck.Clapton@gilead.com>
Subject: Gilead / Remdesivir

Dear Gary,

I want to alert you to the potential timing of FDA action on remdesivir and the need for urgent follow up with you and your colleagues at BARDA, the Strategic National Stockpile and HHS on a few time sensitive questions that will inform Gilead's next steps on procurement and allocation of remdesivir.

On timing, Gilead is assessing whether to submit a request next week to FDA to issue an Emergency Use Authorization. This is based on where we stand with the collection of clinical patient data, as well as the intense demand we are seeing for the drug through our new expanded access treatment IND.

Recognizing that FDA could potentially then grant an EUA very quickly, we will need immediate guidance from BARDA/SNS/HHS on the following issues:

* Distribution: We have developed several alternative options on how Gilead or the government could distribute remdesivir to hospitals in the United States. We want to lay out these options, and get direction on how the Department wants to handle this issue. We need this direction now, if we will need to engage specialty distributors to handle any of the distribution.

* Allocation: In addition to the 7,500 courses of treatment that we have already committed to provide to HHS, plus the additional courses that we are allocating for our U.S. expanded access and clinical trial programs, we need to know how much of our total global supply will need to be allocated to the United States. We have developed several proposals and can walk you through how these would address the medical needs of U.S. patients, sorted by their level of medical need. This decision is time sensitive, as we are also receiving similar requests from European governments requesting supply to meet their urgent public health needs.

* Price: How Gilead can structure the U.S. government's acquisition of remdesivir.

I know that you and your colleagues have all been overwhelmed with demands around ventilators, diagnostics and personal protective equipment. Based on the demand we are already seeing for remdesivir through our expanded access program, we are very concerned that we could see a similar situation develop for the drug, soon after FDA approves an EUA.

In the interest of being transparent and constructive partners with you through this process, we are also going to reach out to the White House, the Vice President's office, HHS Secretary, CMS Administrator and Ambassador Birx to request that we meet and resolve these issues as quickly as possible, in order to ensure that we are able to provide remdesivir to the patients with the greatest medical need as quickly as possible.

As always, I am available on my cell at (b)(6)

Brett Pletcher
EVP, Corporate Affairs, General Counsel and Corporate Secretary Gilead Sciences | Office: 1 (650) 522 6219

Sender:	Disbrow, Gary (OS/ASPR/BARDA) </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0FD5845DEFDA4DC0BB45F8FAC629CF09-DISBROW, GA>
Recipient:	Brett Pletcher <Brett.Pletcher@gilead.com>; Stimson, Brian (HHS/OGC) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=338aa495176d4c92bb314f8f3f51d118-Stimson, Br <Brian.Stimson@hhs.gov>; Chuck Clapton <Chuck.Clapton@gilead.com>
Sent Date:	2020/03/28 11:10:19
Delivered Date:	2020/03/28 11:10:00

From: vinu arumugham <vaccine.safety@aol.com>

To: Sestili, Piero <piero.sestili@uniurb.it>;
<def2004@cumc.columbia.edu>;
<jconigliaro@northwell.edu>;
<ddm1@cumc.columbia.edu>;
<ag3786@cumc.columbia.edu>;
<mo2130@cumc.columbia.edu>;
<jl1333@cumc.columbia.edu>;
<dtuveson@cshl.edu>;
<zj7@cumc.columbia.edu>;
<wt62@cumc.columbia.edu>;
<dwl1@cumc.columbia.edu>;
<tcw21@cumc.columbia.edu>;
<kjtracey@northwell.edu>;
mvcallahan@mgh.harvard.edu /o=ExchangeLabs/ou=Exchange Administrative Group
(FYDIBOHF23SPDLT)/cn=Recipients/cn=20f0e9a3ebeb4ef99d30a96386fb2627-Guest_945f5
<mvcallahan@mgh.harvard.edu>;
<ja660@cumc.columbia.edu>;
<janowitz@cshl.edu>;
<djp65@cam.ac.uk>;
<Darrell.Ricke@ll.mit.edu>;
<[redacted]>;
<yongfeng@email.unc.edu>;
<xphuang@unc.edu>;
<kris.white@mssm.edu>;
<elena.morenodelolmo@mssm.edu>;
<Assaf_Alon@hms.harvard.edu>;
<Andrew_Kruse@hms.harvard.edu>;
<anthony.mittermaier@mcgill.ca>;
<Julianne.Hall@quinnipiac.edu>;
<Robert.Bona@quinnipiac.edu>;
<h.clark@ucl.ac.uk>;
<bryan_roth@med.unc.edu>;
<Victor.Francone@quinnipiac.edu>;
<Norbert.Herzog@quinnipiac.edu>;
<Maurice.Fremont-Smith@quinnipiac.edu>;
<marikpe@evms.edu>;
Commins, Scott P <scommins@email.unc.edu>;
Lawrence Steinman <steiny@stanford.edu>;
<ngkounis@otenet.gr>;
Matzinger, Polly <pcm@helix.nih.gov>;
<pconti@unich.it>

CC: Kadlec, Robert (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group
(FYDIBOHF23SPDLT)/cn=Recipients/cn=a182eda693d040d3832bae6efcf7a255-Kadlec, Rob
<Robert.Kadlec@hhs.gov>;
HHS Secretary (HHS/IOS) /o=ExchangeLabs/ou=Exchange Administrative Group
(FYDIBOHF23SPDLT)/cn=Recipients/cn=5e3fce8f00194d8d94fc91094888d811-HHS Secreta
<secretary@hhs.gov>;
Disbrow, Gary (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group
(FYDIBOHF23SPDLT)/cn=Recipients/cn=0fd5845defda4dc0bb45f8fac629cf09-Disbrow, Ga
<Gary.Disbrow@hhs.gov>;
Christine Laine <claine@acponline.org>;
<fgodlee@bmj.com>;
<howard.bauchner@jamanetwork.org>;
<richard.horton@lancet.com>;
<erubin@hsph.harvard.edu>

Subject: Use mast cell stabilizers, histamine H1/H2 blockers in COVID-19

Date: 2020/07/07 17:43:15

Priority: Normal

Type: Note

Prof. Sestili,

Thank you for your quick response and suggestion.

All,

As Prof. Sestili has suggested, I agree that we should coauthor a paper (or perhaps an open letter like this one?) requesting that authorities rapidly consider and promote the clinical exploitation of medications that address inappropriate mast cell activation and the resulting immune cascade in COVID-19 (these include mast cell stabilizers, histamine H1/H2 blockers, leukotriene antagonists and leukotriene receptor antagonists, Vitamin C, etc.)

We have been able to correctly predict the beneficial effects of these medications since late January 2020 because the mechanism was understood. Hundreds of thousands of lives could have been saved if these medications had been used. If we do not act now, hundreds of thousands more lives will be lost.

Many authors have described the mechanism and role of mast cell dysregulation in severe COVID-19:

Repositioning Chromones for Early Anti-inflammatory Treatment of COVID-19

https://doi.org/10.3389/fphar.2020.00854

COVID-19: Famotidine, Histamine, Mast Cells, and Mechanisms
https://www.researchsquare.com/article/rs-30934/v2

Mast Cells Contribute to Coronavirus-Induced Inflammation: New Anti-Inflammatory Strategy
https://pubmed.ncbi.nlm.nih.gov/32013309/

Immunological mechanisms explaining the role of IgE, mast cells, histamine, elevating ferritin, IL-6, D-dimer, VEGF levels in COVID-19 and dengue, potential treatments such as mast cell stabilizers, antihistamines, Vitamin C, hydroxychloroquine, ivermectin and azithromycin
https://doi.org/10.5281/zenodo.3748303

As I wrote in my comment posted in the Annals of Internal Medicine,

Understanding mechanisms is better than demanding clinical trials in the middle of a pandemic

Please see comments section:

https://protect2.fireeye.com/url?k=3daa65ea-61fe7c96-3daa54d5-0cc47adc5fa2-5378d0b28cd65fc0&u=https://annals.org/aim/fullarticle/2764199/use-hydroxychloroquine-chloroquine-during-covid-19-pandemic-what-every-clinician

Please respond if you would like to be a coauthor and please share any other ideas to make this happen. Please include coworkers who may be interested.

Thanks,

Vinu

On 7/7/20 12:11 AM, Sestili, Piero wrote:

Dear Vinu,

I wrote a paper in March proposing mast cell stabilizers to treat COVID-19 soon after its early clinical presentation.
I am elated to see that many colleagues around the world independently formulated similar thoughts and that evidences are accumulating strengthening this hypothesis.

We could collectively prepare a paper coauthorized by all of us (I see that you have a wide list where Prof. Conti, Prof Kritas and their coworkers could be included) pushing authorities to rapidly consider and promote the clinical exploitation of MCS against COVID.

Here is the DOI of my article
https://doi.org/10.3389/fphar.2020.00854

Please, if you think it might be useful, forward this message to your MCS mail list.

Truly yours and thanks for your relevant effort, ciao

Piero Sestili
Full Professor in Pharmacology,
University of Urbino, Italy

Il giorno mar 7 lug 2020 alle 02:46 vinu arumugham <vaccine.safety@aol.com>ha scritto:

www.bmj.com/content/368/bmj.m1252/rr-1

-------- Forwarded Message --------
SubjectKawasaki disease and COVID-19 are iatrogenic diseases; Try mast cell stabilizers, :H1/H2 blockers
Date: Thu, 14 May 2020 09:42:05 -0700

From: vinu arumugham <vaccine.safety@aol.com>
nchoueit@montefiore.org <nchoueit@montefiore.org>, Brett.Giroir@hhs.gov <Brett.Giroir@hhs.gov>, ufficiostampa@asst-pg23.it <ufficiostampa@asst-pg23.it>, ldantiga@hpg23.it <ldantiga@hpg23.it>, letters@nytimes.com <letters@nytimes.com>, nytnews@nytimes.com <nytnews@nytimes.com>, inytletters@nytimes.com <inytletters@nytimes.com>, editorial@nytimes.com <editorial@nytimes.com>, corrections@nytimes.com <corrections@nytimes.com>, books@nytimes.com <books@nytimes.com>, magazine@nytimes.com <magazine@nytimes.com>, travelmail@nytimes.com <travelmail@nytimes.com>, edu@nytimes.com <edu@nytimes.com>, eileen.murphy@nytimes.com <eileen.murphy@nytimes.com>, danielle.rhoades-ha@nytimes.com <danielle.rhoades-ha@nytimes.com>, booking@nytimes.com <booking@nytimes.com>, bizday@nytimes.com <bizday@nytimes.com>, foreign@nytimes.com <foreign@nytimes.com>, sports@nytimes.com <sports@nytimes.com>, washington@nytimes.com <washington@nytimes.com>, national@nytimes.com <national@nytimes.com>, thearts@nytimes.com <thearts@nytimes.com>, metropolitan@nytimes.com <metropolitan@nytimes.com>, tips@nytimes.com <tips@nytimes.com>, public@nytimes.com <public@nytimes.com>, sarah.mervosh@nytimes.com <sarah.mervosh@nytimes.com>, pam.belluck@nytimes.com <pam.belluck@nytimes.com>, reed.abelson@nytimes.com <reed.abelson@nytimes.com>, (b)(6) <(b)(6)>, n.walsh@medpagetoday.com <n.walsh@medpagetoday.com>, tips@medpagetoday.com <tips@medpagetoday.com>, c.bankhead@medpagetoday.com <c.bankhead@medpagetoday.com>, (b)(6) <(b)(6)>, c.phend@medpagetoday.com <c.phend@medpagetoday.com>, m.walker@medpagetoday.com <m.walker@medpagetoday.com>, ehlavinka@medpagetoday.com <ehlavinka@medpagetoday.com>, iingram@medpagetoday.com <iingram@medpagetoday.com>, k.fiore@medpagetoday.com <k.fiore@medpagetoday.com>, n.lou@medpagetoday.com <n.lou@medpagetoday.com>, Press.Office@exec.ny.gov, r.viner@ucl.ac.uk <r.viner@ucl.ac.uk>, e.whittaker@imperial.ac.uk <e.whittaker@imperial.ac.uk>, m.levin@imperial.ac.uk <m.levin@imperial.ac.uk>, JPIDS.EditorialOffice@oup.com <JPIDS.EditorialOffice@oup.com>, gerberj@email.chop.edu <gerberj@email.chop.edu>, sarah.parker@ucdenver.edu <sarah.parker@ucdenver.edu>, greemd@chp.edu <greemd@chp.edu>, ravi.jhaveri@northwestern.edu <ravi.jhaveri@northwestern.edu>, samir.shah@cchmc.org <samir.shah@cchmc.org>, ashane@emory.edu <ashane@emory.edu>, ilan.youngster@childrens.harvard.edu <ilan.youngster@childrens.harvard.edu>, storch@wustl.edu <storch@wustl.edu>, jsbradley@ucsd.edu <jsbradley@ucsd.edu>, penelope.bryant@mcri.edu.au <penelope.bryant@mcri.edu.au>, chchiu@adm.cgmh.org.tw <chchiu@adm.cgmh.org.tw>, lara.danziger-isakov@cchmc.org <lara.danziger-isakov@cchmc.org>, dhunstad@wustl.edu <dhunstad@wustl.edu>, Huskins.Charles@mayo.edu <Huskins.Charles@mayo.edu>,
To: mlaufer@medicine.umaryland.edu <mlaufer@medicine.umaryland.edu>,

latania_logan@rush.edu <latania_logan@rush.edu>, fernando.p.polack@vanderbilt.edu <fernando.p.polack@vanderbilt.edu>, Adam.Ratner@nyulangone.org <Adam.Ratner@nyulangone.org>, jennifer_read@nih.gov <jennifer_read@nih.gov>, jr3@ualberta.ca <jr3@ualberta.ca>, Lrubin@lij.edu <Lrubin@lij.edu>, Ls5@cumc.columbia.edu <Ls5@cumc.columbia.edu>, mike.sharland@stgeorges.nhs.uk <mike.sharland@stgeorges.nhs.uk>, bill.steinbach@duke.edu <bill.steinbach@duke.edu>, ptamma1@jhmi.edu <ptamma1@jhmi.edu>, ttan@northwestern.edu <ttan@northwestern.edu>, jvallejo@bcm.edu <jvallejo@bcm.edu>, a.warris@abdn.ac.uk <a.warris@abdn.ac.uk>, CGIDRadmin@seattlechildrens.org <CGIDRadmin@seattlechildrens.org>, danielle.zerr@seattlechildrens.org <danielle.zerr@seattlechildrens.org>

Kawasaki disease (KD) and COVID-19 are iatrogenic diseases; Try mast cell stabilizers, H1/H2 blockers.

KD shock syndrome is same mechanism as influenza and dengue shock syndrome covered below ("slow rolling anaphylaxis").

https://twitter.com/ArumughamVinu/status/1259659169046474753?s=20

One can also expect peripheral blood eosinophilia. Have you checked? RCPCH case definition does not include it.

That would be consistent with the body's (iatrogenically induced) anti-parasite response against SARS-CoV-2, instead of just an antiviral response. Consider IgE/IgG4 responses against heat shock proteins.

Immunological mechanisms explaining the role of IgE, mast cells, histamine, elevating ferritin, IL-6, D-dimer, VEGF levels in COVID-19 and dengue, potential treatments such as mast cell stabilizers, antihistamines, Vitamin C, hydroxychloroquine, ivermectin and azithromycin

https://doi.org/10.5281/zenodo.3748303

As I have been predicting for 3+ months, there is now evidence that Famotidine (antihistamine, H2-blocker) helps in COVID-19. Study below. The mechanism involved is explained above.

Famotidine Use is Associated with Improved Clinical Outcomes in Hospitalized COVID-19 Patients: A Retrospective Cohort Study

https://www.medrxiv.org/content/10.1101/2020.05.01.20086694v1

Root cause of COVID-19? Biotechnology's dirty secret: Contamination. Bioinformatics evidence demonstrates that SARS-CoV-2 was created in a laboratory, unlikely to be a bioweapon but most likely a result of sloppy experiments

https://doi.org/10.5281/zenodo.3766462

My comment posted in the Annals of Internal Medicine:

Please see comments section:

https://protect2.fireeye.com/url?k=a9af94e0-f5fb8d9c-a9afa5df-0cc47adc5fa2-df9665c0b2775641&u=https://annals.org/aim/fullarticle/2764199/use-hydroxychloroquine-chloroquine-during-covid-19-pandemic-what-every-clinician

Understanding mechanisms is better than demanding clinical trials in the middle of a pandemic

Hydroxychloroquine and azithromycin use in COVID-19 have been dismissed as "unproven" or "anecdotal", by the medical establishment. But the benefit of ventilators in COVID-19 is equally unproven. Why the clamor for ventilators? And now there are reports that ventilators are not helping. https://www.npr.org/sections/health-shots/2020/04/02/826105278/ventilators-are-no-panacea-for-critically-ill-covid-19-patients

Running protein sequence analysis with the SARS-CoV-2, MERS, SARS viruses, there is a strong similarity to a pig spike protein (coronavirus infected pig). Accession number QGV12786 vs. QHD43416.1 for SARS-CoV-2.

Since vaccines contain porcine proteins derived from pigs infected with any number of diseases, one could develop IgE mediated sensitization to coronavirus spike proteins. We have entire, viable porcine circoviruses in the rotavirus vaccines, for example.
https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/b/excipient-table-2.pdf

Upon infection with any of these viruses, the concurrent allergic reaction can increase disease severity. In such cases, antihistamines and other allergy treatments such as mast cell stabilizers may help reduce infection severity.
This is similar to influenza vaccine induced allergy to the influenza virus, increasing the severity of subsequent influenza infection as described here:

Influenza vaccines and dengue-like disease
https://www.bmj.com/content/360/bmj.k1378/rr-15

There have been reports that elevated ferritin and IL-6 levels are predictors of fatality in COVID-19.
https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30628-0/fulltext

There is an increase in mast cell density during infections:
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4435071/

IgE mediated mast cell degranulation results in increased ferritin levels as well as histamine levels.

Ferritin Particles Accumulate in Human Mast Cell Secretory Granules and Are Released upon FcεRI-mediated Activation
https://protect2.fireeye.com/url?k=a30e59ec-ff5a4090-a30e68d3-0cc47adc5fa2-93b2fd36e460cfa7&u=https://www.jacionline.org/article/S0091-6749(17)32622-2/fulltext

Histamine promotes release of IL-6.

Histamine Promotes the Release of Interleukin-6 via the H1R/p38 and NF-κB Pathways in Nasal Fibroblasts
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4214978/

Also, neutrophils recruited to the lung during infection can release histamine.

Neutrophil histamine contributes to inflammation in mycoplasma pneumonia.
https://www.ncbi.nlm.nih.gov/pubmed/17158962

The antihistamine effect of Vitamin C IV seems to help.

Antihistamine effect of supplemental ascorbic acid and neutrophil chemotaxis

https://www.ncbi.nlm.nih.gov/pubmed/1578094

https://www.nutraingredients.com/Article/2020/03/25/Hospital-turns-to-high-dose-vitamin-C-to-fight-coronavirus

Also, azithromycin reduces histamine induced inflammation.

The anti-inflammatory effects of erythromycin, clarithromycin, azithromycin and roxithromycin on histamine-induced otitis media with effusion in guinea pigs.
https://www.ncbi.nlm.nih.gov/pubmed/29888693

Hydroxychloroquine helps in allergic asthma.

Hydroxychloroquine improves airflow and lowers circulating IgE levels in subjects with moderate symptomatic asthma.
https://www.ncbi.nlm.nih.gov/pubmed/9723661

Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial
https://www.sciencedirect.com/science/article/pii/S0924857920300996
https://protect2.fireeye.com/url?k=4fcadd66-139ec41a-4fcaec59-0cc47adc5fa2-b42c2cf989ad9b11&u=https://www.mediterranee-infection.com/covid-19/

So there are many indicators pointing to the role of mast cell degranulation/histamine release being a major component of COVID-19.
Antihistamines, mast cell stabilizers, Vitamin C, hydroxychloroquine, azithromycin may all address different aspects of this same problem.
Focusing on only the antiviral actions of hydroxychloroquine or azithromycin, will lead us into blind alleys.

--
Prof. Piero Sestili
Ordinario di Farmacologia
Dipartimento di Scienze Biomolecolari,
Università degli Studi di Urbino Carlo Bo
Via "I Maggetti" 26 61029 URBINO (PU)
Phone +39 (0)722 303414;
https://scholar.google.it/citations?user=wlJcsW4AAAAJ&hl=it
https://www.uniurb.it/persone/piero-sestili

Sender: vinu arumugham <vaccine.safety@aol.com>

Recipient:
Sestili, Piero <piero.sestili@uniurb.it>;
<def2004@cumc.columbia.edu>;
<jconigliaro@northwell.edu>;
<ddm1@cumc.columbia.edu>;
<ag3786@cumc.columbia.edu>;
<mo2130@cumc.columbia.edu>;
<jl1333@cumc.columbia.edu>;
<dtuveson@cshl.edu>;
<zj7@cumc.columbia.edu>;
<wt62@cumc.columbia.edu>;
<dwl1@cumc.columbia.edu>;
<tcw21@cumc.columbia.edu>;
<kjtracey@northwell.edu>;
mvcallahan@mgh.harvard.edu /o=ExchangeLabs/ou=Exchange Administrative Group
(FYDIBOHF23SPDLT)/cn=Recipients/cn=20f0e9a3ebeb4ef99d30a96386fb2627-Guest_945f5
<mvcallahan@mgh.harvard.edu>;
<ja660@cumc.columbia.edu>;
<janowitz@cshl.edu>;
<djp65@cam.ac.uk>;
<Darrell.Ricke@ll.mit.edu>;
[redacted];
<yongfeng@email.unc.edu>;
<xphuang@unc.edu>;
<kris.white@mssm.edu>;
<elena.morenodelolmo@mssm.edu>;
<Assaf_Alon@hms.harvard.edu>;
<Andrew_Kruse@hms.harvard.edu>;
<anthony.mittermaier@mcgill.ca>;
<Julianne.Hall@quinnipiac.edu>;
<Robert.Bona@quinnipiac.edu>;
<h.clark@ucl.ac.uk>;
<bryan_roth@med.unc.edu>;
<Victor.Francone@quinnipiac.edu>;
<Norbert.Herzog@quinnipiac.edu>;
<Maurice.Fremont-Smith@quinnipiac.edu>;
<marikpe@evms.edu>;
Commins, Scott P <scommins@email.unc.edu>;
Lawrence Steinman <steiny@stanford.edu>;
<ngkounis@otenet.gr>;
Matzinger, Polly <pcm@helix.nih.gov>;
<pconti@unich.it>;
Kadlec, Robert (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group
(FYDIBOHF23SPDLT)/cn=Recipients/cn=a182eda693d040d3832bae6efcf7a255-Kadlec, Rob
<Robert.Kadlec@hhs.gov>;
HHS Secretary (HHS/IOS) /o=ExchangeLabs/ou=Exchange Administrative Group
(FYDIBOHF23SPDLT)/cn=Recipients/cn=5e3fce8f00194d8d94fc91094888d811-HHS Secreta

	<secretary@hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0fd5845defda4dc0bb45f8fac629cf09-Disbrow, Ga <Gary.Disbrow@hhs.gov>; Christine Laine <claine@acponline.org>; <fgodlee@bmj.com>; <howard.bauchner@jamanetwork.org>; <richard.horton@lancet.com>; <erubin@hsph.harvard.edu>
Sent Date:	2020/07/07 17:41:59
Delivered Date:	2020/07/07 17:43:15

OWS Board Update

Vaccines - Therapeutics

OCTOBER 1ST 2020

Vaccines

Data as of 30SEP2020

Candidate updates | Vaccines

Platform	Developer		Updates / risks
Nucleic acid	moderna	↑	• NEJM manuscript on Phase 1 older cohorts published on 29 Sep 2020 • Trialscope/CVS Health bringing in pre-screened African Americans; on track for 30K enrolled by mid Oct, two-month safety / efficacy monitoring median (15K) will occur on 11/24 • Catalent can now support 15 add'l fill lines, resulting in 20M more doses if all runs succeed as planned
	BIONTECH Pfizer	⊖	• Pfizer requesting that two-month safety/ efficacy monitoring be based on median of 15K patients, instead of 22K patients; if 15K, will reach on ~11/15, if 22K, will reach on ~11/22 • Delivery logistics remain complicated; diluent, kits, shipping, dry ice, administration site complexities • Pfizer is considering sending liaisons to be on-site at both CDC & OWS logistics planning HQs
Viral vector	UNIVERSITY OF OXFORD AstraZeneca	⊖	• Full response to FDA and US DSMB to be submitted Friday; enrollment is likely to be negatively affected by SUSAR (60 sites ready to enroll) • PPQ 1 began in Emergent on 9/28; 1st GMP lot completed in Suite 1, awaiting testing results; 2nd GMP lot started in Suite 3
	janssen	↓	• Single dose data from Phase 1 elderly cohort reviewed on 9/28 • Phase 3 enrollment has been very slow (150 enrolled as of 9/29); actively working with IQVIA, CoVPN, VA to accelerate site activation and enrollment • Current low dose creates opportunity to increase DS output; team exploring if F/F capacity is sufficeint
	MERCK	⊖	• VSV program on track to initiate phase 1 trial in late Oct., pathway to phase 3 is at risk based on NHP efficacy
Protein sub-unit	NOVAVAX Creating Tomorrow's Vaccines Today	⊖	• UK Phase 3: enrollment started 9/28 (n=9K, 1:1 ratio, using 50L material from Emergent) • US Phase 3: Site selection and readiness ongoing; revised protocol to be submitted to FDA by 10/2 • Believed to have identified root cause for run failures, insufficient antigen generation due to poor infection; RTP GMP run 5 (scheduled for 10/2) will have adjustments based on findings
	gsk SANOFI	⊖	• Repeat of NHP Challenge study at VRC initiated • Drug Substance batch 3 (Tech run) completed; analysis of samples ongoing • Phase 3 trial preparations on track with site selection underway

Therapeutics

Date updated: 9/30/20

OWS Therapeutics PCT Updates | Candidate summary

Developer	Key Updates / Areas for Leadership Input
(b)(3):42 U.S.C. § 247d-6b(d)	

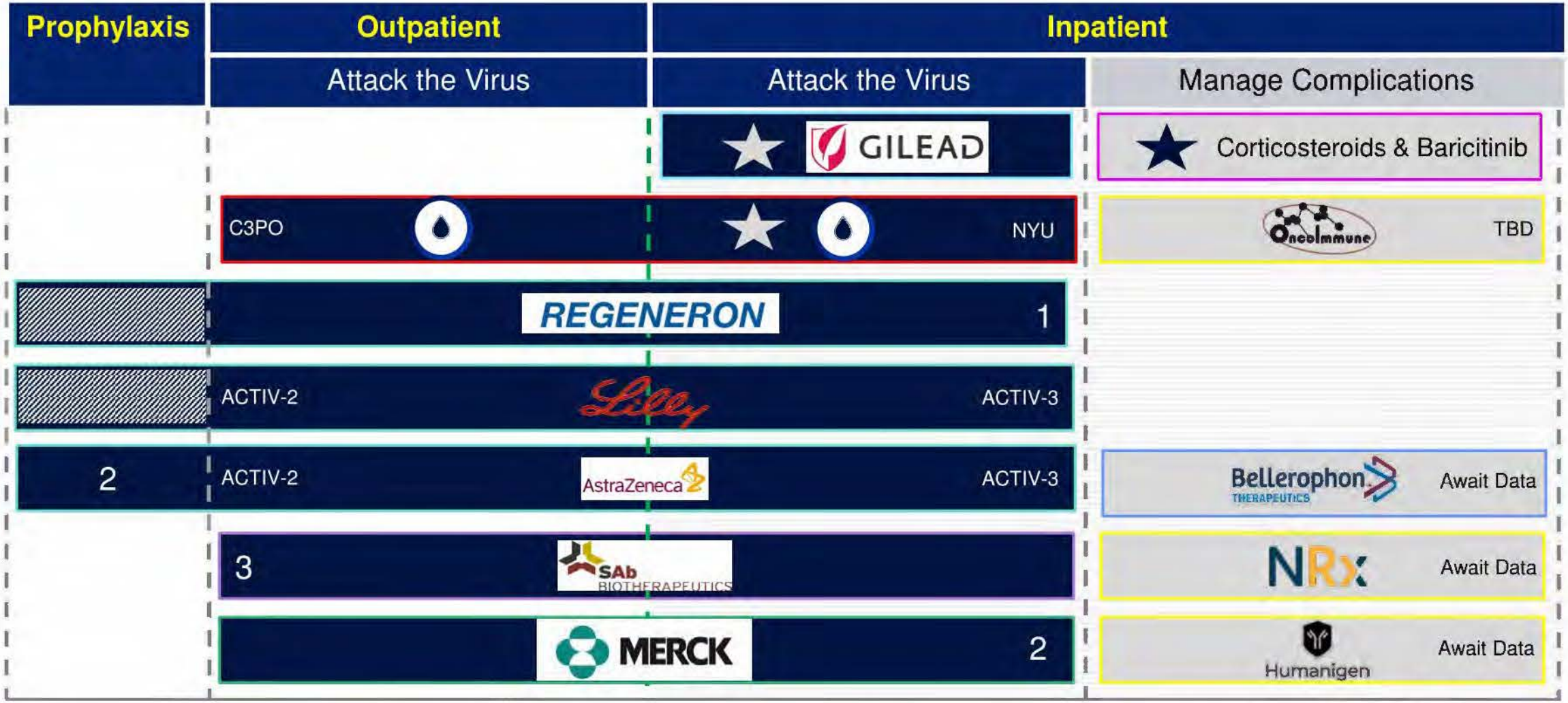
1. Inpatient (IP)

Ideal Target Product Profile for Therapeutics Supported by OWS

Requirements for all therapeutics regardless of indication/formulation:

- Strong safety profile
- Clear target treatment population
- Clinical proof of concept expected by end of year
- EUA expected ideally by end of year but no later than the end of Q1 2021
- 100,000-300,000 doses ideally by end of year but no later than the end of Q1 2021

	Prophylaxis	Outpatient	Inpatient
Oral	-----	**Broader population use** • Reduction of – Hospitalization rate: 30%+ – Symptoms: 30%+	**Stage 2** • Reduction of – Hospitalization length – Progression to ventilator – Mortality **Stage 3 (ventilated patients)** • Reduction of – Hospitalization length – Time on ventilator – Mortality
Intramuscular / Subcutaneous	**nAbs** • Efficacy: 80%+ • Duration of protection: 6mo+ • Covers escape mutants: yes – 2+ Ab cocktail preferred		
Intravenous	-----	**Use in high risk population only** • Reduction of hospitalization rate (30%+)	



Monoclonals | Convalescent Plasma | Immune Modulators | BSA

Polyclonal | Oral Antiviral | Vasodilator | Anticoag

Potential use; not primary focus of OWS

EUA/EAP or Repurposed

1: Considering ACTIV-3
2: Industry lead trials
3: Requesting ACTIV-2

Lilly and Regeneron: Comparison of interim analysis outpatient data

	Lilly	Regeneron
Patient population analyzed	Ambulatory population	Ambulatory population
Number of patients	452 patients • 302 LY-CoV555 & 150 placebo	275 patients (45% [123/275] patients seronegative) • 1:1:1 randomized (high dose : low dose : placebo)
Doses tested	Single IV dose • 0.7g, 2.8g or 7g of LY-CoV555 (monotherapy)	Single IV dose • 2.4g (low) or 8g (high) or of REGN-COV2 (2 mAb cocktail)
Viral load reduction	Primary endpoint (D11): • Significance only met for 2.8g LY-CoV555 arm • Most patients in all arms (including placebo) demonstrated near complete viral clearance by day 11 • At earlier timepoints, viral load reduction seen in all treatment arms	Primary virology endpoint (D7) peak viral load 10^5-10^7: • Both doses performed similarly – Log reduction: high dose (-1.79) & low dose (-2.00) – Between 50-99% total reduction compared to placebo • Negative serological status drove overall viral load reduction effect in full population
Reduction in hospitalization & symptoms	~72% reduction in rate of hospitalizations and ER visits • Based on pooled analysis of all treatment arms – 6% in placebo (9/150) – 1.7% in LY-CoV555 (5/302)	10/12 medically-attended visits[1] occurred in seronegative patients • 15.2% placebo-treated patients • 7.7% high dose patients • 4.9% low dose patients Symptom duration reduced in treatment arm • 13 days in placebo vs. 8/6 days in low/high dose, respectively
Tx resistant variants	• 6% in placebo • 8% across pooled treatment arms	TBD
SAEs	No drug-related SAEs reported across all doses	SAE in 2 placebo patients & 1 low dose patient

1. Defined as hospitalizations, or emergency room, urgent care or telemedicine visits for COVID-19
Note: Regeneron analysis shown only for seronegative population

Immune modulator: (b)(3):42 U.S.C. § 247d-6b(d)

MoA	Current indication & dosing	Covid-19 use case	Manufacturing scale	Existing efficacy evidence[4]	Key risks
(b)(3):42 U.S.C. § 247d-6b(d)					

Trial[1]	Overview	(b)(3):42 U.S.C. § 247d-6b(d)	Jan	Feb	Mar	April	May	Next steps if positive readout
(b)(3):42 U.S.C. § 247d-6b(d)								• Consider support of scale up manufacturing • Consider inclusion in platform clinical trial to test in ICU pts **Asks of OWS** • Mfg expertise and assistance in securing mfg capacity • (b)(3):42 U.S.C. § 247d-6b(d)

of 9/16/20)

(b)(3):42 U.S.C. § 247d-6b(d)

3. Assumes 5 days from LPO based on Oncoimmune's original timeline; accounts for 1 week delay announced 9/2; topline data could be available by end of Sept if DSMB recommends early termination for superior efficacy
4. From OncoImmune presentation on 09/17

(b)(3):42 U.S.C. § 247d-6b(d)

(b)(3):42 U.S.C. § 247d-6b(d)

(b)(3):42 U.S.C. § 247d-6b(d)


DEPARTMENT OF HEALTH & HUMAN SERVICES
USA


OPERATION
WARP SPEED


DEPARTMENT OF DEFENSE
UNITED STATES OF AMERICA

Thank you!

From:	Marinissen, Maria (HHS/OS/OGA) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=5D42FB4D94B041EE88E4F7DD5743E893-MARINISSEN, <Maria.Marinissen@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>
Subject:	Question remdesivir - US Embassy
Date:	2020/05/07 16:09:28
Priority:	Normal
Type:	Note

Dear Gary,
How are you? hearing all going on there and for you now as Acting Director so will make this short.....
We are having a lot of questions from the Mexican Government and private hospitals directed to the Ambassador here about access to remdesivir and wonder if I can talk to someone in your team to understand the terms of use under EUA. It talks about a "USG agency" that will get the product and guide its distribution. FDA tells me it is ASPR.
So, do we own the product or we just distribute it? If MExico wants access, do they need to talk to Gilead directly? Or we got it all?
Please let me know if you have 5 min to chat or if there is someone in your team I can talk with briefly.
Thanks much!
María Julia

Sent from my iPhone

Sender:	Marinissen, Maria (HHS/OS/OGA) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=5D42FB4D94B041EE88E4F7DD5743E893-MARINISSEN, <Maria.Marinissen@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>
Sent Date:	2020/05/07 16:09:27
Delivered Date:	2020/05/07 16:09:28

FBI Warns Chinese Government Targeting Healthcare and Public Health Sector

Executive Summary

The Federal Bureau of Investigation (FBI) Director recently warned that China is attempting to compromise entities in the Healthcare and Public Health (HPH) Sector conducting COVID research. Previously the FBI stated it was investigating attacks by the Chinese military and other Chinese hackers against entities conducting COVID research. On June 9, HC3 briefed that Chinese or suspected Chinese Advance Persistent Threats (APTs) had targeted entities within the HPH Sector that dealt with healthcare, medical devices, pharmaceuticals, biotechnology, and scientific research and consulting. In addition to cyberattacks, U.S.-based Chinese scientists—some of which are naturalized American citizens—are stealing intellectual property to the benefit of the Chinese government. **Mitigation strategies are provided in the full report.** ***Given the frequency of U.S. government warnings and the importance of a COVID-19 vaccine, HC3 analysts assess with high confidence that the Chinese government will maintain or increase its targeting of the U.S. HPH Sector.***

Report

On July 7, 2020, the Washington Post reported that FBI Director Christopher A. Wray warned that "At this very moment, China is working to compromise American health-care organizations, pharmaceutical companies and academic institutions conducting essential COVID-19 research." In May, a joint statement by the FBI and the Department of Homeland Security stated the FBI was investigating "the targeting and compromise of U.S. organizations conducting COVID-19-related research" by the Chinese military and other Chinese hackers. Their investigations showed that Chinese actors were targeting "intellectual property and public health data related to vaccines, treatments, and testing from networks and personnel affiliated with COVID-19-related research."

On June 9, HC3 briefed that Chinese or suspected Chinese Advance Persistent Threats (APTs) had targeted entities within the HPH Sector that dealt with healthcare, medical devices, pharmaceuticals, biotechnology, and scientific research and consulting. The Chinese or suspected Chinese groups identified by HC3 included:

- APT1
- APT 10
- APT18
- APT41
- Deep Panda

In addition to cyberattacks, the Chinese government has benefited from medical research and patents stolen by U.S.-based Chinese scientists, some of which were naturalized American citizens. As of November 2019, "71 institutions, including many of the most prestigious medical schools in the United States" were investigating potential theft of intellectual property. The majority of the investigations related to biomedical research.

Analyst Comment

Given the frequency of U.S. government warnings and the importance of a COVID vaccine, HC3 analysts assess with high confidence that the Chinese government will maintain or increase its targeting of the U.S. HPH Sector. The following actions could mitigate the risk posed by Chinese APTs:

1. Understand Chinese APT tactics, techniques, and procedures, including historical attacks and targeted vulnerabilities.
2. Keep systems updated with the most recent patches and prioritize patching for the most at risk systems based on the TTPs identified in bullet "1."
3. Increase the identification and ingestion of Chinese APT indicators of compromise.
4. Have and practice an incident response plan.

Global Intelligence Note

10 July 2020

SensiGuard. SUPPLY CHAIN INTELLIGENCE CENTER

The SensiGuard® Supply Chain Intelligence Center (SCIC) presents a summary of major incidents and news articles relating to cargo theft and intelligence for the week ending 10 July 2020.

EMEA

Germany

8 July 2020: Tarpaulin slashers were active on the Rodablick parking lot on the A4 towards **Frankfurt**. Shortly after 2:00 p.m., it was noticed that the tarpaulins of four trucks had been damaged by perpetrators to inspect the load. In one of the attacked trucks, they saw worthwhile loot and set about stealing loudspeaker components with a total value of €69,000. So far, there is no evidence of the perpetrators or the vehicles they used to transport the high value cargo.
Read more: PressePortal (Germany)

8 July 2020: Unknown perpetrators cut open the tarpaulins of several trucks in parking lots along Autobahn 7 and stole part of the loads. In the parking lot Schlochau-Ost in the Northeim district, the loading area of a Polish semitrailer was cut open; the thieves stole three table grills.
Read more: HNA (Germany)

From:	Redd, John (OS/ASPR/IO) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=9BA3FED4EE8646EC849A5A87136A24F6-REDD, JOHN <John.Redd@hhs.gov>
To:	Bugin, Kevin (FDA/CDER) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=55c4e5e4038442ff8866f40f603e52ce-kevin.bugin <Kevin.Bugin@fda.hhs.gov>; Woodcock, Janet (FDA/CDER) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5f925e9a0f9147b186d40072d474d13d-janet.woodc <Janet.Woodcock@fda.hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0fd5845defda4dc0bb45f8fac629cf09-Disbrow, Ga <Gary.Disbrow@hhs.gov>
CC:	Thompson, Donna (OS/ASPR/IO) (CTR) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=21f88b26c3544e0aa1ca6b5e71df37da-Thompson, D <Donna.Thompson@hhs.gov>; Johnson, Kelly J. (OS/ASPR/SPPR) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=48bfdc5bee0349a2840980ec07ddc5e2-Johnson, Ke <Kelly.Johnson@hhs.gov>; Thomas, Ashley (FDA/CDER) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=6bcf9a5e75bc42dea48e4009c5342397-ashley.thom <Ashley.Thomas@fda.hhs.gov>
Subject:	Discussion on Distribution Learnings - Remdesivir with OWS
Date:	2020/07/20 08:57:15
Start Date:	2020/07/20 16:00:00
End Date:	2020/07/20 16:30:00
Priority:	Normal
Type:	Schedule.Meeting.Request
Location:	WebEx Meeting - Dial In: 415-527-5035,,,1996534105##
Attendees:	Bugin, Kevin (FDA/CDER); Woodcock, Janet (FDA/CDER); Disbrow, Gary (OS/ASPR/BARDA); Thompson, Donna (OS/ASPR/IO) (CTR); Johnson, Kelly J. (OS/ASPR/SPPR) (Kelly.Johnson@hhs.gov); Thomas, Ashley (FDA/CDER)

Purpose to discuss:

- **Overall lessons learned from the Remdesivir experience**
- **Role of USG in distribution & allocation of doses**
- **Data tracking systems and USG responsibilities as the EUA holder**
- **Reimbursement for drug and non-drug costs associated with the infusion**

I would also like to include Gary from BARDA in this discussion so we can discuss this in the context of our existing contract structures (e.g. Regeneron).

POC: Kevin Bugin (FDA)

-- Do not delete or change any of the following text. --
When it's time, join your Webex meeting here.

Meeting number (access code): (b)(6)

Meeting password: (b)(6)

Join meeting

Tap to join from a mobile device (attendees only)
+1-415-527-5035,,1996534105## US Toll
+1-929-251-9612,,1996534105## USA Toll 2

Join by phone
+1-415-527-5035 US Toll
+1-929-251-9612 USA Toll 2
Global call-in numbers

Join from a video system or application
Dial 1996534105@hhs.webex.com

Join using Microsoft Lync or Microsoft Skype for Business

Dial 1996534105.hhs@lync.webex.com

If you are a host, click here to view host information.

Need help? Go to http://help.webex.com

Sender:	Redd, John (OS/ASPR/IO) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=9BA3FED4EE8646EC849A5A87136A24F6-REDD, JOHN <John.Redd@hhs.gov>
Recipient:	Bugin, Kevin (FDA/CDER) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=55c4e5e4038442ff8866f40f603e52ce-kevin.bugin <Kevin.Bugin@fda.hhs.gov>; Woodcock, Janet (FDA/CDER) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5f925e9a0f9147b186d40072d474d13d-janet.woodc <Janet.Woodcock@fda.hhs.gov>;

	Disbrow, Gary (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0fd5845defda4dc0bb45f8fac629cf09-Disbrow, Ga <Gary.Disbrow@hhs.gov>; Thompson, Donna (OS/ASPR/IO) (CTR) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=21f88b26c3544e0aa1ca6b5e71df37da-Thompson, D <Donna.Thompson@hhs.gov>; Johnson, Kelly J. (OS/ASPR/SPPR) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=48bfdc5bee0349a2840980ec07ddc5e2-Johnson, Ke <Kelly.Johnson@hhs.gov>; Thomas, Ashley (FDA/CDER) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=6bcf9a5e75bc42dea48e4009c5342397-ashley.thom <Ashley.Thomas@fda.hhs.gov>
Sent Date:	2020/07/20 08:57:13
Delivered Date:	2020/07/20 08:57:15

From:	Redd, John (OS/ASPR/SPPR) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=9BA3FED4EE8646EC849A5A87136A24F6-REDD, JOHN <John.Redd@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:	Blatner, Gretta (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=623cb123c2324236b1db6fb9153e0bbf-Blatner, Gr <Gretta.Blatner@hhs.gov>; Oxner, Julie (OS/ASPR/OEA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f96241c6a5f8401a9a218c259f2e614a-Oxner, Juli <Julie.Oxner@hhs.gov>
Subject:	Re: Congressional Testimony
Date:	2020/06/29 06:13:42
Priority:	Normal
Type:	Note

Up-to-date amounts and destinations and a description of the program are found at:

https://www.phe.gov/emergency/events/COVID19/investigation-MCM/Pages/remdesivir.aspx

Just in case

Break a leg!

On Jun 28, 2020, at 10:40 AM, Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>wrote:

Thanks John

Sent from my iPhone

On Jun 28, 2020, at 10:34 AM, Redd, John (OS/ASPR/SPPR) <John.Redd@hhs.gov>wrote:

Sure:

- 940,000 vials donated were donated to HHS in early May
- Enough for at least 120,512 patient courses
- Began distributing on May 4
- Product has gone to all 50 states, Puerto Rico, the US Virgin Islands, the District of Columbia, all of the Pacific &Affiliated Territories (Guam, CNMI, Palau, American Samoa, Marshall Islands, and the Federated States of Micronesia), the Department of Defense, the Veterans Health Administration, the Indian Health Service, and the the State Department.
- As of June 29, all donated product will be allocated. The last shipments go out on June 29th and will be in states by the 4th of July Weekend.

- Donated product is allocated to State Departments of Health based upon proportion by state of the total number of hospitalized patients with confirmed or suspected COVID-19 infection. Then states distribute the medicine to hospitals in their state.
- The USG is not holding any in reserve - all of the donated product will be going to hospitals.
- We are working with Gilead and Amerisource Bergen on plans for the next 2-3 months.

Thanks and ask anything you'd like -

John

On Jun 28, 2020, at 9:30 AM, Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>wrote:

John,

Can you address the questions below for my congressional testimony?

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: [redacted]
Fax: 202-205-0873
email: Gary.Disbrow@HHS.gov

From: Gorman, Susan (ASPR/SNS) <spg4@cdc.gov>
Sent: Sunday, June 28, 2020 9:23 AM
To: Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Adams, Steven A. (ASPR/SNS) <saa1@cdc.gov>
Cc: Oxner, Julie (OS/ASPR/OEA) <Julie.Oxner@hhs.gov>; Blatner, Gretta (OS/ASPR/BARDA)

<Gretta.Blatner@hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>
Subject: Re: Congressional Testimony

Hi Gary
SNS was not involved with this, John Redd was in charge of this for ASPR. However I believe there was distro occurring during June and the last of the product was set to go out June 29. He would be able to confirm.
Sue

Get Outlook for iOS

From: Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>
Sent: Sunday, June 28, 2020 9:15:02 AM
To: Adams, Steven A. (ASPR/SNS) <saa1@cdc.gov>; Gorman, Susan (ASPR/SNS) <spg4@cdc.gov>
Cc: Oxner, Julie (OS/ASPR/OEA) <Julie.Oxner@hhs.gov>; Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>
Subject: Congressional Testimony

Steve and Sue,

Remdesivir question

Response states

940,000 vials donated
Enough for 120,512 individuals
Began distributing in May
As of May 29 all donated product had been distributed

Is that date correct? That is a month ago. Is there more to distribute or where is it coming from now. Did we reserve any? If so, why?

Thanks

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.

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

Sender:	Redd, John (OS/ASPR/SPPR) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=9BA3FED4EE8646EC849A5A87136A24F6-REDD, JOHN <John.Redd@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>; Blatner, Gretta (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=623cb123c2324236b1db6fb9153e0bbf-Blatner, Gr <Gretta.Blatner@hhs.gov>; Oxner, Julie (OS/ASPR/OEA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f96241c6a5f8401a9a218c259f2e614a-Oxner, Juli <Julie.Oxner@hhs.gov>
Sent Date:	2020/06/29 06:13:41
Delivered Date:	2020/06/29 06:13:42

From:	Johnston, Darcie (HHS/IEA) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=F6A8047840CA4406B5AC6BC5CF259937-JOHNSTON, D <Darcie.Johnston@hhs.gov>
To:	Waters, Cicely (OS/ASPR/OEA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=00e638c4ddf64006bcc009e8032dd700-Waters, Cic <Cicely.Waters@hhs.gov>; Trueman, Laura (HHS/IEA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=99dcba4c6ea342c08d58f63e37d997e7-Trueman, La <Laura.Trueman@hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0fd5845defda4dc0bb45f8fac629cf09-Disbrow, Ga <Gary.Disbrow@hhs.gov>; Baker, Michael (OS/IEA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0d44d4176f724d7b92d08f5f989fbfd9-Baker, Mich <Michael.Baker@hhs.gov>; Stevens, Lee (OS/IEA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=user414941c7 <Lee.Stevens@hhs.gov>
Subject:	RE: TPs for regional reps regarding remdesivir
Date:	2020/06/29 08:37:03
Priority:	Normal
Type:	Note

Thank you Cicely.

Darcie L. Johnston
Director, Intergovernmental Affairs
U.S. Department of Health and Human Services
Office of the Secretary
202-690-1058 (office)
(b)(6) (cell)

From: Waters, Cicely (OS/ASPR/OEA) <Cicely.Waters@hhs.gov>
Sent: Monday, June 29, 2020 7:56 AM
To: Trueman, Laura (HHS/IEA) <Laura.Trueman@hhs.gov>; Johnston, Darcie (HHS/IEA) <Darcie.Johnston@hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Baker, Michael (OS/IEA) <Michael.Baker@hhs.gov>; Stevens, Lee (OS/IEA) <Lee.Stevens@hhs.gov>
Subject: TPs for regional reps regarding remdesivir

Good morning, Team IEA:
For your awareness, ASPR plans to issue the attached document to our RECs around 0900 today.

v/r
Cicely

Cicely L. Waters
Director, Office of External Affairs
Assistant Secretary for Preparedness and Response
U.S. Department of Health and Human Services
200 C St, SW Washington, D.C. 20201
(o) 202-205-0714 (m) (b)(6)
cicely.waters@hhs.gov

Sender:	Johnston, Darcie (HHS/IEA) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=F6A8047840CA4406B5AC6BC5CF259937-JOHNSTON, D <Darcie.Johnston@hhs.gov>
Recipient:	Waters, Cicely (OS/ASPR/OEA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=00e638c4ddf64006bcc009e8032dd700-Waters, Cic <Cicely.Waters@hhs.gov>; Trueman, Laura (HHS/IEA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=99dcba4c6ea342c08d58f63e37d997e7-Trueman, La <Laura.Trueman@hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0fd5845defda4dc0bb45f8fac629cf09-Disbrow, Ga <Gary.Disbrow@hhs.gov>; Baker, Michael (OS/IEA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0d44d4176f724d7b92d08f5f989fbfd9-Baker, Mich <Michael.Baker@hhs.gov>; Stevens, Lee (OS/IEA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=user414941c7 <Lee.Stevens@hhs.gov>
Sent Date:	2020/06/29 08:37:02
Delivered Date:	2020/06/29 08:37:03

From:	Johnson, Kelly J. (OS/ASPR/SPPR) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=48BFDC5BEE0349A2840980EC07DDC5E2-JOHNSON, KE <Kelly.Johnson@hhs.gov>
To:	Bugin, Kevin (FDA/CDER) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=55c4e5e4038442ff8866f40f603e52ce-kevin.bugin <Kevin.Bugin@fda.hhs.gov>; Woodcock, Janet (FDA/CDER) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5f925e9a0f9147b186d40072d474d13d-janet.woodc <Janet.Woodcock@fda.hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0fd5845defda4dc0bb45f8fac629cf09-Disbrow, Ga <Gary.Disbrow@hhs.gov>; Lawlor, Ciarán <Lawlor.Ciaran@bcg.com>
CC:	Redd, John (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=9ba3fed4ee8646ec849a5a87136a24f6-Redd, John <John.Redd@hhs.gov>; Thompson, Donna (OS/ASPR/IO) (CTR) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=21f88b26c3544e0aa1ca6b5e71df37da-Thompson, D <Donna.Thompson@hhs.gov>; Thomas, Ashley (FDA/CDER) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=6bcf9a5e75bc42dea48e4009c5342397-ashley.thom <Ashley.Thomas@fda.hhs.gov>; Tewell, Adam (OS/OGA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0172af5d4c93452ea236821fffba4be6-Tewell, Ada <Adam.Tewell@hhs.gov>
Subject:	RE: Follow Up: Meeting - Discussion on Distribution Learnings - Remdesivir with OWS
Date:	2020/07/21 10:06:07
Priority:	Normal
Type:	Note

Hello Kevin:

Thank you for confirming your availability at 4:00 PM on Thursday.

Please stand by for a meeting invitation and call in number.

Respectfully,

Kelly

Kelly J. Johnson, MPH
Management Analyst
Office of the Assistant Secretary for Preparedness and Response (ASPR)
Office of Strategy, Policy, Planning, and Requirements (SPPR)

HEALTH AND HUMAN SERVICES (HHS)
o: (202) 205-5909 m: (b)(6)
kelly.johnson@hhs.gov

From: Bugin, Kevin <Kevin.Bugin@fda.hhs.gov>
Sent: Tuesday, July 21, 2020 10:01 AM
To: Johnson, Kelly J. (OS/ASPR/SPPR) <Kelly.Johnson@hhs.gov>; Woodcock, Janet (FDA/CDER) <Janet.Woodcock@fda.hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Lawlor, Ciarán <Lawlor.Ciaran@bcg.com>
Cc: Redd, John (OS/ASPR/IO) <John.Redd@hhs.gov>; Thompson, Donna (OS/ASPR/IO) (CTR) <Donna.Thompson@hhs.gov>; Thomas, Ashley (FDA/CDER) <Ashley.Thomas@fda.hhs.gov>; Tewell, Adam (OS/OGA) <Adam.Tewell@hhs.gov>
Subject: RE: Follow Up: Meeting - Discussion on Distribution Learnings - Remdesivir with OWS

My apologies. It appears 4:30 no longer works for us. Can we try 4 pm?

Kevin

From: Bugin, Kevin
Sent: Tuesday, July 21, 2020 9:19 AM
To: Johnson, Kelly J (OS) <Kelly.Johnson@hhs.gov>; Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>; Disbrow, Gary (OS) <Gary.Disbrow@hhs.gov>; Lawlor, Ciarán <Lawlor.Ciaran@bcg.com>
Cc: Redd, John T (OS) <John.Redd@hhs.gov>; Thompson, Donna (OS) <Donna.Thompson@hhs.gov>; Thomas, Ashley <Ashley.Thomas@fda.hhs.gov>; Tewell, Adam (OS) <Adam.Tewell@hhs.gov>
Subject: Re: Follow Up: Meeting - Discussion on Distribution Learnings - Remdesivir with OWS

Hi Kelly,

We could do 4:30 on Thursday. Thanks!

Kevin

From: Johnson, Kelly J. (OS/ASPR/SPPR) <Kelly.Johnson@hhs.gov>
Date: July 21, 2020 at 8:37:51 AM EDT
To: Bugin, Kevin <Kevin.Bugin@fda.hhs.gov>, Woodcock, Janet <Janet.Woodcock@fda.hhs.gov>, Disbrow, Gary (OS) <Gary.Disbrow@hhs.gov>, Lawlor, Ciarán <Lawlor.Ciaran@bcg.com>
Cc: Redd, John T (OS) <John.Redd@hhs.gov>, Thompson, Donna (OS) <Donna.Thompson@hhs.gov>, Thomas, Ashley <Ashley.Thomas@fda.hhs.gov>, Tewell, Adam (OS) <Adam.Tewell@hhs.gov>
Subject: Follow Up: Meeting - Discussion on Distribution Learnings - Remdesivir with OWS

Dear Kevin, Janet, Gary, and Ciaran:

Thank you for participating in the call yesterday afternoon with CAPT Redd to discuss the distribution of remdesivir. CAPT Redd is interested in reconvening the group between 4:00 PM and 5:00 PM ET on Thursday, July 23, 2020 for a brief update.

Please advise of your availability to join a 15 minute call on Thursday, July 23, between 4:00 PM and 5:00 PM, by replying to this message. If this time block is not convenient CAPT Redd will follow up by email.

I look forward to hearing from you soon.

Respectfully,

Kelly

Kelly J. Johnson, MPH
Management Analyst
Office of the Assistant Secretary for Preparedness and Response (ASPR)
Office of Strategy, Policy, Planning, and Requirements (SPPR)

HEALTH AND HUMAN SERVICES (HHS)
o: (202) 205-5909 m: (b)(6)
kelly.johnson@hhs.gov

-----Original Appointment-----
From: Johnson, Kelly J. (OS/ASPR/SPPR) **On Behalf Of** Redd, John (OS/ASPR/IO)
Sent: Monday, July 20, 2020 6:29 AM
To: Redd, John (OS/ASPR/IO); Bugin, Kevin (FDA/CDER); Woodcock, Janet (FDA/CDER); Disbrow, Gary (OS/ASPR/BARDA)
Cc: Thompson, Donna (OS/ASPR/IO) (CTR); Johnson, Kelly J. (OS/ASPR/SPPR) (Kelly.Johnson@hhs.gov); Thomas, Ashley (FDA/CDER); Lawlor, Ciarán
Subject: Discussion on Distribution Learnings - Remdesivir with OWS
When: Monday, July 20, 2020 4:00 PM-4:30 PM (UTC-05:00) Eastern Time (US &Canada).
Where: WebEx Meeting - Dial In: 415-527-5035,,,1996534105##

Purpose to discuss:

- **Overall lessons learned from the Remdesivir experience**
- **Role of USG in distribution &allocation of doses**
- **Data tracking systems and USG responsibilities as the EUA holder**
- **Reimbursement for drug and non-drug costs associated with the infusion**

I would also like to include Gary from BARDA in this discussion so we can discuss this in the context of our existing contract structures (e.g. Regeneron).

POC: Kevin Bugin (FDA)

Sender:	Johnson, Kelly J. (OS/ASPR/SPPR) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=48BFDC5BEE0349A2840980EC07DDC5E2-JOHNSON, KE <Kelly.Johnson@hhs.gov>
Recipient:	Bugin, Kevin (FDA/CDER) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=55c4e5e4038442ff8866f40f603e52ce-kevin.bugin <Kevin.Bugin@fda.hhs.gov>; Woodcock, Janet (FDA/CDER) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5f925e9a0f9147b186d40072d474d13d-janet.woodc <Janet.Woodcock@fda.hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0fd5845defda4dc0bb45f8fac629cf09-Disbrow, Ga <Gary.Disbrow@hhs.gov>; Lawlor, Ciarán <Lawlor.Ciaran@bcg.com>; Redd, John (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=9ba3fed4ee8646ec849a5a87136a24f6-Redd, John <John.Redd@hhs.gov>; Thompson, Donna (OS/ASPR/IO) (CTR) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=21f88b26c3544e0aa1ca6b5e71df37da-Thompson, D <Donna.Thompson@hhs.gov>; Thomas, Ashley (FDA/CDER) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=6bcf9a5e75bc42dea48e4009c5342397-ashley.thom <Ashley.Thomas@fda.hhs.gov>; Tewell, Adam (OS/OGA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0172af5d4c93452ea236821fffba4be6-Tewell, Ada <Adam.Tewell@hhs.gov>
Sent Date:	2020/07/21 10:06:05
Delivered Date:	2020/07/21 10:06:07

From:	Redd, John (OS/ASPR/IO) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=9BA3FED4EE8646EC849A5A87136A24F6-REDD, JOHN <John.Redd@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>; Bugin, Kevin (FDA/CDER) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=55c4e5e4038442ff8866f40f603e52ce-kevin.bugin <Kevin.Bugin@fda.hhs.gov>
CC:	Thompson, Donna (OS/ASPR/IO) (CTR) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=21f88b26c3544e0aa1ca6b5e71df37da-Thompson, D <Donna.Thompson@hhs.gov>; Thomas, Ashley (FDA/CDER) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=6bcf9a5e75bc42dea48e4009c5342397-ashley.thom <Ashley.Thomas@fda.hhs.gov>; Johnson, Kelly J. (OS/ASPR/SPPR) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=48bfdc5bee0349a2840980ec07ddc5e2-Johnson, Ke <Kelly.Johnson@hhs.gov>; Woodcock, Janet (FDA/CDER) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5f925e9a0f9147b186d40072d474d13d-janet.woodc <Janet.Woodcock@fda.hhs.gov>; Lawlor, Ciarán <Lawlor.Ciaran@bcg.com>; Tewell, Adam (OS/OGA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0172af5d4c93452ea236821fffba4be6-Tewell, Ada <Adam.Tewell@hhs.gov>
Subject:	RE: Follow up Discussion on Distribution Learnings - Remdesivir with OWS
Date:	2020/07/22 12:16:09
Priority:	Normal
Type:	Note

Thanks for the question re: infrastructure. It's a good one.

The answer re: this is that we really don't have any infrastructure. We do have a team – but the key feature of the system is that we here in DC are the directors of the allocation by state; the movement of product itself is done by Amerisource Bergen, which has purchased the product from Gilead. States themselves direct product to hospitals. I reiterate my strong opinion that attempted Federal allocation to a sub-state level is very high risk.

I would have recommendations for you about how to proceed based upon different models that you may be coming up with for different MCMs, and I would like to continue to do what I can to advise based on our experience getting a scarce product out there.

From: Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>
Sent: Wednesday, July 22, 2020 8:04 AM
To: Bugin, Kevin (FDA/CDER) <Kevin.Bugin@fda.hhs.gov>; Redd, John (OS/ASPR/IO) <John.Redd@hhs.gov>
Cc: Thompson, Donna (OS/ASPR/IO) (CTR) <Donna.Thompson@hhs.gov>; Thomas, Ashley (FDA/CDER) <Ashley.Thomas@fda.hhs.gov>; Johnson, Kelly J. (OS/ASPR/SPPR) <Kelly.Johnson@hhs.gov>; Woodcock, Janet (FDA/CDER) <Janet.Woodcock@fda.hhs.gov>; Lawlor, Ciarán <Lawlor.Ciaran@bcg.com>; Tewell,

+1-415-527-5035 US Toll
+1-929-251-9612 USA Toll 2
Global call-in numbers

Join from a video system or application
Dial 1991700764@hhs.webex.com

Join using Microsoft Lync or Microsoft Skype for Business
Dial 1991700764.hhs@lync.webex.com

If you are a host, click here to view host information.

Need help? Go to http://help.webex.com

Sender:	Redd, John (OS/ASPR/IO) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=9BA3FED4EE8646EC849A5A87136A24F6-REDD, JOHN <John.Redd@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>; Bugin, Kevin (FDA/CDER) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=55c4e5e4038442ff8866f40f603e52ce-kevin.bugin <Kevin.Bugin@fda.hhs.gov>; Thompson, Donna (OS/ASPR/IO) (CTR) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=21f88b26c3544e0aa1ca6b5e71df37da-Thompson, D <Donna.Thompson@hhs.gov>; Thomas, Ashley (FDA/CDER) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=6bcf9a5e75bc42dea48e4009c5342397-ashley.thom <Ashley.Thomas@fda.hhs.gov>; Johnson, Kelly J. (OS/ASPR/SPPR) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=48bfdc5bee0349a2840980ec07ddc5e2-Johnson, Ke <Kelly.Johnson@hhs.gov>; Woodcock, Janet (FDA/CDER) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5f925e9a0f9147b186d40072d474d13d-janet.woodc <Janet.Woodcock@fda.hhs.gov>; Lawlor, Ciarán <Lawlor.Ciaran@bcg.com>; Tewell, Adam (OS/OGA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0172af5d4c93452ea236821fffba4be6-Tewell, Ada <Adam.Tewell@hhs.gov>

Sent Date: 2020/07/22 12:16:09

DONATION AGREEMENT ("Agreement")

between

The U.S. Department of Health & Human Services ("**HHS**")

With offices at 200 Independence Avenue, S.W.
Washington, D.C. 20201

and

Gilead Sciences, Inc. ("**Gilead**")

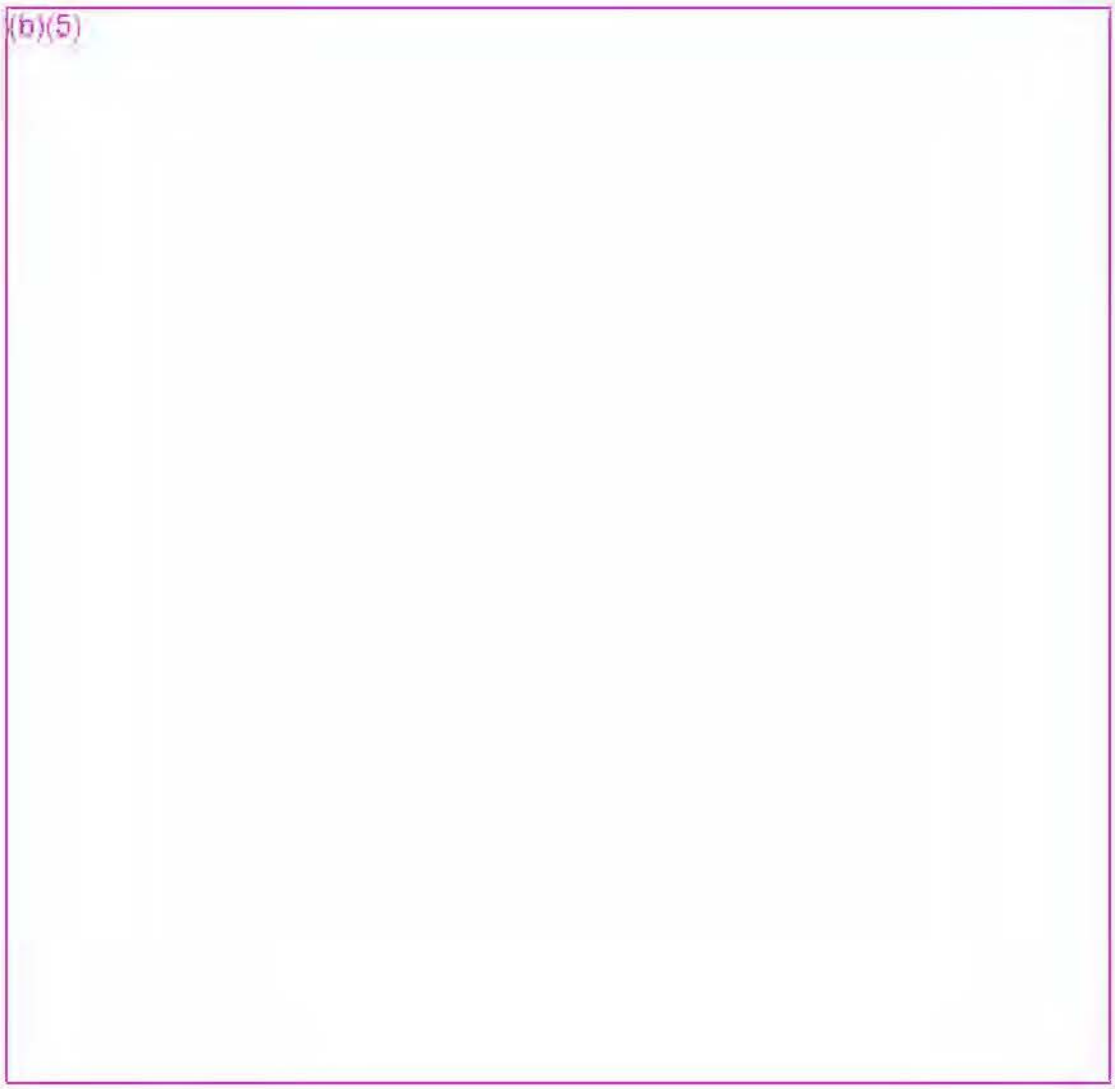
With offices at 333 Lakeside Drive
Foster City, CA 94404

BACKGROUND

Remdesivir is an investigational new drug ("IND") product developed by **Gilead** for the potential treatment of individuals infected with SARS-CoV-2.

(b)(5)

(b)(5)


(b)(5)

SIGNATURE PAGE

IN WITNESS WHEREOF, the parties hereto have executed this **Agreement** by their respective duly authorized officers, who have affixed their signatures hereunto, on the day and year hereinafter written. Each individual signing below represents that he or she has authority to bind the party that he or she represents.

For **HHS**:

_____ _____
Signature of Authorized Official Date

Robert Kadlec, M.D., MTM&H, M.S.
Printed Name

Assistant Secretary for Preparedness and Response
Title

For **Gilead**:

_____ _____
Signature of Authorized Official Date

_____
Printed Name

_____
Title

3) how to coordinate with the Govt of California if this exception is approved, given that they are under lockdown.

We can probably get the answer to #1 via our HHS contacts, but would need help with the others.

Gwen Tobert

Outbreak Response and Biodefense Team Lead

Office of International Health and Biodefense

Bureau of Oceans and International Environmental and Scientific Affairs

U.S. Department of State

TobertGM@state.gov

Desk: 202-647-2208 (Note: I am teleworking fulltime – please use mobile number)

Mobile: (b)(6)

From: Berger, Ryan M <BergerRM@state.gov>
Sent: Friday, March 20, 2020 1:10 PM
To: OES-IHB-DG <OES-IHB-DG@state.gov>; Scovitch, Joseph R <ScovitchJR@state.gov>; Stevens, Kathleen E <StevensKE@state.gov>
Cc: Margolis, Jonathan A <MargolisJA@state.gov>; Areias, Allison V <AreiasAV@state.gov>; Logsdon, Kent D <LogsdonKD@state.gov>
Subject: E Request to OES - Travel Exception from Gilead

OES/IHB Colleagues,

Following U/S Krach and PDAS Bernicat's meeting with the Gilead CEO earlier this month, Gilead's government affairs director reached out to U/S Krach yesterday **(see below)** requesting a waiver for two of its German employees to travel to California next month. We are inquiring whether OES believes that a waiver under this circumstance would be in the national interest.

If you agree, we ask that IHB take the pen on an AM to CA A/S Risch, who now has delegated authority to approve these waivers **(old waiver to S attached)**. Allison and I are happy to work with your designated POC on making this happen. For context, an ALDAC went out last week **(PDF attached)** indicating the categories that would be subject to a waiver.

Thank you for your prompt attention to this matter.

Senate Committee on Appropriations
Hearing on COVID-19
July 2, 2020

Questions and Answers

Budget

1. **Understanding Congress has provided over $27B to the Public Health and Social Services Emergency Fund account, do you have other funding needs that we should consider as we prepare a 5th supplemental appropriation bill?**

- We have made significant progress, as I highlighted in my oral statement, to develop vaccines, therapeutics, and diagnostics utilizing the funding you have provided.

- We are also supporting manufacturing platforms to accelerate the production of vaccines to get them to the public as soon as possible.

- We will keep you all apprised of any future funding needs as they arise.

2. How much of your budget has gone to OWS?

- BARDA has executed approximately $6.5 billion in supplemental funding to support the development of vaccines, therapeutics and diagnostics.
    - The BARDA portfolio now includes over 40 medical countermeasure projects including 9 therapeutics, 26 diagnostics (12 of which have been granted Emergency Use Authorization by the FDA) and five vaccine candidates.

- Three of these five candidates are operating under OWS.
    - $456 million in funds for Janssen's (part of Johnson & Johnson) candidate vaccine
    - $483 million to support Moderna's candidate vaccine
    - Up to $1.2 billion in support for AstraZeneca's candidate vaccine, developed in conjunction with the University of Oxford.

3. What can Congress do to support ASPR's development efforts and ensure long-term goals are met?

- Congress has provided significant funding to support the COVID-19 response. We appreciate everything you have done and provided to date.

- When possible, Congress should consider x-year appropriations in the future to best support investments. This allows the most flexible approaches to support innovation and development efforts.

Operation Warp Speed

4. How is OWS being funded?

- $10 billion from Congressional appropriations was identified to support OWS efforts.

- The almost $10 billion specifically directed includes more than $6.5 billion designated for countermeasure development through BARDA and $3 billion for NIH research.

5. Because BARDA specific funding is falling under OWS, is ASPR/BARDA no longer in full control of its spending of provided supplemental funding?

- The purpose of OWS is to accelerate the development and manufacturing of vaccines to best protect the nation again COVID-19.
    - OWS is bringing together partners unlike ever before and all are working in a coordinated effort to get the job done.

- BARDA sits at the table and has a role in all procurement and investment decisions under OWS.

- In addition, BARDA is benefiting from OWS through leveraging contracting expertise that was otherwise not available to expedite awards.

6. What specific investments is the federal government making with respect to mitigating the cost and schedule risk associated with concurrent vaccine development and manufacturing?

- The OWS team will award contracts with promising vaccine developers to initiate manufacturing prior to completion of Phase 3 clinical trials.
- These contracts will guarantee a certain quantity of vaccine is provided to the US Government in the event clinical trials are successful.
- This approach has the potential to speed up delivery of a vaccine by many months when compared to a more serial approach to development and manufacturing.

7. How much time in the development process will be saved using OWS?

- Under OWS, we have compressed the manufacturing process.

- OWS supports overlapping clinical studies and simultaneous large scale manufacturing. This approach will save years on the traditional countermeasure development timeline.

- We are essentially supporting two steps – vaccine development and manufacturing – at the same time.

- We are making investments in the necessary manufacturing capacity at federal risk, giving companies confidence that they can invest aggressively in development and allowing faster manufacturing and potential distribution of an eventual vaccine.

- Under the terms of the contracts for manufacturing capacity, reservations can be shifted as needed from one candidate vaccine to another more promising candidate based on the findings from clinical trials that are being conducted in parallel with manufacturing scale-up.

8. Is your goal to have 100 million doses ready in November of 2020 and an additional 200 million by January 2021 realistic?

- While this is an ambitious goal for OWS, it is potentially possible and we will continually assess these goals as more information about the vaccine candidates and their manufacturing becomes available.

- However, clinical trials can be lengthy as they work through the science of the effectiveness of the vaccine.

- Only after data is provided to the FDA, and the FDA makes their independent assessment, will a determination be made if a vaccine can be licensed or provided an emergency use authorization. Only vaccines that have been provided a license or EUA can be distributed for wide use.

9. Under OWS, are BARDA program staff being pulled off contracts and contract performance management efforts, thus resulting in a loss of expertise in these high dollar contracts?

- OWS is supporting a whole of government approach to COVID-19 response.

- DoD is lending assistance in a time where we are pushing out a large number of contracts.

- This response is unprecedented. We are working in different ways to execute the mission.

- Working with DoD and NIH partners to facilitate contracts, is being done at OUR request. They are ensuring we are executing and awarding contracts as quickly as possible to support MCM development.

- Bottom line, BARDA is still at the table and supporting contract review.

COVID-19 Response

10. How are you ensuring we have an affordable vaccine for the general public?

- Bottom line, anything BARDA purchases will be available for the general public at no cost.

- In most cases, we do not own the IP or product rights for the COVID-19 vaccines.
  - We are, where possible, negotiating the best price for the American people for further sale, manufacturing, and distribution.

11. Are you under any political pressure to change the science to accelerate vaccine development?

- No. We are adhering to and following all required regulatory and safety requirements required for vaccine development.

- We are not sacrificing the safety of the vaccine in order to expedite its development.

- We are instead supporting two steps at the same time.
  - Vaccine development
  - Manufacturing

- For manufacturing, we are making investments in the necessary manufacturing capacity at federal risk, giving companies confidence that they can invest aggressively in development and allowing faster manufacturing and potential distribution of an eventual vaccine.

12. What could the federal government have done to be better positioned with diagnostics, vaccines, and treatments for COVID-19?

- Key gaps such as personnel shortages, lack of investments in advanced development and licensure of emerging infectious disease vaccines/platforms, and consistent and sustained funding were all obstacles for COVID-19.

- Thanks to Congress, the federal government received significant supplemental appropriations to bridge gaps.

- BARDA has been flat-funded over the last few years with very limited funding available for investments on MCM preparedness for emerging infectious diseases (COVID).
    - Multiyear funding to establish and maintain MCM preparedness for emerging infectious diseases could have supported the development of rapid-response platform technologies and a sustainable flexible US-based manufacturing capacity to enable accelerated initiation of MCM development.

- The positive for this vaccine development campaign is that some previous investments in other related countermeasures are proving to be applicable to COVID-19 treatments so we are not starting from complete scratch.

13. Is the Assistant Secretary for Preparedness and Response the right position to coordinate a whole-of-government response to a pandemic?

- Yes, ASPR is the right position to coordinate a whole-of-government response. Congress has provided the authorities to support this effort and ASPR has demonstrated over the last decade its ability to manage and support a coordinated response.

- For COVID-19, FEMA was named the lead to assist with the various distribution, allocation, and messaging elements of the response.
    - This is the role of FEMA during natural disasters and, due to the large movement of PPE and other logistics requests, the move best supported the need for the response.

- Over the summer, ASPR is transitioning back into its lead role for the response as FEMA moves into hurricane season.

14. What is the appropriate role for HHS and how can FEMA be better integrated into a nationwide pandemic response?

- HHS has the health and medical expertise to support a nationwide pandemic response. FEMA has the general response and logistics expertise to aid community response and recovery.

- Both agencies worked together during the first few months of the response to support a coordinated and thorough response to COVID-19.

15. What is ASPR's role in the distribution of Remdesivir?

- The total donation to 940,000 vials of remdesivir from Gilead Sciences Inc. is enough to treat an estimated 120,512 hospitalized COVID-19 patients.

- We began distribution in early May using a data-driven allocation strategy.
    - ASPR is working hand-in-hand with states and has utilized data input by hospitals to identify changing needs and meet demands in a fair and equitable way.
    - This data-based model will serve as a future distribution blueprint, should we need to distribute another scarcely available drug for COVID-19 or otherwise.

- As of May 29, 2020, all of the original donated amount of remdesivir has been allocated.
    - Less than ten percent of the first donation is being held in reserve in the event "hotspots" emerge in the coming weeks.

16. What is ASPR's role in leading the current national response to COVID-19?

- ASPR's mission is to save lives and protect Americans from 21st century health security threats.

- ASPR's Regional Administrators (RAs) and Regional Emergency Coordinators (RECs) are physically located in regional offices across the nation and have direct links and networks with State and local health and emergency response officials.
    - These officials also communicate and coordinate with their FEMA regional counterparts to support seamless communication on relevant issues.

- RAs and RECs have and continue to assess needs, coordinate with State and local officials, and triage requests as needed to ensure requests for assistance are addressed quickly.

- HHS generally is supporting the transfer of the lead coordination and support function for the response from FEMA.

- In this role, ASPR is taking the internal lead for the Department.

17. How can federal departments and agencies more effectively work together to respond to public health emergencies?

- ASPR would attest to the value of collaborative planning and exercise cycles across the federal government and including state, local and commercial partners.

- The experience of the Crimson Contagion pandemic influenza exercise series in 2019, while not 100% applicable to the coronavirus pandemic, identified critical requirements and limitations for pandemic response for awareness and planning efforts.

- The Crimson Contagion exercise also refreshed or established important relationships and familiarity across federal response agencies that were important to the early stages of the COVID-19 response.

- Increased frequency, and broader participation in this sort of exercise will continue to help identify challenges and enhance preparedness moving forward.

18. Domestic Manufacturing: Please speak to the threat of relying on foreign entities for material to support vaccine formulation and administration.

- ASPR is seeking innovative solutions and partnerships to limit dependence on foreign nations and better protect national security.

- As you all know, during the initial days of the COVID-19 response, we saw the negative consequence of relying on foreign partners when personal protective equipment was in short supply and unavailable for direct purchase.

- ASPR is looking at how this issue can be addressed early during product development when and where possible.

- We are also working closely with partners at the Food and Drug Administration to monitor product availability. With this partnership, we will have better information on potential shortages if and when they occur.

19. What incentives can the federal government offer to the private sector to encourage development of more medical countermeasures with no commercial market?

- BARDA was established to incentivize the private sector to develop countermeasures with no commercial market.
  - It does so by providing drug developers with non-dilutive funding to support the research, development and manufacturing of medical countermeasures against CBRN threats, pandemic influenza and emerging infectious diseases.
  - BARDA also provides access to critical capabilities such as the Centers for Innovation in Advanced Development and Manufacturing, fill and finish capabilities, clinical trial networks to support human clinical studies, and non-clinical networks.
  - BARDA also provides industry partners with access to technical subject matter expertise in such areas of drug development as manufacturing, clinical and non-clinical development, clinical operations, and regulatory and quality affairs among other areas. =

- Consistent funding going forward, in the form of advance appropriations, would enhance developers' confidence in the overall process and would best support product development through to licensure and future acquisition for stockpile.

20. Should the federal government create government-owned-contractor-operated facilities to solve supply chain and manufacturing challenges?

- BARDA has already invested in Centers for Innovation and Advanced Manufacturing (CIADMs) and some of these Centers are already being considered for COVID-19 vaccine production.

- In addition, ASPR/BARDA recently awarded a contract with Phlow to support the development of active pharmaceutical ingredients to reduce reliance on the global supply chain.

21. What is the justification for funding the Phlow contract and how are the medicines they are working on decided?

- The Phlow contract fulfilled 2 government needs:
  - Short term immediate supply of essential medicines that became further on shortage status as hospitalizations due to COVID19 increased
  - Long-term bolstering of the US industrial base for domestic manufacturing API and precursor chemical compounds.

- Increasing API manufacturing on US soil helps to minimize reliance on foreign suppliers and secure the national medical supply chain, especially critical during a national pandemic

- BARDA is working closely with the FDA, SNS and the FEMA Pharmaceutical Supply Chain Task Force to determine the most critical medicine needs.

22. How can the United States build manufacturing systems that can rapidly respond to new threats, whether naturally occurring or manmade?

- The US should invest in accelerating efforts to establish sustainable MCM manufacturing capacity for rapid-response platform technologies that can transition quickly between products.

- A faster response would leverage public-private partnerships with industry to drive our research choice transitioning from the "one bug, one drug" approach to a multifaceted approach.

- Domestic manufacturing capabilities are fairly easy to expand. The challenge is maintaining that expansion, balancing the commercial capabilities required to have an independently functioning organization with the 'march in' requirements necessary to respond to an infectious disease.

- The most efficient approach is to maintain a certain amount of capacity for USG utilization at all times. This, however, requires consistent, flexible funding.

23. What is the appropriate federal role in supporting the manufacturing of medical countermeasures, especially vaccines?

- The role of the federal government in manufacturing differs depending on the threat, existing capabilities, and long-term impact.

- For the current COVID-19 response, because there are no licensed vaccines or therapeutics indicated for any members of the coronavirus family, and no clear evidence of a future commercial market for these products, the federal government had to lead MCM and vaccine development to ensure that safe and effective products are developed, and subsequently produced in large quantities as quickly as possible to limit the impact of the pandemic.

- With respect to manufacturing, it is important that the USG bears the majority of the risks associated with product development.

- For the current COVID-19 response (and future pandemics where no MCM exists prior to the outbreak), to produce products at the speed with which the USG is requiring manufacturers, it is imperative that work streams that are usually sequential be run in parallel.

24. How is ASPR working with states during the current response?

- ASPR has and continues to directly support State and local needs and requirements through the assistance of the ASPR Regional Administrators and Regional Emergency Coordinators.

- ASPR's RAs and RECs are physically located in regional offices across the nation and have direct links and networks with State and local health and emergency response officials.
    - These officials also communicate and coordinate with their FEMA regional counterparts to support seamless communication on relevant issues.

- RAs and RECs have and continue to assess needs, coordinate with State and local officials, and triage requests as needed to ensure requests for assistance are addressed quickly.

- The ASPR Organization was critical in the repatriation of Americans early in the response.

25. Why did BARDA recently suspended areas of interest supporting the development of immune modulators, host-targeted therapeutics including cell based therapies and pre- and post-exposure prophylaxis candidates?

- Areas of interest under BARDA's broad agency announcement (BAA) have adjusted over time to meet HHS priorities and as the scientific community learns more about the virus and its effects on the human body.

- The pathophysiology of coronavirus disease is still unknown. There is not enough data available about the pathophysiology of coronavirus disease to understand which immune modulating or host-targeted therapeutics are the most likely to succeed.

- Rather than focus on individual clinical trials for each candidate with BARDA contracts, the USG is planning to use platform clinical trials to support the evaluation of multiple products, as opposed to supporting expensive clinical trials for each product separately.

- Prophylaxis is not the highest priority for BARDA at this time. Effective treatments for symptomatic and hospitalized COVID-19 are the priority.

26. The majority of BARDA funds have been given to large pharmaceutical companies, while innovation in medicine is often seen in small companies. Why is BARDA focusing their spending only on large pharma?

- Early BARDA awards were given to companies with existing relationships with BARDA. There were many large companies that were supported in this way.

- New awards have been given to both large and small pharmaceutical companies, and BARDA is eager to support promising MCMs no matter the size of the company.

27. What preparations are underway to ensure adequate quantities of the supplies needed to distribute and administer a vaccine, once it receives EUA or licensure?

- BARDA has been working daily with vaccine manufacturers not only to develop COVID-19 vaccines, but also to ensure manufacturing capacity to maximize supply to the American people.

- All of our pandemic plans include increasing capacity of necessary supplies, such as vials, needles, and syringes, needed to carry out a mass vaccination campaign in the United States.

- We have been working daily with our manufacturers to secure those supplies and assist them with any anticipated obstacles in their supply chains.

SNS

28. How can the Strategic National Stockpile be better managed and how can Congress increase oversight and accountability?

- In the case of COVID-19, when the supply chain for PPE collapsed due to the halt in production and shipping from Chinese suppliers, states and private sector entities looked to the SNS to meet all PPE requirements.
    - **This was never the envisioned role of SNS during a pandemic, and the SNS did not have the requirements or the resources to establish and sustain the vast amounts of PPE required to meet the national demand for PPE through a months long pandemic.**

- Using the supplemental appropriations from Congress, HHS is working to resupply the SNS and ensure that HHS is better prepared for future pandemics.

- Under the SNS 2.0 construct SNS would hold a 90-day reserve supply of PPE necessary to meet surge requirements for PPE and other products during a pandemic response until demand is reduced or production is increased to meet all requirements.

29. How can states and hospitals improve their ability to maintain a reserve of supplies in the future to ensure the Strategic National Stockpile is the backup and not the first source of supplies during emergencies?

- Hospital Preparedness Program (HPP) funding allows recipients to purchase supplies (e.g., personal protective equipment (PPE) and other equipment).

- However, the amount of funding provided is limited, and many recipients have deprioritized building and maintaining their own reserves of supplies in order to address other competing needs.

- Additionally, recipients are unable to take advantage of the Shelf Life Extension Program (SLEP), which only applies to federal stockpiles.

30. What steps should be taken to ensure that health care providers and first responders have the supplies they need, such as personal protective equipment?

- Health care providers and first responders are currently disincentivized from stockpiling equipment, relying on "just in time" supply chain models.

- Increasing the funding support for the development of supply reserves, extending SLEP to state, local and private health care stockpiles – or establishing an equivalent program for non-federal stockpiles –may enable health care providers and first responders to better maintain supply reserves during emergencies and mitigate reliance on federal stockpiles.

31. As states and hospitals establish or build their own stockpiles, how will they know what supplies to stockpile? What guidance should the federal government provide on what medical supplies are appropriate?

- Federal stockpiles should focus on maintaining supplies that are not commercially available, and coordinate with states and private health care to address gaps.

32. Could states and hospital systems establish their own vendor managed inventory programs with manufacturers and distributors? Should the federal government or states contribute to such hospital stockpiles?

- While a majority of states and hospital systems do not do this, many states and hospital systems – including health care coalitions funded by HPP – have established their own vendor-managed inventory programs with manufacturers and distributors.

- With increased funding and resources for HPP, this program could set guidelines for health care coalitions to promote and sustain development of these inventory programs.

- One major challenge is that many hospital systems, particularly smaller hospital systems, lack the buying power to sustain and maintain stockpiles of supplies during steady state.

33. Did you support Dr. Kadlec's decision to move the SNS from the CDC to ASPR, in light of opposition?

- The decision to move the SNS from CDC to ASPR was a decision made by Secretary Azar.

- The move was based on a review of operations and identified efficiencies.
    - It was determined the move would improve the country's response capabilities by integrating supporting assets with the organization supporting personnel deployments vs. having components housed separately.

34. What is the current status of Personal Protective Equipment in the SNS?

- Throughout this response, FEMA and HHS has closely coordinated to provide PPE to those who have made requests for assistance.

- Recently, the SNS deployed all PPE holdings except for 10% that will be retained for critical needs of frontline healthcare workers serving in federal response efforts.

- SNS has entered into contacts with PPE manufacturers. Thus far, as shipments are received, supplies are going out to States requesting support vs. resupplying the SNS.
    - The SNS will be resupplied once the supply chain levels out and States and hospitals can receive direct shipments.

35. What is the SNS 2.0 concept that has been discussed recently?

- The goal of SNS 2.0 is to ensure we replenish the PPE components of the SNS to have a 90 day supply for federal use and that, as much as possible, states have 30 day supply on hand.

- To accomplish this, the SNS is utilizing active and open contracts.

- Please note that the SNS has not actively resupplied PPE to pre-COVID-19 levels at this time because we did not want to hinder purchases for frontline healthcare.

- Bottom line, as the supply chain levels out, the SNS is ready to make procurements quickly.

36. Is the stockpile depleted?

- Under the joint direction of FEMA and HHS in support of the COVID-19 response, the SNS has deployed all remaining personal protective equipment (N95 respirators, surgical/face masks, face shields, gloves, coveralls, and gowns) in its inventory.
    - A small percentage (10%) will be retained for critical needs of frontline healthcare workers serving in federal response efforts.

- Although SNS sent out 90% of the PPE it held, the stockpile still maintains $8 billion of antibiotics, vaccines, antitoxins, antivirals, etc.

37. How has PPE been distributed for the COVID-19 response?

- The SNS's role is to serve as a stop-gap measure to supplement state and local supplies during public health emergencies and localized disasters when the commercial supply chain is disrupted.
    - Many states have products stockpiled and are ordering their own supplies, as well.

- In early March, HHS began deploying PPE.
    - The allocation strategy for the first half of the overall PPE inventory in the SNS was primarily based on a pro-rata formula, which used 2010 U.S. Census data and was proportionate to the population size of each jurisdiction. Areas with high transmission received additional allocations by request.
    - It is important to note that the pro-rata allocations were likely less than what states requested. However, all jurisdictions received 100% of their allocations.

- Following the initial population-based strategy, the remaining shipments from the SNS to the 62 jurisdictions were directed through the National Response Coordination Center.

38. We understand the federal government made significant ventilator purchases based on modeling earlier in the response. We now understand the need for ventilators has diminished. How many ventilators were purchased and what is the plan for the excess of product?

- The SNS was maintaining approximately 17K ventilators prior to the start of the COVID-19 pandemic.
    - At the request of States, the SNS deployed 10,640 vents.

- To date, approximately $3.1B of CARES Act supplemental appropriations has been executed to purchase ventilators for the COVID-19 response.

- The ventilator will be stored at SNS locations across the nation as we prepare for a potential fall wave and/or an increase in requests for ventilators.

- To support specific power requirements, the SNS is building out warehouse capabilities (power supply specifically) to keep them charged and ready.

Local/Community Preparedness

39. What changes can be made to Public Health Emergency Preparedness and Hospital Preparedness Program to help states prepare and respond more quickly?

- HPP has focused on advancing regional, tiered systems that engage the private and public sectors to collaboratively respond to national health emergencies.
    - Supporting health care coalitions, developing the National Special Pathogen System, the Regional Disaster Health Response System, and proposing a National Emergency Telemedicine Network.

- The COVID-19 response has provided numerous lessons learned from the private sector, which could be incorporated to a) improve federal/STTL coordination capabilities and b) inform new federal regulatory or policy changes that can address systemic challenges currently limiting the private sector's ability to effectively respond.

- Additional resources will build on these efforts and enhance capabilities.

40. How can the federal government ensure all states are adequately prepared without infringing on states' rights and recognizing states have primary responsibility for response?

- The federal government can work to develop basic national standards, as well as triggers and measures to prompt activation of different levels of surge response, which states can use as targets for their own preparedness efforts.

- Additionally, the federal government can work with states as well as the private sector to leverage private sector modeling and data, which may be more readily available and advanced, and facilitate dissemination of those models/information to support situational awareness at the state and national level.

41. Exercises: How does ASPR test and evaluate plans and assumptions guidance response and recover activities?

- When our plans are developed, they are tested and authenticated. This examination is accomplished through the exercise function, where plans are validated to ensure they are functional and accurate for the various incident scenarios to which they were developed. The exercise testing and validation of a plan is a critical element of a viable plan, as it enables the identification and appropriate mitigation of planning deficiencies.

- Our recent Crimson Contagion Exercise series exemplifies this benefit. This exercise included two tabletop exercises, a seminar, and a functional exercise to examine issues related to response structures, information exchange, coordination of resources, and policy decisions—with a non-traditional Lead Federal Agency—in accordance with the *Biological Incident Annex to the Response and Recovery Federal Interagency Operational Plans* (January 2017).
    - This was the largest pandemic exercise to date and included
        - 12 Federal departments/agencies,
        - 12 states,
        - 96 local jurisdictions,
        - 24 Native American Tribes,
        - 87 hospitals, and more than
        - 100 private sector partners

Oversight

42. The Washington Post reported that Dr. Kadlec failed to disclose his business relationships in his Senate financial disclosures. Is this a conflict of interest?

- I can't comment on someone else's financial disclosures.

- However, please be aware that Dr. Kadlec did submit an ethics filing during his time in the Senate. These filings are required for all Senators and Senate employees earning a pay rate above 120% of a GS-15.

- These reports are publically available and legally required and are available for anyone who has a need to review

.

43. But Kadlec struck a deal for a $2.8 billion to Emergent – one of his former clients, led by a former business partner. Isn't that a conflict?

- Any contract we award is reviewed and approved in accordance with HHS policies and procedures for awarding contracts, which includes Contracting Officers, HCA, SPE, and OGC where required.
    - All contracts are negotiated and executed by independent contracting officers.

- The SNS is required to hold smallpox vaccines to meet requirements to protect against existing identified threats.
    - To fill that requirement, it holds ACAM2000.

- The CDC put out the RFP (SNS was still under its control at that time) for a five-year contract (previous contract was expiring in 2018).
    - As the CDC's RFP noted: Emergent is the only FDA licensed provider of ACAM2000 Smallpox Vaccine and therefore is the only source capable to provide this requirement to the Government.

- The contract was finalized after the SNS moved to ASPR.
    - The cost for 5 years exceeded the amount budgeted. By extending the contract to 10 years, ASPR negotiated a better price that nearly cut in half the price per dose.

44. According to Dr. Kadlec, the PHEMCE was over-bureaucratic and slow. According to the Washington Post: Kadlec "scaled back a long-standing interagency process for spending billions of dollars on stockpile purchases, diminishing the role of government experts and restricting decision-making to himself and a small circle of advisers." He also moved meetings behind closed doors. Was this part of his power-grab?

- The process was streamlined to create greater efficiencies.

- Given the sensitive nature of discussions as pertaining to national security, the conversations were moved to a SCIF.

45. The Washington Post reported that under Kadlec's leadership, ASPR halted an Obama-era initiative to spend $35 million to build a machine that could produce 1.5 million N95 masks per day. Why?

- ASPR entered into a contract with Halyard in 2016 to investigate the feasibility of a high speed N95 mask manufacturing line, using similar technologies as used in high speed diaper manufacturing.

- The project successfully demonstrated the feasibility of the approach and developed an initial design of a high speed mask manufacturing line.

- Building a prototype was not included in the scope of the original contract.
    - Currently, the Supply Chain Task force is considering the use of more proven mask manufacturing techniques, such as this one, to reduce N95 shortages.

Bright Q's:

46. How has the reassignment of Rick Bright impacted BARDA and its efforts to develop medical countermeasures for COVID-19?

- The Rapid Acceleration of Diagnostics (RADx) initiative led out of the National Institutes of Health (NIH) is a new program aimed to rapidly identify new and promising early countermeasures that can be used to respond to COVID-19.

- Given Dr. Bright's success leading BARDA over the last three years as well as the link between this effort and BARDA's portfolio, Dr. Bright was the clear choice to ensure the initiative's success.
    - Dr. Bright understands better than anyone how to identify promising candidates and what support is needed to push them forward in development.

- Dr. Bright's departure from BARDA will not impact overall operations or product development within the BARDA organization.
    - BARDA has already made a number of awards to support COVID-19 vaccines, therapeutics, and diagnostics, and this work will continue to move forward.
- In his new role, Dr. Bright will continue to be a strong partner with BARDA, bridging the gap between parallel efforts.

47. Several of the press reports regarding Dr. Bright's departure indicate that it was due in part to dissatisfaction in his leadership abilities. Do you have confidence that Dr. Bright can competently lead the RADx initiative?

- Given Dr. Bright's success leading BARDA over the last three years as well as the link between this effort and BARDA's portfolio, Dr. Bright was the clear choice to ensure the initiative's success.
    - Dr. Bright understands better than anyone how to identify promising candidates and what support is needed to push them forward in development.

EUA recommendations and implications for distribution & allocation

Initial considerations for Tx

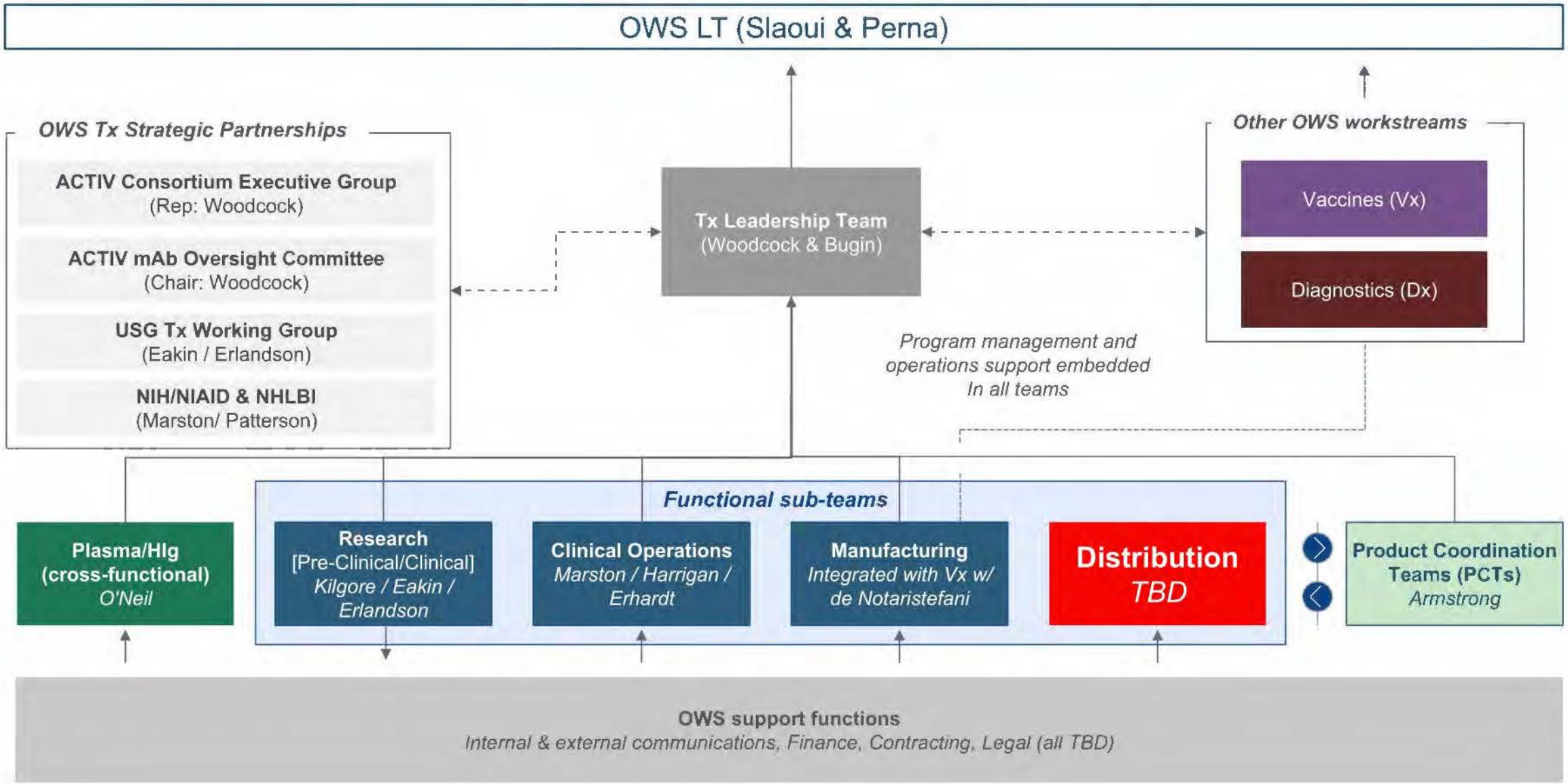
AUG 4TH 2020

BLUF: OWS Tx recommends building key requirements for EUA, labeling, and distribution into contracts with manufacturers, with allocation directed by USG but managed within commercial distribution channels

Objectives for today

- Agree on initial set of recommendations for EUA, distribution and recommendations for Tx
- Review draft view on concept of operations and milestones to prepare for a potential EUA
- Identify potential resourcing to stand-up effort to support distribution and allocation

Recap: Therapeutics (Tx) team structure and interfaces



Context for today's discussion

- Initial set of novel Tx are currently in Ph 2 / 3 studies with the potential for first **read-outs on efficacy in Sep**

- **Regeneron** has articulated Oct as a potential timeframe for when they could apply for an EUA (assuming positive clinical data)

- USG has an **advanced purchase agreements (APA)** with Regeneron and several other manufacturers
  - Manufacturers are seeking USG guidance on EUA & distribution

- USG also needs to develop an **equitable allocation plan** in the event that supply cannot meet demand, which is likely given increase in cases and supply projections in the October timeframe

- USG seeking to pro-actively develop an overall **strategy** as other manufacturers are likely to closely follow behind Regeneron
  - Eli Lilly (treatment) could consider an EUA in a similar timeframe and AZ may have data readouts in late Nov

Principles informing EUA, allocation and distribution strategy

EUA

Ensure contracts and responsibilities are in place before earliest potential EUA date (Oct) to avoid any delays in getting Tx to patients

Allocation

Build on Remdesivir experience to inform recommendations on allocation

Distribution

Utilize existing infrastructure where possible within USG and within current manufacturer distribution channels

Summary of distribution and allocation model with Remdesivir EUA

Gilead holds the EUA for Remdesivir

Oversight body was established for allocation and ethical guidance provided input on two core elements of Remdesivir allocation strategy:

- Geographical equity: all 50 states and US territories have access to drug
- Temporal equity[1]: to ensure continuity of supply and avoid a "first come first serve" approach

Gilead used existing distributor (AmerisourceBergen) and initial distribution strategy utilized county and hospital level data to drive allocation decisions

- Gilead covered distribution costs for Remdesivir
- Initial distribution strategy resulted in misallocation issues due to inaccurate local data reporting / requests
- Hospitals under most stress most likely to make mistakes in reporting / requests for drug

In current model, allocation and distribution happen across states on a "pro-rata" basis driven by hospital utilization rates. Decisions are made on an ongoing basis including:

- Initial allocation recommendation is approved by Dr. Birx
- State governors are notified and product is then released to state health officers
- States can apply to access HHS Protect to see data

1. Temporal equity refers to ensuring that the allocation strategy that spreads allocation over time. It is intended to account for the fact that immediate demand may not meet expected supply and the need to ensure that there is a steady stream of Tx for future patients

Overview of key recommendations for potential Tx EUAs

Key decision	Recommendation
EUA holder	• Each manufacturer will hold their own EUA
Labeling	• Product will be labeled with manufacturer info. only - *Product will not have "property of USG" label*
Storage	• Manufacturer will be responsible for storage of product
Allocation (inpatient)	• USG to develop pre-designed formula for allocation across states - Allocation within state driven by state health officials
Allocation (outpatient)	• NIH will develop guidelines to inform allocation decisions for non-hospitalized patients
Allocation (prophylaxis)	• USG to form ethical review board to develop principles for prophylaxis allocation decisions and use groups dependent on EUA conditions
Distribution	• Utilize existing commercial distributor used by the manufacturer
Data tracking	• Manufacturer will be responsible for all pharmacovigilance • Distributor to provide USG tracking data on inventory • States will provide USG with product utilization (county & hospital level)

Draft view on distribution Concept of Operations

Key
Flow of data
Flow of product

- Reviews EUA application
- Oversees ongoing reporting

- Manages EUA submission
- Prepares product fact sheet
- Updates EUA as needed
- Notifies FDA on any reported safety issues
- BARDA regulatory support available for PCTs

Manufacturer

Quality agreement reqd. between manufacturer & distributor

Distributor

- Contracts directly with manufacturer
- Manages storage of USG product
- Reports data back to USG

- Direct product to appropriate county districts & hospitals

State Governors

Administration sites

- Hospitals
- Nursing homes
- VA
- Pharmacy
- Indian Health Services
- Other

- **Reports case / hospitalizations** to USG
- Provides USG with hospital utilization levels & product usage

- Sets allocation scheme in consultation with NIH & ethicists
- Pays for distribution costs as part of USG product procurement
- Directs distributor on state allotments based on reporting
- Tracks product is delivered/utilized

For discussion: Short-term team needs for distribution and allocation

Current need:

Onboard small team immediately on distribution to:

- Shadow Remdesivir team to replicate current processes (e.g. Governor email distribution lists)
- Join PCTs to lead engagement with external manufacturers & distributors to align on expectations & working model
- Map out ordering and allocation process between USG, states, manufacturer & distributors
- Define data strategy & ensure systems are in place
- Initiate state engagement & ensure state's readiness

For discussion:

Where can we source resources to help pro-actively drive this Tx effort?

- Overall distribution lead who understands commercial Tx distribution
- Logisticians
- Data & analytics support for forecasting
- IT expertise to understand potential system needs (*as required*)

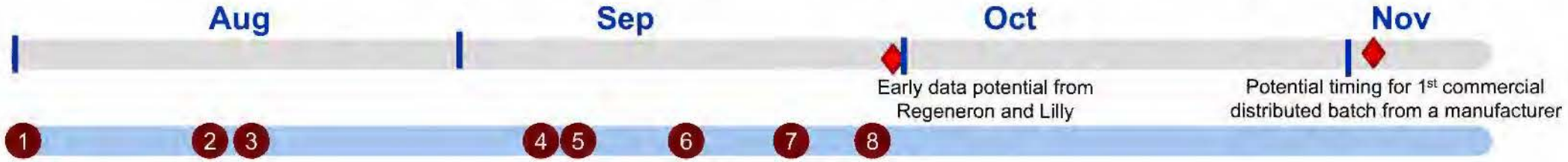
Establish ethical review board, etc on allocation decisions for the various clinical use cases (outpatient, prophylaxis and inpatient)

- Build allocation algorithm & guidelines

Do we need to establish a new review board with NIH, ethicists to manage allocation decisions for nAbs or should we utilize the existing Remdesivir one? Leverage ACTIV?

Work in progress, to be continuously updated

Milestones for Tx EUA, allocation and distribution effort



	Milestone	Timing
1	Synthesized initial recommendations on EUA and responsibilities across USG & manufacturers	ASAP
2	Established USG distribution lead, logisticians and support team	08/14
3	Aligned with manufacturers (Lilly, Regeneron & AZ) on EUA & distribution strategy	08/14
4	Drafted contracts to cover storage (quality agreements) and distribution expectations for data tracking / reporting and ensure all distribution costs are covered by USG	09/11
5	Developed allocation formula and ethical review board (*in collaboration with NIH*)	09/11
6	Established guidelines to inform allocation decisions for non-hospitalized patients and for prophylaxis applications based on guidance from ethicist groups and NIH, within EUA guardrails	09/18
7	Operationalized allocation process including required IT & complete test run on the process to ensure smooth operations between states, USG, manufacturers & distributors	09/18
8	Established guidelines to inform allocation decisions for non-hospitalized patients and for prophylaxis applications based on guidance from ethicist groups and NIH	09/18

Proposed next steps

- **Establish USG distribution lead, logisticians and team for Tx efforts by 08/07**
- **Review proposed recommendations with CAPT Redd and Remdesivir team**
- **Schedule individual calls with Lilly, Regeneron and AZ to align on recommendations & path forward**


DEPARTMENT OF HEALTH & HUMAN SERVICES
USA


OPERATION
WARP SPEED


DEPARTMENT OF DEFENSE
UNITED STATES OF AMERICA

Thank you!

The feasibility of convalescent plasma therapy in severe COVID-19 patients: a pilot study

Kai Duan[1,2*], Bende Liu[3*], Cesheng Li[4*], Huajun Zhang[5*], Ting Yu[6*], Jieming Qu[7*], Min Zhou[7*], Li Chen[8*], Shengli Meng[2], Yong Hu[4], Cheng Peng[5], Mingchao Yuan[9], Jinyan Huang[10], Zejun Wang[2], Jianhong Yu[4], Xiaoxiao Gao[5], Dan Wang[9], Xiaoqi Yu[11], Li Li[2], Jiayou Zhang[2], Xiao Wu[4], Bei Li[5], Yanping Xu[7], Wei Chen[2], Yan Peng[4], Yeqin Hu[2], Lianzhen Lin[4], Xuefei Liu[7], Shihe Huang[2], Zhijun Zhou[4], Lianghao Zhang[2], Yue Wang[4], Zhi Zhang[2], Kun Deng[4], Zhiwu Xia[2], Qin Gong[4], Wei Zhang[4], Xiaobei Zheng[4], Ying Liu[4], Huichuan Yang[1], Dongbo Zhou[1], Ding Yu[1], Jifeng Hou[12], Zhengli Shi[5], Saijuan Chen[10], Zhu Chen[10+],Xinxin Zhang[11+], Xiaoming Yang[1,2+]

1. China National Biotec Group Company Limited, 15F, Block 2, Fortune Tower, No.4 HuiXin East Street, Chaoyang District, Beijing 100029, China
2. National Engineering Technology Research Center for Combined Vaccines, Wuhan Institute of Biological Products Co.Ltd., No.1 Huangjin Industrial Park Road, Jiangxia District, Wuhan 430207, China
3. First People's Hospital of Jiangxia District, No.1 Wenhua Road, Jiangxia District, Wuhan 430200, China
4. Sinopharm Wuhan Plasma-derived Biotherapies Co.,Ltd, No.1A Huangjin Industrial Park Road, Jiangxia District, Wuhan 430207, China
5. CAS Key Laboratory of Special Pathogens, Wuhan Institute of Virology, Center for Biosafety Mega-Science, Chinese Academy of Sciences, 44 Xiao Hong Shan, Wuhan 430071, China
6. WuHanJinyintan Hospital, No.1 Jin Yin Tan Road, Dongxihu District, Wuhan 430023, China
7. Department of Respiratory and Critical Care Medicine, National Research Center for Translational Medicine (Shanghai,NRCTMS), Institute of Respiratory Diseases, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine,No.197 Ruijin 2nd Road, Shanghai 200025, China
8. Clinical Research Center, Department of Gastroenterology, Ruijin Hospital North, Shanghai Jiao Tong University School of Medicine, Xiwang Road 999, Jiading District, Shanghai 200018, China
9. Wuhan Blood Center, No.8 BaoFeng First Road, Qiaokou District, Wuhan 430030, China
10. State Key Laboratory of Medical Genomics, Shanghai Institute of Hematology, NRCTMS, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine,No.197 Ruijin 2nd Road, Shanghai 200025, China
11. Research Laboratory of Clinical Virology, Ruijin Hospital and Ruijin Hospital North, NRCTMS, Shanghai Jiao Tong University School of Medicine, No.197 Ruijin 2nd Road, Shanghai 200025, China

12. National Institute for Food and Drug Control of China, No.29 HuaTuo Road, Daxing District, Beijing 102629, China

+Correspondence:

Xiaoming Yang

China National Biotec Group Company Limited, National Engineering Technology Research Center for Combined Vaccines, Wuhan 430207, China

Email: yangxiaoming@sinopharm.com

Xinxin Zhang

Research Laboratory of Clinical Virology, Ruijin Hospital and Ruijin Hospital North, National Research Center for Translational Medicine (Shanghai), Shanghai Jiao Tong University School of Medicine, No.197 Ruijin 2nd Road, Shanghai 200025, China

Email: zhangx@shsmu.edu.cn

Zhu Chen

State Key Laboratory of Medical Genomics, Shanghai Institute of Hematology, National Research Center for Translational Medicine (Shanghai), Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, No.197 Ruijin 2nd Road, Shanghai 200025, China

Email:zchen@stn.sh.cn

* These authors contributed equally

Classification

BIOLOGICAL SCIENCES; Medical Sciences

Keywords

COVID-19, convalescent plasma, treatment outcome, pilot project

Author Contributions

XZ, ZC, and XY contnbuted to the design of the study. SM, ZW, LL, JZ, WC, YH, SH, LZ, ZZ, ZX, JH, HY, DZ, and DY collected the epidemiological and clinical data. JH, XY, YX, XL, and JZ processed statistical data. KD, BL, CL, HZ, TY, JQ, MZ, ZC and LC drafted the manuscript. ZS, CP, XG, BL, YH, JY, XW, YP, LL, ZZ, YW, KD, QG, WZ, XZ, YL, MY, SC, and DW was responsible for virus detection and summarizing all epidemiological and clinical data. All authors reviewed and approved the final version.

Abstract

Currently, there are no approved specific antiviral agents for 2019 novel coronavirus disease (COVID-19). In this study, ten severe patients confirmed by real-time viral RNA test were enrolled prospectively. One dose of 200 mL convalescent plasma (CP) derived from recently recovered donors with the neutralizing antibody titers above 1:640 was transfused to the patients as an addition to maximal supportive care and antiviral agents. The primary endpoint was the safety of CP transfusion. The second endpoints were the improvement of clinical symptoms and laboratory parameters within 3 days after CP transfusion. The median time from onset of illness to CP transfusion was 16.5 days. After CP transfusion, the level of neutralizing antibody increased rapidly up to 1:640 in five cases, while that of the other four cases maintained at a high level (1:640). The clinical symptoms were significantly improved along with increase of oxyhemoglobin saturation within 3 days. Several parameters tended to improve as compared to pre-transfusion, including increased lymphocyte counts (0.65×10^9/L vs. 0.76×10^9/L) and decreased C-reactive protein (55.98 mg/L vs. 18.13 mg/L). Radiological examinations showed varying degrees of absorption of lung lesionswithin 7 days. The viral load was undetectable after transfusion in seven patients who had previous viremia. No severe adverse effects were observed. This study showed CP therapy was welltolerated and could potentially improve the clinical outcomes through neutralizing viremia in severe COVID-19 cases. The optimal dose and time point, as well as the clinical benefit of CP therapy, needs further investigation in larger well-controlled trials.

Significance Statement

COVID-19is currently a big threat to global health. However, no specific antiviral agents are available for its treatment. In this work, we explored the feasibility of convalescent plasma (CP) transfusion to rescue severe patients. The results from 10 severe adult cases showed that one dose (200 mL) of CP was welltolerated and could significantly increase or maintain the neutralizing antibodies at a high level, leading to disappearance of viremia in 7 days. Meanwhile, clinical symptoms and paraclinical criteria rapidly improved within 3 days. Radiological examination

showed varying degrees of absorption of lung lesions within 7 days. These results indicate that CP can serve as a promising rescue option for severe COVID-19 while the randomized trial is warranted.

Main Text

Introduction

Since December 2019, a pneumonia associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), named as 2019 novel coronavirus disease (COVID-19) by World Health Organization (WHO), emerged in Wuhan, China (1-3). The epidemic spread rapidly worldwidewithin three months and was characterized as a pandemic by WHO on March 11,2020.As of March 12, 2020, a total of80,980confirmed cases and 3,173deaths had been reported in China. Meanwhile, a total of 44,377 confirmed cases and 1,446 deaths was reported in other 108 countries or regions.Currently, there are no approved specific antiviral agents targeting the novel virus, while some drugs are still under investigation, including remdesivir and lopinavir/ritonavir (4, 5). Although remdesivirwas reported to possess potential antiviral effectin one COVID-19 patient from the U.S., randomized controlled trials of this drug are ongoing to determine its safety and efficacy (6). Moreover, the corticosteroid treatment for COVID-19 lung injury remains controversial, due to delayed clearance of viral infection and complications(7,8). Since the effective vaccine and specific antiviral medicines are unavailable, it is an urgent need to look for an alternative strategy for COVID-19 treatment, especially amongsevere patients.

Convalescent plasma (CP) therapy, a classic adaptiveimmunotherapy, has been applied to the prevention and treatment of many infectious diseases for more than one century. Over the past two decades,CP therapy was successfully used in the treatment of SARS, MERS, and 2009 H1N1 pandemic with satisfactory efficacy and safety (9-12). A meta-analysis from 32 studies of SARS coronavirus infection and severe influenza showed a statistically significant reduction in the pooled odds of mortality following CP therapy, compared with placebo or no therapy (odds ratio, 0.25; 95% confidence interval, 0.14-0.45) (13). However, the CP therapy was unable to significantly improve the survival in the Ebola virus disease, probably due to the absence of data of neutralizing antibodytitrationfor stratified analysis (14). Since the virological and clinical characteristics share similarity among SARS, MERS, and COVID-19 (15), CP therapy might be a promising treatment option for COVID-19 rescue(16). Patients who have recovered from COVID-19 with a high neutralizing antibody titermay bea valuable donor source of CP. Nevertheless, the potential clinical benefit and risk of convalescent blood products in COVID-19 remains uncertain. Hence, we performed this pilot study in three participated hospitals to explore the feasibility of CPtreatment in 10 severe COVID-19 patients.

Results

Neutralizing activity of CP against SARS-CoV-2

The neutralizing activity against SARS-CoV-2 was evaluated by classical plaque reduction test using a recently isolated viral strain (1). Among the first batch of CP samples from 40 recovered COVID-19 patients, 39 showed high antibody titers of at least 1:160 whereas only one had a antibody titer of 1:32. This result laid the basis for our pilot clinical trial using CP in severe patients.

General characteristics of Patients in the trial

From January 23, 2020, to February 19, 2020, ten severe COVID-19 patients (six males and four females) were enrolled and received CP transfusion. The median age was 52.5 years (IQR, 45.0–59.5 years) (Table 1). None of the patients had direct exposure to Huanan Seafood Wholesale Market. The median time from onset of symptoms to hospital admission and CP transfusion was 6 days (IQR, 2.5–8.5 days) and 16.5 days (IQR11.0–19.3 days), respectively. Three patients were affected by clustering infection. The most common symptoms at disease onset were fever (seven of ten patients), cough (eight cases), and shortness of breath (eight cases), while less common symptoms included sputum production (five cases), chest pain (two cases), diarrhea (two cases), nausea and vomiting (two cases), headache (one case), and sore throat (one case). Four patients had underlying chronic diseases, including cardiovascular and/or cerebrovascular diseases and essential hypertension. Nine patients received arbidolmonotherapy or combination therapy with remdesivir (in one case not included in the current clinical trial), or ribavirin,or peramivir, while one patient received ribavirin monotherapy(Table 2). Antibacterial or antifungal treatment was used when patients had co-infection. Six patients received intravenousmethylprednisolone (20 mg every 24 hrs).

On computer-assisted tomography (CT), all patients presented bilateral ground-glass opacity and/or pulmonary parenchymal consolidation with predominantly subpleural and bronchovascular bundles distribution in the lungs. Seven patients had multiple lobe involvement and four patients had interlobular septal thickening.

Effects of CP transfusion

Improvement of clinical symptoms All symptoms inthe 10 patients, especially fever, cough, shortness of breath and chest pain, disappeared or largely improved within 1-3 days upon CP transfusion. Prior toCP treatment, three patients received mechanical ventilation, three received

high-flow nasal cannula oxygenation, and two received conventional low-flow nasal cannula oxygenation. After treatmentwith CP, two patients were weaned from mechanical ventilation to high-flow nasal cannula and one patient discontinued high flow nasal cannula. Besides, in one patient treated with conventional nasal cannula oxygenation, continuous oxygenation was shifted to intermittent one (Table 2).

Reduction of pulmonary lesions on chest CT examinations According to chest CTs, all patients showed different degrees of absorption of pulmonary lesions after CP transfusion. Representative chest CT images of patient 9 and patient 10 were shown on Fig. 1. Patient 9, a 49-year-old female admitted on 1 day post onset of illness (dpoi), showed the most obvious pulmonary image improvement. On 10 dpoi, one dose of 200 mL transfusion of CP was given. The SARS-CoV-2 RNA converted to negative on 12 dpoi. Compared with the result on 7 dpoi, massive infiltration and ground-glass attenuation disappeared on CT image performed on 13 dpoi, accompanied bya much better pulmonary function. Patient 10, a 50-year-old male, was admitted on 3 dpoi and was given a 200 mL transfusion of CP on 20 dpoi. His chest CT presented massive infiltration and widespread ground-glass attenuation on admission andstarted to show a gradual absorption of lung lesions 5 days after CP transfusion. The SARS-CoV-2 RNA became negative on 25 dpoi.

Amelioration ofroutine laboratory criteria and pulmonary function Lymphocytopenia, an important index for prognosis inCOVID-19 (2), tended to beimprovedafter CP transfusion (median: 0.65×10^9 per L vs. 0.76×10^9 per L), seven out of ten patients showingan increase of lymphocyte counts (Fig. 2). Concerning other laboratory tests, we observed a tendency of decrement of parameters indicative of inflammation and/or liver dysfunction as compared to the statusbefore CP therapy. These included C-reactive protein (CRP) (median: 55.98 mg/L vs. 18.13 mg/L), alanine aminotransferase (median: 42.00 U/L vs. 34.30 U/L) and aspartate aminotransferase (median: 38.10 U/L vs. 30.30 U/L) (Table 3). The total bilirubin (median: 12.40 μmol/L vs. 13.98 μmol/L) remained unchanged except an obvious increment in patient 1 (Fig. 2). An increase of SaO_2 (median:93.00% vs. 96.00%), a measurement constantly performed in most patients in our trial, was found, which could indicaterecovering lung function.This temporal relationship was notable despite the provision of maximal supportive care and antiviral agents.

Remarkably, patient 1, a 46-year-old male admitted on 8 dpoi, had a very quick recovery with much improved result of laboratory tests. He received antiviral drugs (arbidol and ribavirin) treatment and high flow nasal cannula on admission. Mechanical ventilation was given on 10 dpoi for critical care support. CP transfusion was performed on 11 dpoi. On 12 dpoi, the SARS-CoV-2test turned to negative, with a sharp decrease of CRP from 65.04 mg/L to 23.57 mg/L and incrementof SaO_2 from 86% to 90% (Fig. 3). The mechanical ventilation was successfully weaned off 2 days after CP

transfusion. On 15 dpoi, a steady elevation oflymphocyte count and a drop ofaminopherase levelwere observed, indicating improvement ofimmunological and hepatic function.

Increase of neutralizing antibody titers and disappearanceof SARS-CoV-2 RNA We determined neutralizing antibody titers before and after CP transfusion in all patients except one (patient2) (Table 4). The neutralizing antibody titers of five patients increased and four patients remained atthe same level after CP transfusion.SARS-CoV-2 RNA, assayed by reverse transcriptase-polymerase chain reaction (RT-PCR), was positive in seven patients and negative in three cases before CP transfusion. Of note, SARS-CoV-2 RNA was decreased to anundetectable level in 3 patients on day 2, 3 patients on day 3 and 1 patients on day 6 after CP therapy.These results were in support of anneutralizing effectof CP on serum SARS-CoV-2.

Outcome of patients treated with CP as compared to a recent historic control group Ahistoric control group was formed by random selection of10 patients from the cohort treated in the same hospitals andmatched by age, gender and severity of the diseases to the 10 cases in our trial. Baseline characteristics of patients between CP treatment group and control group showed no significant differences, while clinical outcomesof these two groups weredifferent: 3 cases dischargedwhile 7 cases in much improved status and ready for discharge in CP group, as compared to 3 deaths, 6 cases in stablized status and one case in improvement in the control group ($p<0.001$, Supplementary table 1).

Adverse effects of CP transfusions

Patient 2 showed an evanescent facial red spot. No serious adverse reactions or safety events were recorded after CP transfusion.

Discussion

To our knowledge, this is the first study to explore the feasibility of CP therapy in COVID-19. All enrolled severe COVID-19 patients achieved primary and secondary outcomes. One dose of 200 mL CP transfusion was welltolerated, while the clinical symptoms significantly improved with the increase of oxyhemoglobin saturation within 3 days, accompanied by rapid neutralization of viremia. Severe pneumonia caused by human coronavirus was characterized by rapid viral replication, massive inflammatory cell infiltration, and elevated proinflammatory cytokines or even cytokine storm in alveoli of lungs, resulting in acute pulmonary injury and acute respiratory distress

syndrome (ARDS) (17). Recent studies on COVID-19 demonstrated that the lymphocyte counts in the peripheral blood were remarkably decreased and the levels of cytokines in the plasma from patients requiring ICU support, including IL-6, IL-10, TNF-α, GM-CSF, were significantly higher than those who did not require ICU conditions (2, 18). CP, obtained from recovered COVID-19 patients who had established humoral immunity against the virus, contains a large quantity of neutralizing antibodies capable of neutralizing SARS-CoV-2 and eradicating the pathogen from blood circulation and pulmonary tissues (19). In the present study, all investigated patients achieved serum SARS-CoV-2 RNA negativity after CP transfusion, accompanied by the increase of oxygen saturation and lymphocyte counts, and the improvement of liver function and C-reactive protein. The results suggested that the inflammation and overreaction of the immune system were alleviated by antibodies contained in CP. The case-fatality rates (CFRs) in the present study were 0% (0/10), which was comparable to the CFRs in SARS which varied from 0% (0/10) to 12.5% (10/80) in four non-comparative studies using CP treatment (9, 20-22). Based on our preliminary results, CP therapy can be an easy-accessible, promising and safe rescue option for severe COVID-19 patients. It is nevertheless worth mentioning that the absorption of pulmonary lesions was often behind the improvement of clinical symptoms, as shown in patients 9 and 10 in this trial.
The first key factor associated with CP therapy is the neutralizing antibody titer. A small sample study in MERS-CoV infection showed that the neutralizing antibody titer should exceed 1:80 to achieve effective CP therapy (12). To find eligible donors who have high levels of neutralizing antibody is a prerequisite. Cao (23) et al showed that the level of specific neutralizing antibody to SARS-CoV decreased gradually 4 months after the disease process, reaching undetectable levels in 25.6% (IgG) and 16.1% (neutralizing antibodies) of patients at 36 months after disease status. A study from the MERS-CoV infected patients and the exposed healthcare workers showed that the prevalence of MERS-CoVIgGseroreactivity was very low (2.7%), and the antibodies titer decreased rapidly within 3 months (24). These studies suggested that the neutralizing antibodies represented short-lasting humoral immune response and plasma from recently recovered patients should be more effective. In the present study, recently recovered COVID-19 patients, who were infected by SARS-CoV-2 with neutralizing antibody titer above 1:640and recruited from local hospitals should be considered as suitable donors. The median age of donors was lower than that of recipients (42.0 vs. 52.5 years). Among the nine cases investigated, the neutralizing antibody titers of five patients increased while four patients kept the same level to 1:640 within two days. The antibody titers in CP in COVID-19 seem thus higher than those used in the treatment of MERS patient (1:80) (12).
The second key factor associated with efficacy is the treatment time point. A better treatment outcome was observed among SARS patients who were given CP before 14 dpoi (58.3% vs 15.6%; $P < 0.01$), highlighting the importance of timely rescue therapy (9). The mean time from onset of illness to CP transfusion was 16.5 days. Consistent with previous research, all three patients

receiving plasma transfusion given before 14 dpoi (patients 1, 2 and 9) in our study showed a rapid increase of lymphocyte counts and a decrease of CRP, with remarkable absorption of lung lesions in CT. Notably, patients who received CP transfusion after 14 dpoi showed much less significant improvement, such as patient 10. However, the dynamics of the viremia of SARS-CoV-2 was unclear, so the optimal transfusion time point needs to be determined in the future.

In the present study, no severe adverse effects were observed. One of the risks of plasma transfusion is the transmission of the potential pathogen. Methylene blue photochemistry was applied in this study to inactivate the potential residual virus and to maintain the activity of neutralizing antibodies as much as possible, a method known to be much better than ultraviolet C light (25). No specific virus was detected before transfusion. Transfusion-related acute lung injury (TRALI) was reported in an Ebola virus disease woman who received CP therapy (26). Although uncommon in the general population receiving plasma transfusion, this specific adverse reaction is worth noting, especially among critically illed patients experiencing significant pulmonary injury (27). Another rare risk worth mentioning during CP therapy is antibody-dependent infection enhancement, occurring at sub-neutralizing concentrations, which could suppress innate antiviral systems and thus could allow logarithmic intracellular growth of the virus (28). The special immune enhancement was reportedly more common in Dengue fever, but also could be found in SARS-CoV infection *in vitro* (29). No such pulmonary injury and infection enhancement were observed in our patients, probably owing to high levels of neutralizing antibodies, timely transfusion, and appropriate plasma volume.

There were some limitations to the present study. First, except for CP transfusion, the patients received other standard cares. All patients received antiviral treatment despite the uncertainty of the efficacy of drugs used. As a result, the possibility thatthese antiviral agents could contribute to the recovery of patients, or synergize with the therapeutic effect of CP, could not be ruled out. Furthermore, some patients received glucocorticoid therapy, which might interfere with immune response and delay virus clearance. Second, the median time from onset of symptoms to CP transfusion was 16.5 days (IQR11.0-19.3 days). Although the kinetics of viremia during natural history remains unclear, the relationship between SARS-CoV-2 RNA reduction and CP therapy, as well asthe optimal concentration of neutralizing antibodies and treatment schedule, should be further clarified. Third, the dynamic changes of cytokines during treatment were not investigated. Nevertheless, the preliminary results of this trial seem promising, justifying a randomized controlled clinical trial in a larger patient cohort.

In conclusion, this pilot study on CP therapy showed a potential therapeutic effect and low risk in the treatment of severe COVID-19 patients. One dose of CP with high concentration of neutralizing

antibodies can rapidly reduce the viral load and tends to improve clinical outcomes. The optimal dose and treatment time point, as well as the definite clinical benefits of CP therapy, need to be further investigated in randomized clinical studies.

Materials and Methods

Patients

From January 23, 2020, to February 19, 2020, ten patients in three participating hospitals (Wuhan Jinyintan Hospital, the Jiangxia District Hospital of Integrative Traditional Chinese and Western Medicine, Wuhan, and the First People's Hospital of Jiangxia District, Wuhan) were recruited in this pilot study. All patients were diagnosed as having severe COVID-19 according to the WHO Interim Guidance (30) and the Guideline of Diagnosis and Treatment of COVID-19 of National Health Commission of China (version 5.0) (31), with confirmation by real-time RT-PCR assay. The enrollment criteria were one of the conditions (2 to 4) plus condition (1): 1). Age ≥18 years; 2).Respiratory distress, RR ≥30 beats/min; 3).Oxygen saturation level less than 93% in resting state; 4). Partial pressure of oxygen (PaO_2)/oxygen concentration (FiO_2) ≤300 mmHg (1 mmHg=0.133 kPa). The exclusion criteria were as follows: 1). Previous allergic history to plasma or ingredients (Sodium Citrate); 2). Cases with serious general conditions, such as severe organ dysfunction, who were not suitable for CP transfusion; Written informed consent according to the Declaration of Helsinki was obtained from each patient or legal relatives. This study was approved by the Ethics Committee of the China National Biotec Group Co., Ltd. (Approval number:2020-0001). The registration number of this trial was ChiCTR2000030048.

Donors for convalescent plasma transfusion

Tendonor patients who recovered from COVID-19 were recruited from three participating hospitals. The recovery criteria were as follows: 1). Normality of body temperature for more than 3 days; 2). Resolution of respiratory tract symptoms; 3). Two consecutively negative results of sputum SARS-CoV-2 of real-time reverse transcriptase-polymerase chain reaction (RT-PCR) assay (one-day sampling interval). The donor's blood was collected after three weeks post-onset of illness and 4 days post-discharge. Written informed consent was obtained from each patient.

Plasma preparation procedure and quality control

Apheresis was performed using a Baxter CS 300 cell separator (Baxter, Deerfield, IL, USA). Convalescence plasma for treatment was collected from 40donors. The median age was 42.0 years (IQR, 32.5–49 years). A 400–600 mL ABO-compatible plasma sample was harvested from each

donor depending on the age and body weight, and each sample was divided and stored as 200 mL aliquots at 4℃ without any detergent or heat treatment. The CP was then treated with methylene blue and light treatment for 30 minutes in the medical plasma virus inactivation cabinet (Shandong Zhongbaokang Medical Appliance Co., Ltd).

Serology test and real-time RT–PCR detection of SARS-CoV-2 and other pathogens

The neutralized activity of plasma was determined by plaque reduction neutralization test using SARS-CoV-2 virusin the high biosafy level (BSL-4) laboratory of Wuhan Institute of Virology, Chinese Academy of Sciences.Neutralization titer was defined as the highest serum dilution with 50 % reduction in the number of plaques, as compared with the number of plaques in wells in the absence of novel coronavirus antibody as blank control. The neutralization activity of the receptor-binding domain (RBD) of antibody in the CP was detected by a sandwich ELISA.SARS-CoV-2-IgG antibody titer was tested by enzyme-linked immunosorbent assay. SARS-CoV-2 RNA was detected by RT-PCR assay and the result was presented as cycle threshold (Ct) value (Shanghai BioGerm Medical Biotechnology Co., Ltd). Methylene blue residue was detected by the verified ultraviolet method. The serology screening for hepatitis B and C virus, human immunodeficiency virus, and syphilis spirochete was negative. The protocols for SARS-CoV-2 serology and RNAtest are presented in the supplementary materials.

Treatment

All patients were admitted to the intensive care unit (ICU) and received antiviral therapy and other supportive care, while somepatients received antibiotic treatment, antifungal treatment, glucocorticoid and oxygen support at the appropriate situation. One dose of 200 mL inactivated CP with neutralization activity >1:640 was transfused into the patients within 4 hours following the WHO blood transfusion protocol.

Data collection

Clinical information of all enrolled patients was retrieved from the hospital electronic history system, including the baseline demographic data, days of illness duration, presenting symptoms, different kinds of examination and methods of treatment. Bacterial co-infection was identified by a positive culture from respiratory, urinary or blood culture within 48h of hospital admission. Complications including acute renal failure, acute coronary syndrome, myocarditis, acute respiratory distress syndrome, and nosocomial infection were recorded. The applications of assisted mechanical ventilation, intranasal oxygen inhalation, and medication regimen were recorded. The SARS-CoV-2 RNA from the serum sample was monitored during treatment.

Outcome Measures and Definitions

The clinical symptoms were recorded by attending physicians daily. The blood test and biochemical tests were carried out every 1-2 days. SARS-CoV-2 RNA was detected every 2-3 days. CT scan was repeated every 3-5 days. The primary endpoint was the safety of CP transfusion. The second endpoints were the improvement of clinical symptoms, laboratory and radiological parameters within 3 days after CP transfusion. The clinical symptoms improvement was defined as temperature normalization, relief of dyspnea, and oxygen saturation normalization, and the radiological improvement was defined as different degrees of absorption of lung lesions.

Statistical analysis

Continuous variables were presented as the median and interquartile range (IQR). Graphs were plotted using GraphPad Prism 7.0. Statistical software used included SPSS 24.0.

Data Availability statement

The data that support the findings of this study are available from the corresponding author on reasonable request. Participant data without names and identifiers will be made available after approval from the corresponding author. After publication of study findings, the data will be available for others to request. The research team will provide an email address for communication once the data are approved to be shared with others.
The proposal with detailed description of study objectives and statistical analysis plan will be needed for evaluation of the reasonability to request for our data. The corresponding author will make decision based on these materials. Additional materials may also be required during the process.

Acknowledgments

This study was funded by Key projects of the Ministry of Science and Technology China "Preparation of specific plasma and specific globulin from patients with a recovery period of COVID-19 infection" (project number: 2020YFC0841800).This work was also supported by Shanghai Guangci Translational Medicine Development Foundation. We thank all patients and donors involved in this study.

References

1. P. Zhou *et al.* A pneumonia outbreak associated with a new coronavirus of probable bat

origin. *Nature*. (2020)

2. N. Chen *et al.*, Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet***395**, 507-513 (2020).
3. WHO. Coronavirus disease 2019. Available at https://www.who.int/emergencies/diseases/novel-coronavirus-2019. Deposited 20 Feb 2020.
4. H. Lu, Drug treatment options for the 2019-new coronavirus (2019-nCoV). *Biosci Trends* 10.5582/bst.2020.01020 (2020).
5. M. Wang *et al.*, Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. *Cell Res* 10.1038/s41422-020-0282-0 (2020).
6. M. L. Holshue *et al.*, First Case of 2019 Novel Coronavirus in the United States. *N Engl J Med* 10.1056/NEJMoa2001191 (2020).
7. C. D. Russell, J. E. Millar, J. K. Baillie, Clinical evidence does not support corticosteroid treatment for 2019-nCoV lung injury. *Lancet***395**, 473-475 (2020).
8. L. Shang, J. Zhao, Y. Hu, R. Du, B. Cao, On the use of corticosteroids for 2019-nCoV pneumonia. *Lancet***395**, 683-684 (2020).
9. Y. Cheng *et al.*, Use of convalescent plasma therapy in SARS patients in Hong Kong. *Eur J ClinMicrobiol Infect Dis***24**, 44-46 (2005).
10. B. Zhou, N. Zhong, Y. Guan, Treatment with convalescent plasma for influenza A (H5N1) infection. *N Engl J Med***357**, 1450-1451 (2007).
11. I. F. Hung *et al.*, Convalescent plasma treatment reduced mortality in patients with severe pandemic influenza A (H1N1) 2009 virus infection. *Clin Infect Dis***52**, 447-456 (2011).
12. J. H. Ko *et al.*, Challenges of convalescent plasma infusion therapy in Middle East respiratory coronavirus infection: a single center experience. *AntivirTher***23**, 617-622 (2018).
13. J. Mair-Jenkins *et al.*, The effectiveness of convalescent plasma and hyperimmune immunoglobulin for the treatment of severe acute respiratory infections of viral etiology: a systematic review and exploratory meta-analysis. *J Infect Dis***211**, 80-90 (2015).
14. J. van Griensven *et al.*, Evaluation of Convalescent Plasma for Ebola Virus Disease in Guinea. *N Engl J Med***374**, 33-42 (2016).
15. P. I. Lee, P. R. Hsueh, Emerging threats from zoonotic coronaviruses-from SARS and MERS to 2019-nCoV. *J MicrobiolImmunol Infect* 10.1016/j.jmii.2020.02.001 (2020).
16. L. Chen, J. Xiong, L. Bao, Y. Shi, Convalescent plasma as a potential therapy for COVID-19. *Lancet Infect Dis* 10.1016/S1473-3099(20)30141-9 (2020).
17. R. Channappanavar, S. Perlman, Pathogenic human coronavirus infections: causes and consequences of cytokine storm and immunopathology. *SeminImmunopathol***39**, 529-539

(2017).

18. C. Huang *et al.*, Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet***395**, 497-506 (2020).
19. G. Marano *et al.*, Convalescent plasma: new evidence for an old therapeutic tool? *Blood Transfus***14**, 152-157 (2016).
20. V. W. Wong, D. Dai, A. K. Wu, J. J. Sung, Treatment of severe acute respiratory syndrome with convalescent plasma. *Hong Kong Med J***9**, 199-201 (2003).
21. K. M. Yeh *et al.*, Experience of using convalescent plasma for severe acute respiratory syndrome among healthcare workers in a Taiwan hospital. *J AntimicrobChemother***56**, 919-922 (2005).
22. L. K. Kong, B. P. Zhou, Successful treatment of avian influenza with convalescent plasma. *Hong Kong Med J***12**, 489 (2006).
23. W. C. Cao, W. Liu, P. H. Zhang, F. Zhang, J. H. Richardus, Disappearance of antibodies to SARS-associated coronavirus after recovery. *N Engl J Med***357**, 1162-1163 (2007).
24. Y. M. Arabi *et al.*, Feasibility of Using Convalescent Plasma Immunotherapy for MERS-CoV Infection, Saudi Arabia. *Emerg Infect Dis***22**, 1554-1561 (2016).
25. M. Eickmann *et al.*, Inactivation of Ebola virus and Middle East respiratory syndrome coronavirus in platelet concentrates and plasma by ultraviolet C light and methylene blue plus visible light, respectively. *Transfusion***58**, 2202-2207 (2018).
26. M. Mora-Rillo *et al.*, Acute respiratory distress syndrome after convalescent plasma use: treatment of a patient with Ebola virus disease contracted in Madrid, Spain. *Lancet Respir Med***3**, 554-562 (2015).
27. A. B. Benson, M. Moss, C. C. Silliman, Transfusion-related acute lung injury (TRALI): a clinical review with emphasis on the critically ill. *Br J Haematol***147**, 431-443 (2009).
28. S. B. Halstead, Dengue Antibody-Dependent Enhancement: Knowns and Unknowns. *MicrobiolSpectr***2** (2014).
29. S. F. Wang *et al.*, Antibody-dependent SARS coronavirus infection is mediated by antibodies against spike proteins. *BiochemBiophys Res Commun***451**, 208-214 (2014).
30. WHO. Clinical management of severe acute respiratory infection when Novel coronavirus (nCoV) infection is suspected: interim guidance. Available at https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected. Deposited 20 Feb 2020.
31. National Health Commission of China. Guideline for diagnosis and treatment for novel coronavirus pneumonia (fifth edition). Deposited 4 Feb 2020.

Figures and Tables

Figure 1. Chest CTs of two patients

(*A*) Chest CT of patient 9 obtained on Feb 9 (7 dpoi) before convalescent plasma transfusion (10 dpoi)showed ground glass opacity with uneven density involving the multilobal segments of both lungs. The heart shadow outline was not clear. The lesion was close to the pleura. (*B*) CT Image of patient 9 taken on Feb 15(13 dpoi) showed the absorption of bilateral ground glassopacity after convalescent plasma transfusion. (*C*)Chest CT of patient 10 was obtained on Feb 8 (19 dpoi) before convalescent plasma transfusion (20 dpoi). The brightness of both lungs was diffusely decreased and multiple shadows of high density in both lungs were observed.(*D*) Chest CTof patient 10 on Feb 18 (29dpoi) showed those lesions improvedafter convalescent plasma transfusion.

Figure 2. Dynamic changes of laboratory parameters in all patients.

The dotted horizontal line represents the reference value range. CP=convalescent plasma. CRP=C-reactive protein. SaO_2=oxyhemoglobin saturation. TBIL=total bilirubin. ALT=alanine aminotransferase. AST=aspartate aminotransferase.

Figure 3. Change of laboratory parameters in patient 1

X-axis represents the day post convalescent plasma transfusion. The dotted horizontal line represents the reference value range. CP=convalescent plasma. CRP=C-reactive protein. SaO_2=oxyhemoglobin saturation. TBIL=total bilirubin. ALT=alanine aminotransferase. AST=aspartate aminotransferase.

Table 1. Clinical characteristics of patients receiving convalescent plasma transfusion.

No.	Sex	Age	Clinical classification	Days of admission from symptom onset	Days of convalescent plasma therapy from symptom onset	Clustering infection	Principal symptoms	Comorbidity
1	M	46	Severe	8	11	No	Fever, cough, sputum production, shortness of breath, chest pain	Hypertension
2	F	34	Severe	0	11	Yes	Cough, shortness of breath, chest pain, nausea and vomiting	None
3	M	42	Severe	8	19	Yes	Fever, cough, sputum production, shortness of breath, sore throat, diarrhea	Hypertension
4	F	55	Severe	10	19	No	Fever, cough, sputum production, shortness of breath	None
5	M	57	Severe	4	14	No	Fever, shortness of breath	None
6	F	78	Severe	8	17	Yes	Fever, cough, sputum production, shortness of breath, muscle ache	None
7	M	56	Severe	4	16	No	Fever, cough, sputum production, arthralgia	None
8	M	67	Severe	10	20	No	Fever, cough, headache, diarrhea, vomiting	Cardiovascular andcerebrovascular diseases
9	F	49	Severe	1	10	No	Cough, shortness of breath	None
10	M	50	Severe	3	20	No	Shortness of breath	Hypertension

M=male. F=female.

Table 2. Other treatments of ten patients receiving convalescent plasma transfusion.

No.	Drugs administered			Oxygen support	
	Antiviral treatment	Antibiotic or antifungal treatment	Corticosteroids treatment	Before convalescent plasma therapy	After convalescent plasma therapy
1	Arbidol0.2g q8h po. Ribavirin 0.5g qdi.v	Cefoperazone Sodium i.v.	None	High-flow nasal cannula, mechanical ventilation	Mechanical ventilation
2	Arbidol0.2g q8hpo.	Cefoperazone Sodium i.v.	None	None	None
3	Arbidol0.2g q8hpo.	Moxifloxacini.v.	Methylprednisolone i.v.	High-flow nasal cannula, mechanical ventilation	High-flow nasal cannula
4	Ribavirin 0.5g qdi.v.	Linezolid i.v.Imipenem - Sitastatin Sodium i.v.	Methylprednisolone i.v.	Mechanical ventilation	High-flow nasal cannula
5	Arbidol0.2g q8hpo. Remdesivir0.2gqdi.v. Interferon-o 500MIUqdinh.	Moxifloxacini.v.Cefoperagone Sodium and Tazobactam Sodium i.v.	Methylprednisolone i.v.	Low-flow nasal cannula	Low-flow nasal cannula
6	Arbidol0.2g q8h po.	Cefoperazone Sodium i.v. Levofloxacin i.v.	Methylprednisolone i.v.	High-flow nasal cannula	High-flow nasal cannula
7	Arbidol0.2g q8h po.	Cefoperagone Sodium and Tazobactam Sodium i.v. Fluconazole i.v.	Methylprednisolone i.v.	High-flow nasal cannula	none
8	Arbidol0.2g q8h po. Ribavirin 0.5g qdi.v.	None	None	None	None
9	Arbidol0.2g q8h po. Oseltamivir75mg q12h po. Peramivir0.3gqdi.v	None	None	Low-flow nasal cannula	Low-flow nasal cannula (intermittent)
10	Arbidol0.2g q8h po. Interferon-o 500MIU qdinh.	Cefoperazone Sodium i.v.Caspofungini.v.	Methylprednisolone i.v.	High-flow nasal cannula	High-flow nasal cannula

po.=peros. i.v.=intravenous injection. inh.=inhalation.

Table 3. Comparison of laboratory parameters before and after convalescent plasma transfusion

Clinical Factors	BeforeCP transfusion	After CPtransfusion
C-reactive protein (mg/L, normal range 0-6)	55.98 (15.57-66.67)	18.13 (10.92-71.44)
Lymphocyte (10^9 per L, normal range 1.1-3.2)	0.65 (0.53-0.90)	0.76 (0.52-1.43)
Alanine aminotransferase (U/L, normal range 9-50)	42.00 (28.25-61.85)	34.30 (25.75-53.90)
Aspartate aminotransferase (U/L, normal range 15-40)	38.10 (28.50-44.00)	30.30 (17.30-38.10)
Total bilirubin (μmol/L, normal range 0-26)	12.40 (11.71-22.05)	13.98 (12.20-20.80)
SaO_2 (%, normal range ≥95)	93.00 (89.00-96.50)	96.00 (95.00-96.50)

SaO_2=oxyhemoglobin saturation.

Table 4. Comparison of serum neutralizing antibody titers and SARS-CoV-2 RNA load before and after convalescent plasma therapy

patient No.	CP transfusionDate	Before CP transfusion			After CP transfusion		
		Date	Serum neutralizing antibody titres	Serum SARS-CoV-2 RNA load (Ct value)	Date	Serum neutralizing antibody titres	Serum SARS-CoV-2 RNA load (Ct value)
1	February 9	February 8	1:160	37.25	February 10	1:640	negative
2	February 9	February 8	Unavailable	35.08	February 11	Unavailable	negative
3	February 13	February 12	1:320	38.07	February 14	1:640	negative
4	February 13	February 12	1:160	37.68	February 14	1:640	negative
5	February 12	February 11	1:640	negative	February 14	1:640	negative
6	February 12	February 11	1:640	negative	February 14	1:640	negative
7	February 12	February 11	1:320	34.64	February 14	1:640	negative
8	February 12	February 11	1:640	35.45	February 14	1:640	negative
9	February 12	February 11	1:160	negative	February 14	1:640	negative
10	February 9	February 8	1:640	38.19	February 14	1:640	negative

Figure 1:

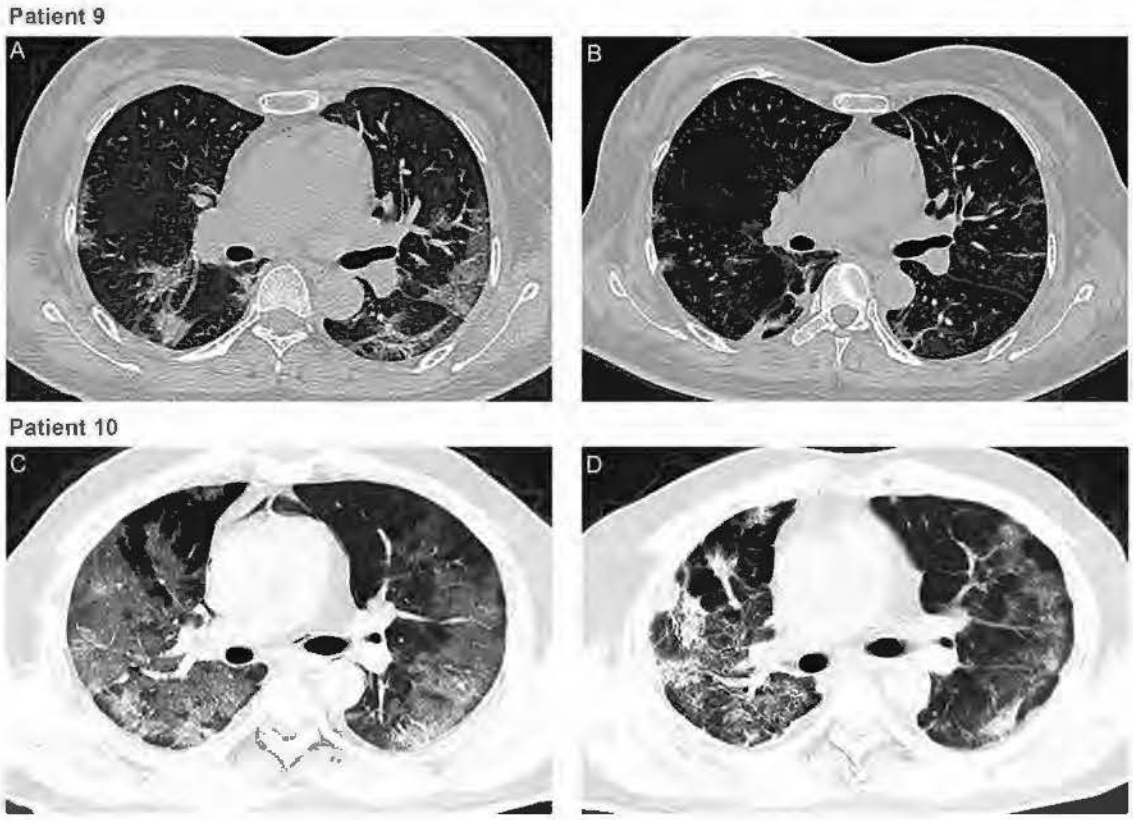


Figure 2:

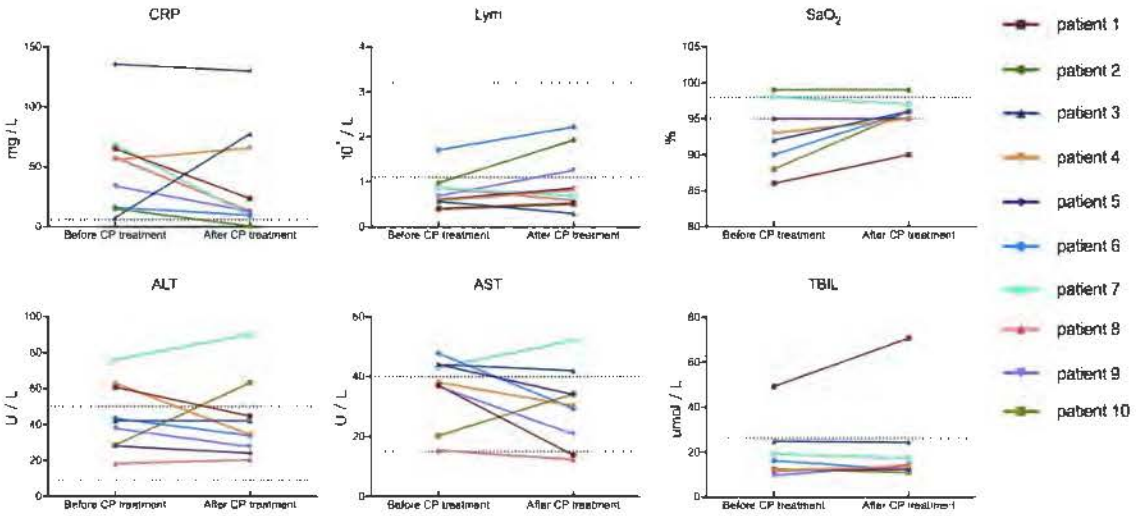
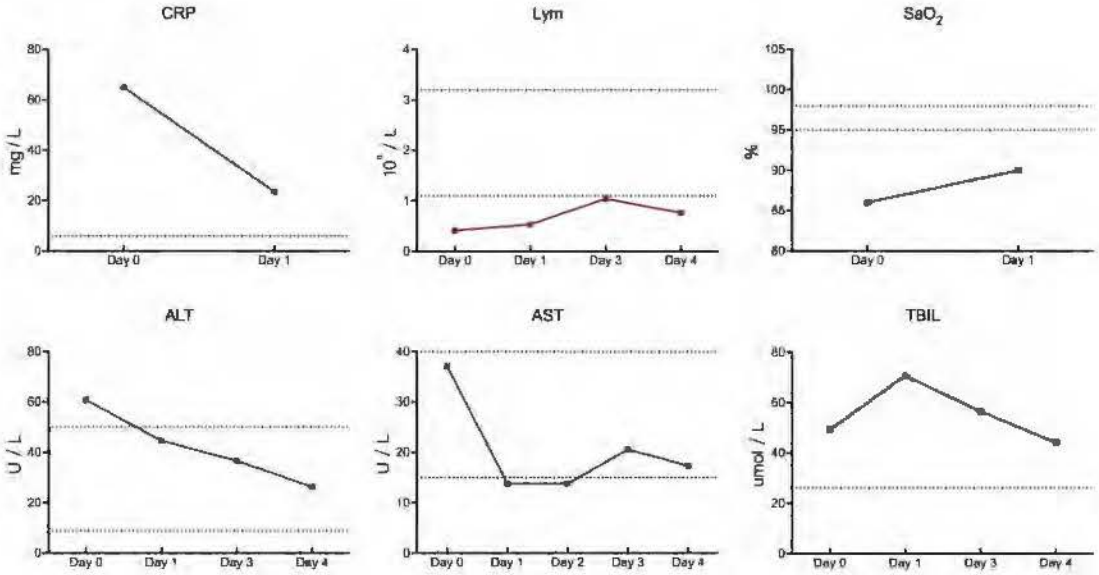


Figure 3:



Courses of Action (COAs) to Increase the Availability and Access to Remdesivir for Trials and Potential Treatment of COVID-19

Background

Drug information: Remdesivir, developed by the U.S. company Gilead Science Inc. (Gilead), is an investigational broad-spectrum antiviral being developed to treat multiple viral pathogens including Ebola, Marburg, MERS and SARS. Remdesivir is currently in clinical trials for COVID-19 in the United States and China. Remdesivir is not yet licensed or approved anywhere globally and has only early clinical data against Ebola and pre-clinical data against SARS and MERS.

(b)(5)

(b)(5)

(b)(5)

(b)(5)

(b)(5)

From:	Disbrow, Gary (OS/ASPR/BARDA) </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0FD5845DEFDA4DC0BB45F8FAC629CF09-DISBROW, GA>
To:	'Ken Nelson' <knelson@bardydx.com>
CC:	Disbrow, Gary (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0fd5845defda4dc0bb45f8fac629cf09-Disbrow, Ga <Gary.Disbrow@hhs.gov>
Subject:	RE: Follow Up - BardyDx & BARDA - COVID-19 Remote Patient Monitoring & Hydroxychloroquine Clinical Studies
Date:	2020/05/06 05:56:13
Priority:	Normal
Type:	Note

Ken,

Apologies for the delayed response, these are very busy times. If you have not already submitted your ideas to the MCM portal, please do so. The link is copied below. This will allow a discussion with your company. We are experiencing high volumes of submissions under the market research portal but we are moving them quickly through the process. I thank you for your interest is potentially partnering with BARDA.

I hope you, your family and those in your company are staying safe.

The federal government established a single point of entry for product developers to submit their research on 2019 novel coronavirus medical countermeasures If you are interested in partnering with with BARDA and PHEMCE partners about medical countermeasures against COVID-19, submit your ideas via the BARDA 2019 Novel Coronavirus Market Research Initiative. This is for market research only and a submission is not a submission to the solicitations listed below for potential funding. This does allow for a conversation and potential TechWatch.

For additional questions about the Market Research Initiative, please contact: TechWatchInbox@hhs.gov.

Regards,

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

From: Ken Nelson <knelson@bardydx.com>
Sent: Friday, May 1, 2020 11:03 AM
To: Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>
Subject: Follow Up - BardyDx &BARDA - COVID-19 Remote Patient Monitoring &Hydroxychloroquine Clinical Studies
Importance: High

Gary,

A few days ago, on April 29th we presented to multiple individuals at BARDA and HHS via the BARDA/ MedTech Innovator COVID-19 Solutions Event for about 3 hours. As a follow up to those presentations, we are trying to determine the appropriate people at BARDA to follow up with to further explore the potential use of our BardyDx CAM Patch in some of the COVID-19 clinical studies that BARDA is funding and collaborating with others on, especially ones related to monitoring QT intervals for COVID-19 patients taking Hydroxychloroquine (HCQ), Azithromycin (Z-Pak), or any other experimental or investigational drugs that may prolong QT intervals and/ or lead to other potentially lethal cardiac arrhythmias. The BardyDx CAM Patch is the only external cardiac monitoring patch clinically validated to monitor QT intervals.

Any help with directing me to the right individuals at BARDA would be greatly appreciated so that we can get a follow up call scheduled to discuss in more detail.

In the mean time, below is a very high level summary of BardyDx, our CAM Patch, and the COVID-19 related educational resources for mailing directly to patients and for home applications with remote patient monitoring, based on the rapid shift to telehealth in the current COVID-19 environment.

BardyDx Overview &Summary of COVID-19 Remote Patient Monitoring Solutions

- • ***Company*** - Bardy Diagnostics, Inc. ("BardyDx") is an innovator in digital health and remote patient monitoring, with a focus on providing the highest fidelity rhythm strips and most diagnostically-accurate and patient-friendly cardiac patch monitors in the industry.
- • ***Product*** – Our BardyDx CAM Patch is a single use and disposable, non-invasive, P-wave centric™ ambulatory cardiac monitor and arrhythmia detection device, that is uniquely

designed to accurately monitor QT intervals and detect any other cardiac arrhythmias. CAM records every heart beat continuously for up to 14 Days.

- • ***COVID-19 Solution*** –
  - • Monitoring QT intervals for COVID-19 patients taking Hydroxychloroquine (HCQ), Azithromycin (Z-Pak), or any other experimental or investigational drugs that may prolong QT intervals and/ or lead to other potentially lethal cardiac arrhythmias.
  - • The BardyDx CAM Patch is the only external cardiac monitoring patch clinically validated to monitor QT intervals.
- • ***Current COVID-19 Studies*** – CAM Patch is currently being used in significant clinical studies of COVID-19 patients including one at Walter Reed, several at UW Medicine in Seattle, and others at leading institutions across the country.
- • ***Proprietary*** – The CAM Patch's proprietary design includes patented circuit board design and signal processing with 60+ U.S. patents issued and more pending to help protect it.
- • ***Clinical Evidence*** - In addition, 3 separate head to head clinical studies have been done providing clinical evidence to help back up the superior rhythm fidelity and detection accuracy, with 2 peer reviewed and published in the American Heart Journal.

- • **Monitor Life-Threatening QT Prolongation In COVID-19 Patients** Using Hydroxychloroquine (HCQ), Azithromycin (Z-Pak), or Other Drugs (e.g., Remdesivir) Via BardyDx CAM Patch.
  - • There are 3 key ECG monitoring facts regarding proper QT monitoring with COVID-19:
    - • First, proper QT interval monitoring should include the ability to record low amplitude, low frequency content at the tail end of the T wave. The CAM Patch is designed for this very function.
    - • Second, the BardyDx CAM Patch has been clinically validated in a peer-reviewed clinical trial demonstrating excellent correlation with standard QT measurement tools.
      - • A head-to-head clinical study published in the *American Heart Journal* comparing the CAM Patch and a traditional multi-vector (3 lead) Holter monitor provides clinical evidence that the CAM Patch ECG intervals PR, QRS and QT correlated well with the traditional 3-channel Holter ECG intervals having correlation coefficients of 0.93, 0.86, and 0.94 respectively.
    - • Third, it has been reported in studies that COVID-19 may generate a myocarditis or cardiomyopathy leading to other arrhythmias if the patient receives a Z-pak or HCQ.

Sources:

1. ACC Clinical Bulletin on COVID-19 Clinical Guidance for Cardiovascular Care Team
2. Wang D, Hu B, Hu C, et al.Clinical Characteristics of 138 Hospitalized Patients with2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA. Published online February 07, 2020. doi:10.1001/jama.2020.1585
3. Chun-Yu Chen, Feng-Lin Wang &Chih-Chuan Lin (2006) Chronic Hydroxychloroquine Use Associated with QT Prolongation and Refractory Ventricular Arrhythmia. Clinical Toxicology. 44:2. 173-175, DOI: 10.1080/15563650500514558
4. Smith WM., et al. Comparison of diagnostic value using a small, single channel, P-wave centric sternal ECG monitoring patch with a standard 3-lead Holter system over 24 hours. American Heart Journal. March 2017 (See Figure 3-c)

5. • https://www.prnewswire.com/news-releases/bardy-diagnostics-announces-use-of-the-carnation-ambulatory-monitor-patch-to-measure-qt-segments-in-covid-19-patients-using-hydroxychloroquine-301029840.html

We are all fighting the COVID-19 pandemic together, and in order to help with transitioning the care of both research and non-research patients in need of cardiac monitoring to telehealth, we wanted to make you aware of the following options to consider, along with associated educational resources (available at https://protect2.fireeye.com/url?k=02f92029-5ead3955-02f91116-0cc47adc5fa2-e66e1f9b29fa0b0e&u=https://www.bardydx.com/patients along with a patient home application video):

1. • New Mail To Patient / Home Application Offering for CAM Patches &Patient Education Resources
2. • One Time Use (Disposable) BardyDx CAM Patches
3. • Monitor Life-Threatening QT Interval Prolongation and related arrhythmias in COVID-19 Patients With BardyDx CAM Patches
    a. • COVID-19 patients using hydroxychloroquine, Azithromycin or other drugs (e.g., Remdesivir)

- • **Mail To Patient/ Home Application Resources**
    - Please to visit https://protect2.fireeye.com/url?k=f924621b-a5707b67-f9245324-0cc47adc5fa2-db5090d36ce53c52&u=https://www.bardydx.com/patients to learn more and view the home application video.

Thanks and we look forward to next steps,

Ken

Kenneth W. Nelson III
Chief Commercial Officer
knelson@bardydx.com

Bardy Diagnostics, Inc.
+1-844-77P-WAVE | +1-844-777-9283
316 Occidental Ave South, Suite 310
Seattle, WA 98104
https://protect2.fireeye.com/url?k=2dad2024-71f93958-2dad111b-0cc47adc5fa2-12adc0da1d592919&u=http://www.bardydx.com/

Sender:	Disbrow, Gary (OS/ASPR/BARDA) </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0FD5845DEFDA4DC0BB45F8FAC629CF09-DISBROW, GA>
Recipient:	'Ken Nelson' <knelson@bardydx.com>; Disbrow, Gary (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0fd5845defda4dc0bb45f8fac629cf09-Disbrow, Ga <Gary.Disbrow@hhs.gov>
Sent Date:	2020/05/06 05:56:13

Department of Health and Human Services

HHS and our federal partners are working together with state, local, tribal and territorial governments, public health officials, health care providers, researchers, private sector organizations and the public to execute a whole-of-America response.

(b)(5)

Page 231

Withheld pursuant to exemption

(b)(5)

of the Freedom of Information Act

From:	Disbrow, Gary (OS/ASPR/BARDA) </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0FD5845DEFDA4DC0BB45F8FAC629CF09-DISBROW, GA>
To:	Angelastro, Michael (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=583e910528e7473d9dcdfce9d1a80b83-Angelastro, <Michael.Angelastro@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0851e89240324306b78740a4a60745e2-Johnson, Ro <Robert.Johnson@hhs.gov>; Armstrong, Kimberly (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5b778c7e17734740b14fbae4d3ed652c-Armstrong, <Kimberly.Armstrong@hhs.gov>
CC:	Figlio, Joseph (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=user3f14f4ea <Joseph.Figlio@hhs.gov>; Joyner, Arlene (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=35b6b138479f47d0bb14a6955bf3165b-Joyner, Arl <Arlene.Joyner@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>; Bright, Rick (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=53034752f35a4317aa74f46348442d39-Bright, Ric <Rick.Bright@hhs.gov>; Houchens, Christopher (HHS/ASPR) (Christopher.Houchens@hhs.gov) /o=HHS EES/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=Christopher.Houchens.os <Christopher.Houchens@hhs.gov>
Subject:	RE: Gilead call April 1, my notes and what I can recall.
Date:	2020/04/04 11:29:00
Priority:	Normal
Type:	Note

Team,

Just had a call with the WH...will have a follow up on Monday so need to get information put together by tomorrow COB.

We need to reach out to Regeneron and Genentech and understand the following

Treatment courses the currently have available in the US (if they give vials we need to know concentration of drug and what concentration they are using so we can estimate on a 70kg individual)

Do they have any drug substance available, if so, how much where is it and how long does it take to convert to DP and where is that done

What is their plan for additional manufacturing of ds and dp...what are the timelines for each step and capacity to complete each step and where are those activities done (US outside the US)

Do they have sufficient raw materials to manufacture additional DS and if so, how many runs

Trying to see what the supply for each will look like in the next several weeks to determine potential drug supply

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

From: Angelastro, Michael (OS/ASPR/BARDA) <Michael.Angelastro@hhs.gov>
Sent: Saturday, April 4, 2020 11:23 AM
To: Johnson, Robert (OS/ASPR/BARDA) <Robert.Johnson@hhs.gov>; Armstrong, Kimberly (OS/ASPR/BARDA) <Kimberly.Armstrong@hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>
Cc: Figlio, Joseph (OS/ASPR/BARDA) <Joseph.Figlio@hhs.gov>; Joyner, Arlene (OS/ASPR/BARDA) <Arlene.Joyner@hhs.gov>; Donis, Ruben (OS/ASPR/BARDA) <Ruben.Donis@hhs.gov>
Subject: RE: Gilead call April 1, my notes and what I can recall.

Robert,
Correct. Gilead appears to have things under control -- as a company, they are throwing all their heavy hitters/ 'A-team' at this one.

Best BARDA can do (at this time) is maintain a level of visibility into their rapidly evolving production plans – and hope they continue to be willing to share.

-M

From: Johnson, Robert (OS/ASPR/BARDA) <Robert.Johnson@hhs.gov>
Sent: Saturday, April 4, 2020 8:01 AM
To: Angelastro, Michael (OS/ASPR/BARDA) <Michael.Angelastro@hhs.gov>; Armstrong, Kimberly (OS/ASPR/BARDA) <Kimberly.Armstrong@hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>
Cc: Figlio, Joseph (OS/ASPR/BARDA) <Joseph.Figlio@hhs.gov>; Joyner, Arlene (OS/ASPR/BARDA) <Arlene.Joyner@hhs.gov>; Donis, Ruben (OS/ASPR/BARDA) <Ruben.Donis@hhs.gov>
Subject: RE: Gilead call April 1, my notes and what I can recall.

Mike,

Thanks a lot for the really nice summary below. in reading Bob's e-mail, it sounds like at this time there is not much the USG can do in terms of additional support to obtain raw materials sooner, but please let me know if you have a different take.

Thanks.

Robert

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

contractor must disregard that portion of the communication and contact the Contracting Officer for direction

---

From: Angelastro, Michael (OS/ASPR/BARDA) <Michael.Angelastro@hhs.gov>
Sent: Thursday, April 2, 2020 1:41 PM
To: Johnson, Robert (OS/ASPR/BARDA) <Robert.Johnson@hhs.gov>; Armstrong, Kimberly (OS/ASPR/BARDA) <Kimberly.Armstrong@hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>
Cc: Figlio, Joseph (OS/ASPR/BARDA) <Joseph.Figlio@hhs.gov>; Joyner, Arlene (OS/ASPR/BARDA) <Arlene.Joyner@hhs.gov>; Donis, Ruben (OS/ASPR/BARDA) <Ruben.Donis@hhs.gov>
Subject: FW: Gilead call April 1, my notes and what I can recall.

All,
We had a 'manufacturing/ supply chain' call with folks at Gilead last night – just to check-in on things.

Bob captured the detailed notes below (if you want to nerd-out on the chemistry).

I'm awaiting a revised/ updated synthesis map, bill of materials (BOM) for RSMs/API, and their current scale out plan.

My take… Gilead appears to be working very hard to onboard redundant suppliers and add'l CMO capacity.

The Gilead team is appreciative of the 'recommendations & support' that the BARDA small molecule/ materiel management SMEs are providing.

-M

From: Stahl, Robert (OS/ASPR/BARDA) (CTR) <Robert.Stahl@hhs.gov>
Sent: Thursday, April 2, 2020 12:58 PM
To: Angelastro, Michael (OS/ASPR/BARDA) <Michael.Angelastro@hhs.gov>; Figlio, Joseph (OS/ASPR/BARDA) <Joseph.Figlio@hhs.gov>; Singer, Lawrence (OS/ASPR/BARDA) (CTR) <Lawrence.Singer@hhs.gov>
Cc: Joyner, Arlene (OS/ASPR/BARDA) <Arlene.Joyner@hhs.gov>
Subject: Gilead call April 1, my notes and what I can recall.

Team,

Here is what I can gather from the call last evening. Please add or correct what I have missed.

The meeting focused on the March 20, supply chain map for the API and the March 23, Drug Product Sourcing.

Relative to the supply chain for Asia, India and all countries in general, there has been a tightening of supply with prices increasing and tightening of the key starter materials from china. Current key starter materials from china would be the (b)(3):42 U.S.C. § 247d-6b(d) (b)(3):42 U.S.C. § 247d-6b(d). The commodity raw materials are still tight but the manufacturing is starting to return to normal. (b)(3): is a key commodity sourced from China which is currently in tight supply.

There are transportation issues particularly with air shipment. The logistics are such that there is a lot of competition. Joe Figlieo did state that BARDA working with FEMA would be able to assist if needed to expedite shipments with the resources of the US government. Shipment by sea will work as long as the lead time can be factored and is adequate.

Gilead is still stockpiling raw materials and reagents especially those that will be hard to come by as a result of the world pandemic. (b)(3):42 U.S.C. § 247d-6b(d) The goal is to have the stockpile set aside and not used unless necessary. There are (b) key important compounds for this stockpile needed for (b)(3):42 although others will be added. (b)(3):42 U.S.C. § 247d-6b(d) commodity, (b)(3):42 Germany and (b)(3):42 from Japan. (b)(3):4 is to eventually be manufactured by (b)(3) (b)(3):42 U.S.C. § via fermentation. This will take several months perhaps 6, to develop the process and start before product is out the door. For (b)(3) from (b)(3) Germany, this is currently in short supply and the stock pile will take a while. There was significant concern about (b)(3):42 as well as this is key to the final prodrug portion and close to the end of the synthesis. (b)(3): is key to the (b)(3):42 The chemistry to potentially eliminate the need for (b)(3):42 U.S.C. § 247d-6b(d) is ongoing and uses (b)(3):42 We should verify this sourcing of the (b)(3):42 I can help with the structures and the specifics.

The less critical but not readily available reagents and compounds for the stockpile are (b)(3):42 U.S.C. § Germany and with shipping issues, (b)(3):42 U.S.C. § 247d-6b(d) and (b)(3):42 U.S.C. § 247d-6b(d) all foreign sourced with no US source and source not revealed but likely Asia, (b)(3):42 U.S.C. § source not revealed. Remaining sources are likely commodity and should be part of the return to normal scenario. Gilead is more confident in the supply of these compounds. However, a shortage of any will shut down the manufacture of remdesivir.

(b)(3):42 U.S.C. § 247d-6b(d) (gas dissolved in liquid) is a raw material that was specifically discussed as this requires (b) metric ton per ton of Remdesivir. Tank truck quantities will be required. This will be manufactured on site via purchase of (b)(3):42 U.S.C. § (b)(3):4 (A 1 molar solution is required, I will do the calculation for you) This is still tank trucks of (b)(3):42 U.S.C.

(b)(3):42 U.S.C. § is backed up by a supply of (b)(3):42 U.S.C. § stocked for (b)(3):4 converted to (b)(3):42 I believe the important issue here is that we make sure that this supply or that a sufficient quantity of this supply is reserved for Remdesivir. Looking at the chemistry, this requires almost (b)(3):4 tons per ton of Remdesivir. Gilead did not specify if (b)(3): was stockpiled. (b)(3): is supplied from Russia or China for now.

L-Alanine is evidently available in massive quantities essentially as a commodity from Japan as there are many uses. Gilead was confident to the supply. I believe it is up to BARDA to verify the need. (b)(3): (b)(3):42 U.S.C. § could manufacture this with the correct strain to start the fermentation. Start-up could take several months. Gilead was not keen to this. I would suggest BARDA to ultimately consider.

The chemistry to manufacture (b)(3):42 U.S.C. § 247d-6b(d) Gilead felt was best left to Japan. We queried about the ability for the entire synthesis from (b)(3): being transferred to (b)(3):42 However, (b)(3):42 is a relatively small facility only suited for the synthesis of the final (b)(3):42 from (b)(3):42 (b)(3):42 U.S.C. § 247d-6b(d)

Gilead thanked BARDA for the leads relative to the CMO's to the different manufacturing steps. However, they specifically mentioned (b)(3):42 for the fused (b)(3):42 U.S.C. § . I believe it is probably safe to assume that Albemarle has a handle on the new chemistry.

Additionally from a manufacturing perspective, there was significant optimization work taking place at the (b)(3):42 U.S.C. § which also uses the (b)(3). We had hoped to get some information on the stoichiometry for this reaction and the other reactions to get a better idea of the what the raw material requirements we were being faced with. However, almost every step has some form of optimization work taking place. I suspect as the process is being transferred from (b)(3):42 U.S.C. § both sites chosen because of continuous capability in part, that these sites would want to do in house work to optimize the process steps for use of reagents and fit to facility. The entire synthesis at this point is a moving target with the exception of (b)(3): which received the process essentially as published in the (b)(3):42 This they told us on the first call. Mike was able to get they to send us the raw material list for the primary synthesis essentially from where I and BARDA Quality/Regulatry would consider the regulatory starting materials to be.

The limiting reagent for the primary synthesis is the (b)(3):42 U.S.C. § which requires (b)(tons per ton of Remdesivir. Not only is this the limiting reagent from a stoichiometric perspective it is also limiting from the supply perspective. This presents a unique problem relative to capacity. Gilead never revealed how much of the (b)(3):42 U.S.C. that they have estimated that would be needed. However, it is easy to guess that this would be huge. The (b)(3):4 is also evidently not a commodity unlike the (b)(3): for the other compound for the (b)(3):42 the (b)(3) (b)(3):42 The problem becomes that even if we brought (b)(3):42 U.S.C. § on line to manufacture simultaneous with AMPAC, there would be insufficient supplies of the (b)(3) to supply both facilities for simultaneous operation. Part of the process is continuous and the (b)(3): would need to be stockpiled for months before the start.

Gilead for the IND was able to file (b)(3):42 U.S.C. § 247d-6b(d) At the time because of the situation, this was acceptable. (b)(3):42 U.S.C. § This is essentially (b)(3):42 U.S.C. § (b)(3):42 from the final product. (b)(3):42 U.S.C. § 247d-6b(d) (b)(3):42 U.S.C. § 247d-6b(d) (b)(3):42 U.S.C. § 247d-6b(d) BARDA needs to make every effort to work with Gilead and the FDA to be sure that this regulatory strategy is accepted to streamline the registration.

Additional.

The lead time for the (b)(3): is 5 months.
The (b)(3):42 reaction to the (b)(3):42 takes 2 weeks. Gilead will supply timing for the manufacturing operations.

Currently, the entire API production is rate limiting to the manufacturing as compared to the (b)(3):4 operation. Eventually, the (b)(3):4 will be the rate limiting operation.

There are (b US as main sites (b)(3):42 U.S.C. § . The (b)(3):4 is using API in hand. There are added US based sites pending contracts to increase the capacity as well as sites overseas.

(I will let those better versed in (b)(3):42 U.S.C. § sites cover this in detail) For now (b)(3):4 is not limiting. Capacity is being added. The API is supplied from (b)(3):

Once again, it was pointed out that the US based manufacturing is desired.

Gilead will provide reagent lists and quantities from the (b)(3): process and processing times for reactions/delivery times for key reagents.

All The Best,
Bob

Robert J. Stahl Ph.D.

Tunnell Government Services (contractor) supporting the mission of:
Division of Pharmaceutical Countermeasures Infrastructure (PCI)
Biomedical Advanced Research and Development Authority (BARDA)
Office of Assistant Secretary of Preparedness and Response (ASPR)
U.S. Department of Health & Human Services (HHS)
330 Independence Ave. SW, Room G640, Washington DC 20201

(202) 205-3723 (W)
(b)(6) (C)
(202) 205-8442 (F)

robert.stahl@hhs.gov
www.medicalcountermeasures.gov

Sender:	Disbrow, Gary (OS/ASPR/BARDA) </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0FD5845DEFDA4DC0BB45F8FAC629CF09-DISBROW, GA>
Recipient:	Angelastro, Michael (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=583e910528e7473d9dcdfce9d1a80b83-Angelastro, <Michael.Angelastro@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0851e89240324306b78740a4a60745e2-Johnson, Ro <Robert.Johnson@hhs.gov>; Armstrong, Kimberly (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5b778c7e17734740b14fbae4d3ed652c-Armstrong, <Kimberly.Armstrong@hhs.gov>; Figlio, Joseph (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=user3f14f4ea <Joseph.Figlio@hhs.gov>; Joyner, Arlene (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=35b6b138479f47d0bb14a6955bf3165b-Joyner, Arl <Arlene.Joyner@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>; Bright, Rick (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=53034752f35a4317aa74f46348442d39-Bright, Ric <Rick.Bright@hhs.gov>; Houchens, Christopher (HHS/ASPR) (Christopher.Houchens@hhs.gov) /o=HHS EES/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=Christopher.Houchens.os <Christopher.Houchens@hhs.gov>
Sent Date:	2020/04/04 11:29:39
Delivered Date:	2020/04/04 11:29:00

From:	Kadlec, Robert (OS/ASPR/IO) </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=A182EDA693D040D3832BAE6EFCF7A255-KADLEC, ROB>
SentVia:	Disbrow, Gary (OS/ASPR/BARDA) </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0FD5845DEFDA4DC0BB45F8FAC629CF09-DISBROW, GA>
To:	Walker, Robert (OS/ASPR/BARDA) (Robert.Walker@hhs.gov) <Robert.Walker@hhs.gov>
Subject:	FW: IMPORTANT CALL Remdesivir: URGENT
Date:	2020/04/30 17:53:14
Start Date:	2020/04/30 18:05:00
End Date:	2020/04/30 18:35:00
Priority:	Normal
Type:	Schedule.Meeting.Request
Location:	Tele Conf Call - 8776120731,,,3127927#

-----Original Appointment-----
From: Kadlec, Robert (OS/ASPR/IO) <Robert.Kadlec@hhs.gov>
Sent: Thursday, April 30, 2020 5:52 PM
To: Kadlec, Robert (OS/ASPR/IO); Yeskey, Kevin (OS/ASPR/IO); Adams, Steven A. (ASPR/SNS); Shuy, Bryan (OS/ASPR/IO); Disbrow, Gary (OS/ASPR/BARDA); Houchens, Christopher (OS/ASPR/BARDA); Johnson, Robert (OS/ASPR/BARDA); Hassell, David (Chris) (OS/ASPR/IO); Callahan, Victoria (OS/ASPR/IO) (CTR); Redd, John (OS/ASPR/SPPR); Moreno, Rafael (OS/ASPR); Ayala, Ana (OS/OGA)
Subject: IMPORTANT CALL Remdesivir: URGENT
When: Thursday, April 30, 2020 6:05 PM-6:35 PM (UTC-05:00) Eastern Time (US & Canada).
Where: Tele Conf Call - 8776120731,,,3127927#

From: Kadlec, Robert (OS/ASPR/IO) <Robert.Kadlec@hhs.gov>
Sent: Thursday, April 30, 2020 5:40 PM
To: Yeskey, Kevin (OS/ASPR/IO) <Kevin.Yeskey@hhs.gov>; Adams, Steven A. (ASPR/SNS) <saa1@cdc.gov>; Shuy, Bryan (OS/ASPR/IO) <Bryan.Shuy@hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Houchens, Christopher (OS/ASPR/BARDA) <Christopher.Houchens@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) <Robert.Johnson@hhs.gov>; Hassell, David (Chris) (OS/ASPR/IO) <David.Hassell@hhs.gov>; Ford-Barnes, Arwenthia (OS/ASPR/IO) <Arwenthia.FordBarnes@hhs.gov>; Callahan, Victoria (OS/ASPR/IO) (CTR) <Victoria.Callahan@hhs.gov>; Redd, John (OS/ASPR/SPPR) <John.Redd@hhs.gov>
Subject: Fwd: Remdesivir: URGENT

Folks let's
Convene on a call at 6 pm tonite to
Discuss.

Issues to determine.

1. Is the approach outlined appropriate and operationally supportable
2. Who in ASPR should

Be be the POC for
Allocation decisions.
Sent from my iPhone

Sender:	Kadlec, Robert (OS/ASPR/IO) </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=A182EDA693D040D3832BAE6EFCF7A255-KADLEC, ROB>; Disbrow, Gary (OS/ASPR/BARDA) </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0FD5845DEFDA4DC0BB45F8FAC629CF09-DISBROW, GA>
Recipient:	Walker, Robert (OS/ASPR/BARDA) (Robert.Walker@hhs.gov) <Robert.Walker@hhs.gov>
Sent Date:	2020/04/30 17:53:13
Delivered Date:	2020/04/30 17:53:14
From:	Kadlec, Robert (OS/ASPR/IO) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=A182EDA693D040D3832BAE6EFCF7A255-KADLEC, ROB <Robert.Kadlec@hhs.gov>
To:	Yeskey, Kevin (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=6fe6cf13518445fd9c3a1c254e166b3f-Yeskey, Kev <Kevin.Yeskey@hhs.gov>; Adams, Steven A. (ASPR/SNS) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f98462fe8d124743a437c7a80b3f60dd-Adams, Stev <saa1@cdc.gov>; Shuy, Bryan (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fdeb5ca04b6b4ed19fec2209b5f571e7-Shuy, Bryan <Bryan.Shuy@hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0fd5845defda4dc0bb45f8fac629cf09-Disbrow, Ga <Gary.Disbrow@hhs.gov>; Houchens, Christopher (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7ac94a574bd04528b7c91bbd61893975-Houchens, C <Christopher.Houchens@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0851e89240324306b78740a4a60745e2-Johnson, Ro <Robert.Johnson@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>; Ford-Barnes, Arwenthia (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d533abc24cbe44b79f6fddc6b08737a6-Ford-Barnes <Arwenthia.FordBarnes@hhs.gov>; Callahan, Victoria (OS/ASPR/IO) (CTR) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=95162cb185624a6ebe5fadf08484c141-Callanhan, <Victoria.Callahan@hhs.gov>; Redd, John (OS/ASPR/SPPR) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=9ba3fed4ee8646ec849a5a87136a24f6-Redd, John <John.Redd@hhs.gov>
Subject:	Fwd: Remdesivir: URGENT
Date:	2020/04/30 17:40:06
Priority:	Normal
Type:	Note

Folks let's
Convene on a call at 6 pm tonite to
Discuss.

Sender:	Kadlec, Robert (OS/ASPR/IO) /O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=A182EDA693D040D3832BAE6EFCF7A255-KADLEC, ROB <Robert.Kadlec@hhs.gov>
Recipient:	Yeskey, Kevin (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=6fe6cf13518445fd9c3a1c254e166b3f-Yeskey, Kev <Kevin.Yeskey@hhs.gov>; Adams, Steven A. (ASPR/SNS) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f98462fe8d124743a437c7a80b3f60dd-Adams, Stev <saa1@cdc.gov>; Shuy, Bryan (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fdeb5ca04b6b4ed19fec2209b5f571e7-Shuy, Bryan <Bryan.Shuy@hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0fd5845defda4dc0bb45f8fac629cf09-Disbrow, Ga <Gary.Disbrow@hhs.gov>; Houchens, Christopher (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7ac94a574bd04528b7c91bbd61893975-Houchens, C <Christopher.Houchens@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0851e89240324306b78740a4a60745e2-Johnson, Ro <Robert.Johnson@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>; Ford-Barnes, Arwenthia (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d533abc24cbe44b79f6fddc6b08737a6-Ford-Barnes <Arwenthia.FordBarnes@hhs.gov>; Callahan, Victoria (OS/ASPR/IO) (CTR) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=95162cb185624a6ebe5fadf08484c141-Callanhan, <Victoria.Callahan@hhs.gov>; Redd, John (OS/ASPR/SPPR) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=9ba3fed4ee8646ec849a5a87136a24f6-Redd, John <John.Redd@hhs.gov>
Sent Date:	2020/04/30 17:40:05
Delivered Date:	2020/04/30 17:40:06

From:	Disbrow, Gary (OS/ASPR/BARDA) </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0FD5845DEFDA4DC0BB45F8FAC629CF09-DISBROW, GA>
To:	Blatner, Gretta (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=623cb123c2324236b1db6fb9153e0bbf-Blatner, Gr <Gretta.Blatner@hhs.gov>
Subject:	RE: Additional Information for Thursday
Date:	2020/05/06 11:49:20
Priority:	Normal
Type:	Note

Gretta,

For diagnostics, Rodney had an email that had simply answers for the diagnostic test we are supporting.

Can you find that and print it larger enough for me to take. The tables are great but I don't want to flip through pages.

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

From: Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>
Sent: Tuesday, May 5, 2020 6:25 PM
To: Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>
Subject: Additional Information for Thursday

1. Attached are the updated profiles of members.
    a. I added COVID Awards in each state and only added non-COVID awards for Mass, as Julie's polling says she is going to speak about awards in Mass and how decisions around awards are made.
    b. Also attached are the letter from Patty Murray re BARDA and the letter from Tim Kane and the VA delegation regarding Phlow - FYSA
2. The DCD/RQA information about CQ/HCQ is also attached, as we discussed, it is long.
3. For the EUA, according to Tremel, we could ask the FDA to remove the EUA designation or FDA could also remove the EUA designation for CQ/HCQ. Our current statement is as follows:
    a. BARDA continues to consider the benefits and risks of hydroxychloroquine and chloroquine in light of the EUA for remdesivir as a treatment for hospitalized patients with COVID. In consultation with our interagency partners we will continue to weigh ongoing safety and efficacy data as well as product availability for both products in our decision making.
4. I'll have a note card on the little Cue device.
    a. RT-PCR Test
    b. Sample to answer in 20 mins
    c. Cost of the cube approximately (b)(3):42 U.S.C. §
    d. EUA possible in less than 3 weeks
    e. Likely not authorized for home use at that time, but very useful in outpatient clinics and doctor's offices etc.
5. New Hologic Award for the Panther system
    a. EUA to be applied for tomorrow and could be approved in (b)(3):42 U.S.C. rolling review ongoing now)
    b. Will be able to ship approximately 1M tests per week after EUA
    c. "work horse" machine currently found in reference labs and hospital labs
6. Rodney is sending new shipment information for BARDA supported tests – over 7 weeks approximately 2.6M tests shipped.

<< File: HELP Member Profiles_updated.docx >> << File: HCQ CQ Safety QA 20200504.docx >> << File: 3.23.2020 Virginia Delegation Letter to HHS.pdf >> << File: April 30 - BARDA letter FINAL.pdf >>

Gretta Blatner, MS MPH
Special Assistant to the Director, BARDA
Office Telephone: 202-401-9386
Cell: (b)(6)

Sender:	Disbrow, Gary (OS/ASPR/BARDA) </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0FD5845DEFDA4DC0BB45F8FAC629CF09-DISBROW, GA>
Recipient:	Blatner, Gretta (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=623cb123c2324236b1db6fb9153e0bbf-Blatner, Gr <Gretta.Blatner@hhs.gov>
Sent Date:	2020/05/06 11:49:20

From:	Disbrow, Gary (OS/ASPR/BARDA) </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0FD5845DEFDA4DC0BB45F8FAC629CF09-DISBROW, GA>
To:	Johnson, Robert (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0851e89240324306b78740a4a60745e2-Johnson, Ro <Robert.Johnson@hhs.gov>; Armstrong, Kimberly (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5b778c7e17734740b14fbae4d3ed652c-Armstrong, <Kimberly.Armstrong@hhs.gov>
CC:	Oshansky, Christine (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d7bd764440b44b06af644cdcd22e42d6-Oshansky, C <Christine.Oshansky@hhs.gov>; Donis, Ruben (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=af00dcf720cb429f8e2accbe06ee32ff-Donis, Rube <Ruben.Donis@hhs.gov>; Kozak, Marina (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a01168b63ebb4402ba3d5a67f5d583c1-Kozak, Mari <Marina.Kozak@hhs.gov>
Subject:	RE: COVID-19: Kevzara 2040 study Question
Date:	2020/05/20 07:55:19
Priority:	Normal
Type:	Note

Yes. That would be my assumption.

Please loop in Steve Adams and Victor Harper.

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: [redacted]
Fax: 202-205-0873
email: Gary.Disbrow@HHS.gov

contractor must disregard that portion of the communication and contact the Contracting Officer for direction

---

From: Johnson, Robert (OS/ASPR/BARDA) <Robert.Johnson@hhs.gov>
Sent: Wednesday, May 20, 2020 7:54 AM
To: Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Armstrong, Kimberly (OS/ASPR/BARDA) <Kimberly.Armstrong@hhs.gov>
Cc: Oshansky, Christine (OS/ASPR/BARDA) <Christine.Oshansky@hhs.gov>; Donis, Ruben (OS/ASPR/BARDA) <Ruben.Donis@hhs.gov>; Kozak, Marina (OS/ASPR/BARDA) <Marina.Kozak@hhs.gov>
Subject: RE: COVID-19: Kevzara 2040 study Question

Gary,

Thanks. one last question-should we alert SNS? I'm assuming that since this is a licensed product if the USG decided to buy any doses, it would come from them?

Thanks.

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: Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>
Sent: Wednesday, May 20, 2020 7:52 AM
To: Johnson, Robert (OS/ASPR/BARDA) <Robert.Johnson@hhs.gov>; Armstrong, Kimberly (OS/ASPR/BARDA) <Kimberly.Armstrong@hhs.gov>
Cc: Oshansky, Christine (OS/ASPR/BARDA) <Christine.Oshansky@hhs.gov>; Donis, Ruben

(OS/ASPR/BARDA) <Ruben.Donis@hhs.gov>; Kozak, Marina (OS/ASPR/BARDA) <Marina.Kozak@hhs.gov>
Subject: RE: COVID-19: Kevzara 2040 study Question

Yes, if not donated. If procurement occurs, then the below could be true for either delivery to SNS or stored by Sponsor.

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

From: Johnson, Robert (OS/ASPR/BARDA) <Robert.Johnson@hhs.gov>
Sent: Wednesday, May 20, 2020 7:48 AM
To: Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Armstrong, Kimberly (OS/ASPR/BARDA) <Kimberly.Armstrong@hhs.gov>
Cc: Oshansky, Christine (OS/ASPR/BARDA) <Christine.Oshansky@hhs.gov>; Donis, Ruben (OS/ASPR/BARDA) <Ruben.Donis@hhs.gov>; Kozak, Marina (OS/ASPR/BARDA) <Marina.Kozak@hhs.gov>
Subject: RE: COVID-19: Kevzara 2040 study Question

Gary,

Hi. if it's not donated, and since it is a licensed product, wouldn't the company be directly responsible for providing the drug? unless the USG made a buy?

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: Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>
Sent: Wednesday, May 20, 2020 7:44 AM
To: Johnson, Robert (OS/ASPR/BARDA) <Robert.Johnson@hhs.gov>; Armstrong, Kimberly (OS/ASPR/BARDA) <Kimberly.Armstrong@hhs.gov>
Cc: Oshansky, Christine (OS/ASPR/BARDA) <Christine.Oshansky@hhs.gov>; Donis, Ruben (OS/ASPR/BARDA) <Ruben.Donis@hhs.gov>; Kozak, Marina (OS/ASPR/BARDA) <Marina.Kozak@hhs.gov>
Subject: RE: COVID-19: Kevzara 2040 study Question

If there is an EUA, I would assume that it would go through the same process that is being used for HCQ and Remdesivir. States make request to FEMA who then coordinates with ASPR/SNS for distribution if delivered to the SNS or with ASPR/SNS/Company if maintained under the company's quality control system.

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.

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

---

From: Johnson, Robert (OS/ASPR/BARDA) <Robert.Johnson@hhs.gov>
Sent: Wednesday, May 20, 2020 7:29 AM
To: Armstrong, Kimberly (OS/ASPR/BARDA) <Kimberly.Armstrong@hhs.gov>
Cc: Oshansky, Christine (OS/ASPR/BARDA) <Christine.Oshansky@hhs.gov>; Donis, Ruben (OS/ASPR/BARDA) <Ruben.Donis@hhs.gov>; Kozak, Marina (OS/ASPR/BARDA) <Marina.Kozak@hhs.gov>; Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>
Subject: RE: COVID-19: Kevzara 2040 study Question

Kim,

Hi. looping in Gary for awareness. No, BARDA would not be involved in procurement/distribution.

In our presentation to Janet tomorrow, let's give her a heads up on Regeneron's plan.

Thanks.

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

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.

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

---

From: Armstrong, Kimberly (OS/ASPR/BARDA) <Kimberly.Armstrong@hhs.gov>
Sent: Tuesday, May 19, 2020 3:49 PM
To: Johnson, Robert (OS/ASPR/BARDA) <Robert.Johnson@hhs.gov>
Cc: Oshansky, Christine (OS/ASPR/BARDA) <Christine.Oshansky@hhs.gov>; Donis, Ruben (OS/ASPR/BARDA) <Ruben.Donis@hhs.gov>; Kozak, Marina (OS/ASPR/BARDA) <Marina.Kozak@hhs.gov>
Subject: FW: COVID-19: Kevzara 2040 study Question
Importance: High

Robert,
Regeneron would like to know if BARDA will be involved in product distribution as a part of an EUA for sarulimab. I don't think we can expect a donation to the SNS.

I will respond that we will participate in the writing and FDA discussions regarding an EUA, but I need to know how to respond on the distribution/acquisition question. They want a response by Thurs morning.

I don't believe the interim analysis will be that strong of a signal that they will be getting an EUA, but the data can always surprise us. Keep in mind Genentech will have a study read out in about a month, we should figure out what the plan is.

Thanks,
Kim

From: Yasmin Khan <Yasmin.Khan@regeneron.com>
Sent: Tuesday, May 19, 2020 3:30 PM
To: Armstrong, Kimberly (OS/ASPR/BARDA) <Kimberly.Armstrong@hhs.gov>
Cc: Yasmin Khan <Yasmin.Khan@regeneron.com>; Leah Lipsich <Leah.Lipsich@regeneron.com>
Subject: COVID-19: Kevzara 2040 study Question
Importance: High

Dear Kim,

We wanted to inform you of the next steps for the 2040 study- phase 3 study interim analysis. The DBL for the interim analysis is planned for May 20th with a blinded IDMC review scheduled on May 22, 2020. The IDMC would inform REGN of the recommendation to alter and/or stop the study and the decision by select members of executive management have decided to accept the IDMC recommendation . If the IDMC recommendation is not accepted or the recommendation is to continue the study as planned, no further disclosure of the data will occur.

If the data is promising, REGN would be prepared to submit an EUA on May 26 (target). We wanted to know if BARDA will participate at any level (including distribution) for the EUA? This will enable our planning and next steps.

We will need to inform our management of any BARDA involvement and would appreciate your prompt response (Thursday morning latest).

Thank you for your help,
Yasmin

Warm Regards,
Yasmin Khan
Director, Development Program Manager
Regeneron Pharmaceuticals Inc.
Office: 914-847-3187
Cell: (b)(6)

Sender:	Disbrow, Gary (OS/ASPR/BARDA) </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0FD5845DEFDA4DC0BB45F8FAC629CF09-DISBROW, GA>
Recipient:	Johnson, Robert (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0851e89240324306b78740a4a60745e2-Johnson, Ro <Robert.Johnson@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>; Donis, Ruben (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=af00dcf720cb429f8e2accbe06ee32ff-Donis, Rube <Ruben.Donis@hhs.gov>; Kozak, Marina (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a01168b63ebb4402ba3d5a67f5d583c1-Kozak, Mari <Marina.Kozak@hhs.gov>
Sent Date:	2020/05/20 07:55:18
Delivered Date:	2020/05/20 07:55:19

From:	Disbrow, Gary (OS/ASPR/BARDA) </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0FD5845DEFDA4DC0BB45F8FAC629CF09-DISBROW, GA>
To:	Blatner, Gretta (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=623cb123c2324236b1db6fb9153e0bbf-Blatner, Gr <Gretta.Blatner@hhs.gov>
Subject:	Re: Updated: draft BARDA All Hands Agenda 19 June
Date:	2020/06/17 10:07:48
Priority:	Normal
Type:	Note

Yes it is a holiday

Sent from my iPhone

On Jun 17, 2020, at 9:59 AM, Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>wrote:

Do you want to skip the all hands on Friday July 3rd?

From: Lambert, Linda (OS/ASPR/BARDA) <Linda.Lambert@hhs.gov>
Sent: Wednesday, June 17, 2020 8:52 AM
To: Belton, Amy (OS/ASPR/BARDA) <Amy.Belton@hhs.gov>; Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>
Cc: Deibes, Yuliya (OS/ASPR/BARDA) <Yuliya.Deibes@hhs.gov>
Subject: RE: Updated: draft BARDA All Hands Agenda 19 June

Hi Amy
I'm good either way but think a Friday off before the weekend makes sense.

Gretta – can you check in with Gary and let us know?

Linda C. Lambert, PhD
Director, Medical Countermeasures Program Support Services
Biomedical Advanced Research and Development Authority (BARDA)
Assistant Secretary for Preparedness and Response (ASPR)
Department of Health and Human Services
Washington, D.C. 20201
Phone: 202-841-9481
email: Linda.Lambert@hhs.gov

Note to contractors: nothing in this e-mail is intended to constitute contractuol direction or to impact cost, price, or schedule contained in the contract. If the contractor believes there is an impact, the contractor must disregord thot portion of the communication and contact the Contracting Officer for direction.

From: Belton, Amy (OS/ASPR/BARDA) <Amy.Belton@hhs.gov>
Sent: Wednesday, June 17, 2020 8:46 AM
To: Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>; Lambert, Linda (OS/ASPR/BARDA) <Linda.Lambert@hhs.gov>
Cc: Deibes, Yuliya (OS/ASPR/BARDA) <Yuliya.Deibes@hhs.gov>
Subject: RE: Updated: draft BARDA All Hands Agenda 19 June

Hi,

Are we having an All Hands meeting on July 3rd?

I am asking because that is the Friday before a holiday weekend. If we are not it may be a good idea to have all of the ORISE fellows briefings on 6/26 (Program Managers and Fellows) because if not then there will be a two week gap between the groups (6/26 to 7/10).

Thoughts?

Amy

From: Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>
Sent: Tuesday, June 16, 2020 2:41 PM
To: Belton, Amy (OS/ASPR/BARDA) <Amy.Belton@hhs.gov>; Lambert, Linda (OS/ASPR/BARDA) <Linda.Lambert@hhs.gov>
Cc: Deibes, Yuliya (OS/ASPR/BARDA) <Yuliya.Deibes@hhs.gov>
Subject: RE: Updated: draft BARDA All Hands Agenda 19 June

Ask Sam if he or someone on his staff would be interested.

From: Belton, Amy (OS/ASPR/BARDA) <Amy.Belton@hhs.gov>
Sent: Tuesday, June 16, 2020 2:41 PM
To: Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>; Lambert, Linda (OS/ASPR/BARDA) <Linda.Lambert@hhs.gov>
Cc: Deibes, Yuliya (OS/ASPR/BARDA) <Yuliya.Deibes@hhs.gov>
Subject: RE: Updated: draft BARDA All Hands Agenda 19 June

Good idea. Hurricane season is approaching!!!

Amy

From: Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>
Sent: Tuesday, June 16, 2020 2:40 PM
To: Belton, Amy (OS/ASPR/BARDA) <Amy.Belton@hhs.gov>; Lambert, Linda (OS/ASPR/BARDA) <Linda.Lambert@hhs.gov>
Cc: Deibes, Yuliya (OS/ASPR/BARDA) <Yuliya.Deibes@hhs.gov>
Subject: RE: Updated: draft BARDA All Hands Agenda 19 June

This might be out there, but … what about inviting Sam Imbriale or someone else from the SOC to talk about plans for hurricane season?

From: Belton, Amy (OS/ASPR/BARDA) <Amy.Belton@hhs.gov>
Sent: Tuesday, June 16, 2020 2:02 PM
To: Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>; Lambert, Linda (OS/ASPR/BARDA) <Linda.Lambert@hhs.gov>
Cc: Deibes, Yuliya (OS/ASPR/BARDA) <Yuliya.Deibes@hhs.gov>
Subject: Updated: draft BARDA All Hands Agenda 19 June

Hi,

The updated draft BARDA ALL Hands agenda can be found below as well as the final agendas for the past couple months.

Good news: Tremel and Bob have agreed to provide updates on the HQ EUA
Bad News: The ORISE presentations will have to be pushed back to 6/26 and 7/3.

I am still waiting on Joe Figlio to confirm his participation.

If Joe confirms then we just need **one additional non-COVID speaker**.

Please forward topics as well as the names and POC's for speakers.

19 June

Bring the BAH to Order – Linda Lambert
Opening Remarks and Perspectives – Gary Disbrow 5 min
Update on the COVID-19 IMT – Christine Oshansky 4 min
DCMA- Flu Update-TBD 3 min
Hydroxychloroquine EUA Update-Tremel Faison/Robert Walker 3 min
COVID- TBD 3 min
FedStrive: Nutrition and Wellness- Adair Anderson 12 min (10 min. briefing/2 min Q&A)

Non-COVID- TBD 3 min
Q&A – Linda Lambert/All As required
Moment of Silence – Linda Lambert 1 min
Closing remarks – Gary Disbrow As required

Thanks,

Amy

From: Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>
Sent: Tuesday, June 16, 2020 8:54 AM
To: Belton, Amy (OS/ASPR/BARDA) <Amy.Belton@hhs.gov>; Lambert, Linda (OS/ASPR/BARDA) <Linda.Lambert@hhs.gov>
Cc: Deibes, Yuliya (OS/ASPR/BARDA) <Yuliya.Deibes@hhs.gov>
Subject: RE: draft BARDA All Hands Agenda 19 June

Mark Albrecht and Felicia run the program and Corey, Carol, Will, Shannon and Saddef are participants.

This could be two presentations, maybe this week we hear about that the program is from Mark and Felicia and then next week we hear about the impact of the program from a fellow (or past fellow)

From: Belton, Amy (OS/ASPR/BARDA) <Amy.Belton@hhs.gov>
Sent: Tuesday, June 16, 2020 6:47 AM
To: Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>; Lambert, Linda (OS/ASPR/BARDA) <Linda.Lambert@hhs.gov>
Cc: Deibes, Yuliya (OS/ASPR/BARDA) <Yuliya.Deibes@hhs.gov>
Subject: RE: draft BARDA All Hands Agenda 19 June

Hi Gretta,

Please confirm the following POCs and the purpose of their update:

ORISE Program-Provide overall info on the program and plans for recruiting more fellows in 2020
Felecia Harris
Mark ?
ORISE Fellows-Provide insight into program overall and its impact on their personal and professional development
Corey Hoffman
William Coley
Shannon Loelius
Saddef Haq

Also, is this going to be one or two updates?

Thanks,

Amy

From: Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>
Sent: Monday, June 15, 2020 12:34 PM
To: Belton, Amy (OS/ASPR/BARDA) <Amy.Belton@hhs.gov>; Lambert, Linda (OS/ASPR/BARDA) <Linda.Lambert@hhs.gov>
Cc: Deibes, Yuliya (OS/ASPR/BARDA) <Yuliya.Deibes@hhs.gov>
Subject: RE: draft BARDA All Hands Agenda 19 June

Thoughts…

- • Orise fellows – we are about to put out applications for new Orise fellows, might be good to hear about the program (Mark or Felicia) or from a graduate/current fellow (Corey, Carol, Will, Shannon, others?)
- • HQ/HCQ EUA data - ?? - FDA just pulled the EUA – ask Tremel or Bob Walker if anything can be presented.
- • Capacity building for vials – Joe Figlio

That's all I've got at the moment
g

From: Belton, Amy (OS/ASPR/BARDA) <Amy.Belton@hhs.gov>
Sent: Monday, June 15, 2020 12:16 PM
To: Lambert, Linda (OS/ASPR/BARDA) <Linda.Lambert@hhs.gov>; Blatner, Gretta (OS/ASPR/BARDA) <Gretta.Blatner@hhs.gov>
Cc: Deibes, Yuliya (OS/ASPR/BARDA) <Yuliya.Deibes@hhs.gov>
Subject: draft BARDA All Hands Agenda 19 June

Hi,

The draft BARDA ALL Hands agenda can be found below as well as the final agendas for the past couple months. Please forward topics for this weeks all hands as well as the names and POC's for speakers.

19 June

Bring the BAH to Order – Linda Lambert
Opening Remarks and Perspectives – Gary Disbrow 5 min
Update on the COVID-19 IMT – Christine Oshansky 4 min
DCMA- Flu Update-TBD 3 min
Hydroxychloroquine EUA Update-Tremel Faison/Robert Walker 3 min
COVID- TBD 3 min

FedStrive: Nutrition and Wellness- Adair Anderson 12 min (10 min. briefing/2 min Q&A)
Non-COVID- TBD 3 min
Q&A – Linda Lambert/All As required
Moment of Silence – Linda Lambert 1 min
Closing remarks – Gary Disbrow As required

12 June

Bring the BAH to Order – Linda Lambert
Opening Remarks and Perspectives – Gary Disbrow 5 min
Update on the COVID-19 IMT – Christine Oshansky 4 min
DCMA- CMA/PCI Update- Carol Lavrich 3 min
Regeneron Spike Program Update-Karl Erlandson 3 min
Evidation Project Update-Justin Yang 3 min
BARDA Industry Day Update-Amy Belton/Hillary Reynolds 3 min
Using Microsoft Office on Your Phone-Joe Chapman **(via WebEx)** 3 min
JLABS-Ashley Cecere **(via WebEx)** 3 min
Q&A – Linda Lambert/All As required
Moment of Silence – Linda Lambert 1 min
Closing remarks – Gary Disbrow As required

5 June

Bring the BAH to Order – Linda Lambert
Opening Remarks and Perspectives – Gary Disbrow 5 min
Update on the COVID-19 IMT – Christine Oshansky 4 min
DCMA- DRIVe Update- Matthew McCord 3 min
COVID Diagnostics Update-Rodney Wallace 3 min
COVID Operations and Comms Update-Kathyrn Amass 5 min
Biostatistics Branch Services – Yonghong Gao 3 min
Opioids Update- Nellie Byun 3 min
Q&A – Linda Lambert/All As required
Moment of Silence – Amy Belton 2 min
Closing remarks – Gary Disbrow As required

May 29

Bring the BAH to Order – Linda Lambert
Opening Remarks and Perspectives – Gary Disbrow 5 min
Update on the COVID-19 IMT – Christine Oshansky 4 min
DCMA- SSACB Update- Rosemary Hill 3 min
Vaccine Update- Armen Donabedian 3 min
Advanced Vaccination and

Immunity Management –Chuong Huynh 5 min
Blood Centers-Brian Tse 3 min
Tips for Restoring Balance-Rayshad Holmes 3 min
Q&A – Linda Lambert/All As required
Moment of Silence – Linda Lambert 1 min
Closing remarks – Gary Disbrow As required

May 15

Bring the BAH to Order – Linda Lambert
Opening Remarks and Perspectives – Gary Disbrow 5 min
Update on the COVID-19 IMT – Christine Oshansky 4 min
Antiviral Screening Project Update-Peter Adams 3 min
CARB-X Update-Tina Guina 4 min
Power BI Demo-Joe Chapman (via Screenshare on WebEx) 3 min
100 Days of COVID Briefing-Gary Disbrow (via Screenshare on WebEx) 8 min
BARDA Strong Survey Results- Tyler Merkeley (via Screenshare on WebEx) 3 min
Q&A – Linda Lambert/All As required
Moment of Silence for those who are sick and who we've lost– Linda Lambert 1 min
Closing remarks – Gary Disbrow As required

May 8

Bring the BAH to Order – Linda Lambert
Opening Remarks and Perspectives – Gary Disbrow 5 min
Update on the COVID-19 IMT – Christine Oshansky 4 min
Project Warp Speed - Daniel Wolfe 4 min
Quality Efforts for COVID19 - Pennie Hylton 3 min
DMID/NIAID Remdesivir Trial - Karen Martins 3 min
Public Service Recognition Week - Linda Lambert 3 min
Q/A – Linda Lambert/All As required min
Moment of Silence for those who are sick and who we've lost– Linda Lambert 1 min
Closing remarks – Gary Disbrow As required min

May 1

Bring the BAH to Order – Linda Lambert
Opening Remarks and Perspectives – Gary Disbrow 5 min
Update on the COVID-19 IMT – Christine Oshansky 4 min
COVID-19 Contracting Update- Carol Lavrich 3 min
CoV Animal Models-Allison Totura 10 min
DRIVe Update–Sandeep Patel 3 min
Regeneron Sarulimab (Kevzara) Trial-Marina Kozak 5 min
Q/A – Linda Lambert/All As required min
Moment of Silence for those who are sick and who we've lost– Linda Lambert 1 min

Closing remarks – Gary Disbrow As required min

April 24

Bring the BAH to Order – Linda Lambert
Opening Remarks and Perspectives – Gary Disbrow 5 min
Update on the COVID-19 IMT – Christine Oshansky 4 min
Alternate Routes of Vaccine Administration-Tanima Sinha 4 min
Clinical Trials-Robin Mason 4 min
COVID-19 Contracting Update- Joffrey Benford 4 min
CBRN Update- Amanda Zarrabian 4 min
JLabs Quickfire Update-Bonnie Shen 2 min
Q/A – Linda Lambert/All As required min
Moment of Silence for those who are sick and who 1 min
we've lost – Linda Lambert
Closing remarks – Gary Disbrow As required min

April 17

Bring the BAH to Order – Linda Lambert
1. Opening Remarks and Perspectives – Rick Bright 5 min
2. COVID-19 Funding Update – Gary Disbrow 2 min
3. Update on the COVID-19 IMT – Christine Oshansky 4 min
4. Convalescent Plasma Collections and COVID-19 Considerations 4 min
- Mary Homer
5. Planned Procurement of Midazolam Autoinjector 4 min
- Efrain Garcia
6. Development of Ultrasound with Integrated Learning 4 min
Algorithms for Lung Injuries and Critical Care Response
– Janelle Hurwitz
7. Q/A – Linda Lambert/All As required min
8. Moment of Silence for those who are sick and who we've lost 1 min
– Linda Lambert
9. Closing remarks – Rick Bright As required min

April 10

1. Opening Remarks and Perspectives – Rick Bright 4 min
2. Update on the IMT – Christine Oshansky 4 min
3. HHS/FEMA Structure and Overall Approach to COVID-19
– Christopher Houchens 5 min
4. BARDA Engagement with MCM Task Force and other

Task Forces – David Boucher 5 min
5. DRIVe Efforts – Kim Sciarretta 3 min
6. JLABS Update – Ashley Cecere 3 min
7. New Approaches for Antimicrobials – Sheila Miknyoczki 3 min
8. Q/A – Linda Lambert/All As required min
9. Moment of Silence for those who are sick and who we've lost 1 min – Linda Lambert
10. Closing remarks – Rick Bright As required min

April 3

11. Opening Remarks and Perspectives – Rick Bright 4 min
12. Update on the IMT – Christine Oshansky 3 min
13. Funding and Budget – Gary Disbrow 3 min
14. Contracting – Rosemary Hill 3 min
15. CBRN Efforts – Mary Hosmer 4 min
16. Regulatory and Quality Affairs Efforts – Tremel Faison 4 min
17. Non-Clinical Development Efforts – Ashley Smith 4 min
18. Clinical Development Efforts – Robin Mason 4 min
19. Q/A – Linda Lambert/All 3 min

Closing remarks – Rick Bright

March 27

1. Opening remarks and perspectives –
Rick Bright, Gary Disbrow, Joffrey Benford, Linda Lambert 6 min
2. Update on the IMT – Christine Oshansky 3 min
3. Funding – Gary Disbrow 3 min
4. Contracting – James Harris 3 min
5. Diagnostics Efforts – Rodney Wallace 4 min
6. Therapeutic Efforts – Karl Erlandson 4 min
7. Vaccine Efforts – Armen Donabedian 4 min
8. Q/A – Linda Lambert/All 5 min

Closing remarks – Rick Bright

March 20

1. Opening remarks – Rick Bright 3 min
2. Update on the IMT – Christine Oshansky 3 min
3. Funding– Gary Disbrow 3 min
4. Contracting– James Harris 3 min
5. Diagnostics Efforts – Rodney Wallace or designee 4 min
6. Therapeutic Efforts – Kim Armstrong 4 min
7. Vaccine Efforts - Armen Donabedian 4 min

Rapidly Deployable Capabilities (RDC) Efforts – Kim Sciarretta 4 min
8. Q/A – Linda/All 6 min

March 13

1. Opening remarks – Rick Bright (from the car) 3 min
2. Update on the IMT – Christine Oshansky or Robert Johnson 5 min
3. Funding update – Gary Disbrow 3 min
4. Contracting update – James Harris 3 min
5. COOP update – Craig Hughes 3 to 5 min
6. COVID-19 guidance/key points – Linda Lambert 3 min
7. Q/A 5 min

Amy M. Belton, PhD
Biologist, Office of the Director
Biomedical Advanced Research and Development Authority (BARDA)
Assistant Secretary for Preparedness and Response (ASPR)
Department of Health and Human Services
200 C St, S.W.
Washington, D.C. 20201
Mobile: (b)(6)
email: Amy.Belton@hhs.gov

Sender:	Disbrow, Gary (OS/ASPR/BARDA) </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0FD5845DEFDA4DC0BB45F8FAC629CF09-DISBROW, GA>
Recipient:	Blatner, Gretta (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=623cb123c2324236b1db6fb9153e0bbf-Blatner, Gr <Gretta.Blatner@hhs.gov>
Sent Date:	2020/06/17 10:07:48

DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary

Office of the Assistant Secretary for
Preparedness & Response
Biomedical Advanced Research &
Development Authority (BARDA)
Washington, D.C. 20201

June 5, 2020

Stephen M. Hahn, MD
Commissioner
Food and Drug Administration
10903 New Hampshire Ave.
Silver Spring, MD 20993-0002

Re: Request for Withdrawal of EUA 039
Use of Chloroquine Phosphate or Hydroxychloroquine Sulfate Supplied From the Strategic National Stockpile for Treatment of 2019 Coronavirus Disease (COVID-19)

Dear Dr. Hahn,

We refer to the Emergency Use Authorization (EUA) request dated March 28, 2020, for emergency use of oral formulations of chloroquine phosphate and hydroxychloroquine sulfate for the treatment of 2019 coronavirus disease (COVID-19) distributed from the Strategic National Stockpile.

We also refer to the Food and Drug Administration (FDA) letter dated March 28, 2020, in which the Agency authorized the emergency use of chloroquine phosphate and hydroxychloroquine sulfate for the treatment of COVID-19.

Based on the assessment of clinical data accumulated since the issuance of this EUA, the consensus of clinical experts is that there seems to be no clinical benefit of the use of chloroquine phosphate and hydroxychloroquine sulfate for the treatment of COVID-19. Therefore, the purpose of this submission is to inform the Agency that BARDA believes that the most appropriate course of action is to withdraw this EUA.

If you have any questions or comments regarding this submission, please contact Tremel Faison, Director of Regulatory and Quality Affairs at Tremel.Faison@hhs.gov or at 301-956-3096.

Sincerely,

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

From:	Disbrow, Gary (OS/ASPR/BARDA) </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0FD5845DEFDA4DC0BB45F8FAC629CF09-DISBROW, GA>
To:	Merkeley, Tyler (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=userf1f9626f <Tyler.Merkeley@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0851e89240324306b78740a4a60745e2-Johnson, Ro <Robert.Johnson@hhs.gov>
CC:	Kane, Elleen (OS/ASPR/OEA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=user25dbd6c7 <Elleen.Kane@hhs.gov>; BARDA SARS2 IMT Comms /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cc2f0a7acd3a4ba2906aaf7d39e65a1a-BARDASARS2I <BARDASARS2IMTComms@hhs.gov>
Subject:	RE: URGENT for ASPR: Deadline q: price of remdesivir
Date:	2020/04/07 17:02:00
Priority:	Normal
Type:	Note

No we did not. HHS was in the process of setting up a donation agreement but it was stalled pending discussions at the WH Task Force level.

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

From: Merkeley, Tyler (OS/ASPR/BARDA) <Tyler.Merkeley@hhs.gov>
Sent: Tuesday, April 7, 2020 4:59 PM
To: Disbrow, Gary (OS/ASPR/BARDA) <Gary.Disbrow@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) <Robert.Johnson@hhs.gov>

Cc: Kane, Elleen (OS/ASPR/OEA) <Elleen.Kane@hhs.gov>; BARDA SARS2 IMT Comms <BARDASARS2IMTComms@hhs.gov>
Subject: RE: URGENT for ASPR: Deadline q: price of remdesivir

Gary or Robert
Can you please answer below question.
Thanks
Tyler

TYLER G. MERKELEY
Biomedical Advanced Research and Development Authority (BARDA)
Office of Assistant Secretary of Preparedness and Response (ASPR)
U.S. Department of Health &Human Services (HHS)

O'Neill Building
200 C Street SW
Washington, DC 20024

C (b)(6) | O 202.260.0315 F 202.205.8442 Connect on LinkedIn

MedicalCounterMeasures.gov
DRIVe.HHS.gov

From: Kane, Elleen (OS/ASPR/OEA) <Elleen.Kane@hhs.gov>
Sent: Tuesday, April 7, 2020 4:58 PM
To: BARDA SARS2 IMT Comms <BARDASARS2IMTComms@hhs.gov>
Subject: FW: URGENT for ASPR: Deadline q: price of remdesivir
Importance: High

Did BARDA purchase remdesivir from Gilead?

Thanks!

From: Oakley, Caitlin B. (OS/ASPA) <Caitlin.Oakley@HHS.GOV>
Sent: Tuesday, April 7, 2020 4:55 PM
To: Shuy, Bryan (OS/ASPR/IO) <Bryan.Shuy@hhs.gov>; Hayes, Jonathan (OS/ASPR/IO) <Jonathan.Hayes@hhs.gov>; Michael, Gretchen (OS/ASPR/OEA) <Gretchen.Michael@hhs.gov>; Kane, Elleen (OS/ASPR/OEA) <Elleen.Kane@hhs.gov>; Waters, Cicely (OS/ASPR/OEA) <Cicely.Waters@hhs.gov>
Cc: Murphy, Ryan (OS/ASPA) <Ryan.Murphy1@hhs.gov>; McKeogh, Katherine (OS/ASPA) <Katherine.McKeogh@hhs.gov>
Subject: URGENT for ASPR: Deadline q: price of remdesivir
Importance: High

Hi ASPR—See inquiry from NY Times below.

Is this the correct cost we paid and did we order the additional 90.000?

They're on urgent deadline.

If this isn't ASPR, who would it be?

Happy to chat at 202-868-9798, thanks!

DRAFT PRE_DECISIONAL DELIBERTIVE

From: Thomas, Katie <katie.thomas@nytimes.com>
Sent: Tuesday, April 7, 2020 4:46 PM
To: Oakley, Caitlin B. (OS/ASPA) <Caitlin.Oakley@HHS.GOV>
Subject: Deadline q: price of remdesivir

Hi Caitlin,

I'm working on a deadline story (ASAP) about the price of remdesivir

In the leaked memo from Navarro:
https://www.axios.com/exclusive-navarro-deaths-coronavirus-memos-january-da3f08fb-dce1-4f69-89b5-ea048f8382a9.html

It says that HHS paid Gilead $2,200 per dose for 4,500 doses of remdesivir, and that it was imperative that they secure 90,000 more doses for a total cost of $198 million

Wondering if HHS can comment on what it has paid for remdesivir, and if that additional order for 90,000 additional doses was placed. If not, what is the total amount of remdesivir that has been ordered and at what price?

I'm sorry for the quick turnaround but just got the story and we are trying to put it out quickly. If my timing changes I'll try to give you as much of a heads up as I can.

Katie

Katie Thomas
Staff Writer, New York Times
(b)(6)
Twitter: @katie_thomas

https://images.axios.com/O6BhT0g7n3c39IYi2QEtHCHr6eA=/2020/04/07/1586225117615.jpg

Sender:	Disbrow, Gary (OS/ASPR/BARDA) </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0FD5845DEFDA4DC0BB45F8FAC629CF09-DISBROW, GA>
Recipient:	Merkeley, Tyler (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=userf1f9626f <Tyler.Merkeley@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0851e89240324306b78740a4a60745e2-Johnson, Ro <Robert.Johnson@hhs.gov>; Kane, Elleen (OS/ASPR/OEA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=user25dbd6c7 <Elleen.Kane@hhs.gov>; BARDA SARS2 IMT Comms /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cc2f0a7acd3a4ba2906aaf7d39e65a1a-BARDASARS2I <BARDASARS2IMTComms@hhs.gov>
Sent Date:	2020/04/07 17:02:07
Delivered Date:	2020/04/07 17:02:00

From:	Disbrow, Gary (OS/ASPR/BARDA) </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0FD5845DEFDA4DC0BB45F8FAC629CF09-DISBROW, GA>
To:	Stimson, Brian (HHS/OGC) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=338aa495176d4c92bb314f8f3f51d118-Stimson, Br <Brian.Stimson@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>; Shuy, Bryan (OS/ASPR/IO) (Bryan.Shuy@hhs.gov) <Bryan.Shuy@hhs.gov>
Subject:	FW: Can you please send word doc for Remdesivir
Date:	2020/03/04 16:51:00
Priority:	Normal
Type:	Note

Brian,
Email from Seth below.
Attached document is the draft donation agreement that was put on hold after they disclosed retaining 40kg in Canada with a desire to ship to China for filling.

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

-----Original Message-----
From: Jonas, Seth H. EOP/NSC <(b)(6)
Sent: Wednesday, March 4, 2020 4:31 PM

The Lancet

Remdesivir in Adults with Severe COVID-19: Results of a Randomized, Double-blind, Placebo-controlled, Multicenter Trial

--Manuscript Draft--

Manuscript Number:	
Article Type:	Fast Track (Randomised Controlled Trial)
Keywords:	COVID-19, Remdesivir, Clinical Trial, Severe Illness.
Corresponding Author:	Bin Cao China - Japan Friendship Hospital Beijing, CHINA
First Author:	Yeming Wang
Order of Authors:	Yeming Wang
	Dingyu Zhang
	Guanghua Du
	Ronghui Du
	Jianping Zhao
	Yang Jin
	Shouzhi Fu
	Ling Gao
	Zhenshun Cheng
	Qiaofa Lu
	Yi Hu
	Guangwei Luo
	Ke Wang
	Yang Lue
	Huadong Li
	Shuzhen Wang
	Shunan Ruan
	Chengqing Yang
	Chunlin Mei
	Yi Wang
	Dan Ding
	Feng Wu
	Xin Tang
	Xianzhi Ye
	Yingchun Ye
	Bing Liu
	Jie Yang
	Wen Yin
	Aili Wang

	Guohui Fan
	Fei Zhou
	Zhibo Liu
	Xiaoying Gu
	Jiuyang Xu
	Lianhan Shang
	Yi Zhang
	Lianjun Cao
	Tingting Guo
	Yan Wan
	Hong Qin
	Yushen Jiang
	Thomas Jaki
	Frederick G. Hayden
	Peter W. Horby
	Bin Cao
	Chen Wang
Manuscript Region of Origin:	CHINA
Abstract:	Background No specific antiviral has been proven effective for treatment of severe COVID-19. Remdesivir (GS-5734), a nucleoside analogue prodrug, has inhibitory effects on pathogenic animal and human coronaviruses, including SARS-CoV-2 in vitro, and inhibits MERS-CoV and SARS-CoV replication and disease in animal models. Methods: We conducted a randomized, double-blind, placebo-controlled, multicentre trial. Adults hospitalized with laboratory confirmed SARS-CoV-2 infection, and interval from illness onset to enrollment of ≤12 days, SaO 2 ≤94% on room air or a PaO 2 /FiO 2 ratio less than 300mmHg, and radiologically confirmed pneumonia were randomly assigned in a 2:1 ratio to intravenous remdesivir (200 mg on day 1 followed by 100 mg on days 2-9 in single daily infusions), or placebo for 10 days. Subjects were permitted the use of lopinavir-ritonavir. The primary endpoint was time to clinical improvement (censored at Day 28), defined as the time (in days) from randomization to study treatment (remdesivir or placebo) until a decline of two categories on a six-category ordinal scale of clinical status (1 discharged; 6 death) or discharged alive from hospital, whichever came first. This trial is registered with ClinicalTrials.gov, number NCT04257656. Findings: 237 patients with laboratory-confirmed COVID-19 underwent randomization (158 remdesivir; 79 control); one patient in the control group withdrew before receiving any study treatment. Remdesivir use was not associated with a difference in time to clinical improvement (hazard ratio 1.23, 95% CI 0.87-1.75), mortality at 28 days (13.9% vs 12.8%, difference 1.1; 95% CI, -8.1, 10.3), or in time to SARS-CoV-2 PCR negativity. Adverse events were reported in 65.2% of remdesivir recipients versus 64.1% in placebo recipients. Remdesvir was stopped early in 18 (11.6%) patients because of adverse effects, compared to 4 (5.1%) in the control group. Interpretation: In this study of hospitalized adult patients with severe COVID-19 that was terminated prematurely, remdesivir was not associated with clinical or virological benefits.

Title: Remdesivir in Adults with Severe COVID-19: Results of a Randomized, Double-blind, Placebo-controlled, Multicenter Trial

Running title: A Trial of Remdesivir in Adults with Severe COVID-19

Yeming Wang[#] 1,2, Dingyu Zhang[#] 3, Guanghua Du[#] 4, Ronghui Du[#] 5, Jianping Zhao[#] 6, Yang Jin[#] 7, Shouzhi Fu[#] 8, Ling Gao[#] 9, Zhenshun Cheng[#] 10, Qiaofa Lu[#] 11, Yi Hu[#] 12, Guangwei Luo 13, Ke Wang 4, Yang Lue 4, Huadong Li 3, Shuzhen Wang 3, Shunan Ruan 3, Chengqing Yang 5, Chunlin Mei 5, Yi Wang 6, Dan Ding 6, Feng Wu 7, Xin Tang 7, Xianzhi Ye 8, Yingchun Ye 9, Bing Liu 10, Jie Yang 11, Wen Yin 12, Aili Wang 13, Guohui Fan 14, Fei Zhou 1, Zhibo Liu 1, Xiaoying Gu 14, Jiuyang Xu 15, Lianhan Shang 1,16, Yi Zhang 1, Lianjun Cao 17, Tingting Guo 17, Yan Wan 17, Hong Qin 18, Yushen Jiang 19, Thomas Jaki 20, Frederick G. Hayden 21, Peter W. Horby 22, Bin Cao* 1,2,23,24 Chen Wang* 1,23,24,25

1. Department of Pulmonary and Critical Care Medicine, Center of Respiratory Medicine, National Clinical Research Center for Respiratory Diseases, China-Japan Friendship Hospital, Beijing, China
2. Department of Respiratory Medicine, Capital Medical University, Beijing, China
3. Jin Yin-tan Hospital; Wuhan, Hubei Province, China
4. Institute of Materia Medica, Chinese Academy of Medical Sciences& Peking Union Medical College
5. Wuhan Lung Hospital
6. Tongji Hospital, Tongji Medical College of Huazhong University of Science & Technology
7. Union Hospital, Tongji Medical College of Huazhong University of Science & Technology

8. Wuhan Third hospital

9. Renmin Hospital of Wuhan University

10. Zhongnan Hospital of Wuhan University

11. Wuhan Fourth hospital

12. The Central Hospital of Wuhan

13. Wuhan First hospital

14. Institute of Clinical Medical Sciences, China-Japan Friendship Hospital

15. Tsinghua University School of Medicine

16. Beijing University of Chinese Medicine

17. Tigermed Consulting Co., Ltd.

18. Teddy Clinical Research Laboratory

19. Hangzhou DI'AN Medical Laboritory

20. Lancaster University, UK

21. University of Virginia School of Medicine, Charlottesville, Virginia, USA

22. ISARIC, University of Oxford, Oxford, UK

23. Institute of Respiratory Medicine, Chinese Academy of Medical Science

24. Tsinghua University-Peking University Joint Center for Life Sciences

25. Peking Union Medical College, Beijing, China

* Co-corresponding authors

Bin Cao: caobin_ben@163.com

Chen Wang: cyh-birm@263.net

Research in context

Evidence before this study

We searched PubMed database, up to April 10, 2020, for published clinical trials evaluating the effect of remdesivir among patients with laboratory confirmed coronavirus disease 2019 (COVID-19). The search terms used were ("COVID-19" OR "2019-nCoV" or "SARS-CoV-2") AND "remdesivir" AND ("clinical trial" or "randomized controlled trial"). We identified no published clinical trials of the effect of remdesivir in patients with COVID-19.

Added value of this study

Our study is the first randomized, double-blind, placebo-controlled clinical trial evaluating the effect of intravenous remdesivir in adults hospitalized with severe COVID-19. The study was terminated before attaining the pre-specified sample size and was underpowered for an efficacy evaluation. In the intention-to-treat population, the primary endpoint of time to clinical improvement was numerically shorter in the remdesivir group compared to the control group (median 21.0 days vs. 23 days), but was not statistically significant different (hazard ratio 1.23; 95% CI 0.87 to 1.75). For other secondary endpoints, including 28-day mortality, duration of invasive mechanical ventilation, and time to SARS-CoV-2 PCR negativity, no statistically significant differences were observed.

Implications of all the available evidence

No significant benefits were observed for remdesvir treatment beyond standard of care. Our trial did not attain the predetermined sample size because the outbreak of COVID-19 was brought under control in China. Future studies of remdesivir, including earlier treatment in COVID-19 patients and higher dose regimens or in combination with other antivirals or SARS-CoV-2

neutralizing antibodies in those with severe COVID-19 are needed to better understand its potential effectiveness.

ABSTRACT

Background No specific antiviral has been proven effective for treatment of severe COVID-19. Remdesivir (GS-5734), a nucleoside analogue prodrug, has inhibitory effects on pathogenic animal and human coronaviruses, including SARS-CoV-2 in vitro, and inhibits MERS-CoV and SARS-CoV replication and disease in animal models.

Methods: We conducted a randomized, double-blind, placebo-controlled, multicentre triad. Adults hospitalized with laboratory confirmed SARS-CoV-2 infection, and interval from illness onset to enrollment of ≤12 days, SaO_2 ≤94% on room air or a PaO_2/FiO_2 ratio less than 300mmHg, and radiologically confirmed pneumonia were randomly assigned in a 2:1 ratio to intravenous remdesivir (200 mg on day 1 followed by 100 mg on days 2-9 in single daily infusions), or placebo for 10 days. Subjects were permitted the use of lopinavir-ritonavir. The primary endpoint was time to clinical improvement (censored at Day 28), defined as the time (in days) from randomization to study treatment (remdesivir or placebo) until a decline of two categories on a six-category ordinal scale of clinical status (1 = discharged; 6 = death) or discharged alive from hospital, whichever came first. This trial is registered with ClinicalTrials.gov, number NCT04257656.

Findings: 237 patients with laboratory-confirmed COVID-19 underwent randomization (158 remdesivir; 79 control); one patient in the control group withdrew before receiving any study treatment. Remdesivir use was not associated with a difference in time to clinical improvement (hazard ratio 1.23, 95% CI 0.87-1.75), mortality at 28 days (13.9% vs 12.8%, difference 1.1; 95% CI, -8.1, 10.3), or in time to SARS-CoV-2 PCR negativity. Adverse events were reported in 65.2% of remdesivir recipients versus 64.1% in placebo recipients. Remdesvir was stopped early in 18 (11.6%) patients because of adverse effects, compared to 4 (5.1%) in the control group.

Interpretation: In this study of hospitalized adult patients with severe COVID-19 that was terminated prematurely, remdesivir was not associated with clinical or virological benefits.

Funding: Chinese Academy of Medical Sciences (CAMS) Emergency Project of COVID-19 (2020HY320001); National Key Research and Development Program of China (2018YFC1200102); The Beijing Science and Technology Project (Z191107006600000).

Keywords: COVID-19, Remdesivir, Clinical Trial, Severe Illness.

INTRODUCTION

The ongoing pandemic of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infections has caused over 1,777,666 illnesses and 108,867 deaths globally as of 12 April 2020[1]. Although most infections are self-limited, approximately 15% of infected adults develop severe pneumonia that requires treatment with supplemental oxygen and an additional 5% progress to critical illness with hypoxemic respiratory failure, acute respiratory distress syndrome, and multi-organ failure that necessitates ventilatory support, often for several weeks [2–4]. One-half or more of patients with coronavirus infectious disease-2019 (COVID-19) patients requiring invasive mechanical ventilation have died in hospital [4,5], and the associated burden on healthcare systems, especially intensive care units, has been overwhelming in several affected countries.

Although several approved drugs and investigational agents have shown antiviral activity against SARS-CoV-2 in vitro [6,7], at present there are no antiviral therapies of proven value in treating severely ill COVID-19 patients. Small observational studies enrolling predominantly those with mild illness have reported possible clinical benefit of hydroxychoroquine (alone or combined with azithromycin)[8], An RCT enrolling patients within 12 days of symptom onset found that favipiravir was superior to arbidol in the proportion of those with mild illness who had recovered clinically by day 7 (56% vs 71%), but not in those with critical illness (0 vs 6%) [9]. In severe illness, one uncontrolled study of five patients given convalescent plasma suggested possible benefit, although the patients already had detectable anti-SARS-CoV-2 neutralizing antibodies before receipt of the plasma [10]. An open-label RCT of oral lopinavir-ritonavir found no significant effect on the primary outcome measure of time to clinical improvement (median, 16 days) and no evidence of reduction in viral RNA titers compared to control [11]. However, per-protocol analyses suggested possible

reductions in time to clinical improvement (difference of 1 day), particularly in those treated within 12 days of symptom onset. Further studies of lopinavir-ritonavir and other agents are ongoing.

Remdesivir (also GS-5734) is monophosphoramidate prodrug of an adenosine analog that has a broad antiviral spectrum including filo-, paramyxo-, pneumo- and coronaviruses [12,13]. Remdesivir is inhibitory in vitro for all human and animal coronaviruses tested to date including SARS-CoV-2 [13–15] and has shown antiviral and clinical effects in animal models of SARS-CoV and Middle East Respiratory Syndrome (MERS)-CoV infections [13,16,17]. In a lethal murine model of MERS, remdesivir was superior to a regimen of combined interferon-beta and lopinavir-ritonavir [16]. Remdesivir is a potent inhibitor of SARS-CoV-2 replication in human nasal and bronchial airway epithelial cells [18]. Intravenous remdesivir was studied for treatment of Ebola virus disease, in which it was adequately tolerated but less effective than several monoclonal antibody therapeutics [19], and has been used through individual compassionate use basis in over the last several months in certain countries to date [20]. Case studies have suggested benefit in severely ill COVID-19 patients [5,20,21]. However, the clinical and antiviral efficacy of remdesivir remains to be established. Here we report the results of an RCT of remdesivir in severe COVID-19 illness.

METHODS

Trial design and oversight

This was an investigator-initiated, individually randomized, placebo-controlled, double-blind trial to evaluate the efficacy and safety of intravenous remdesivir planned in 453 adults (≤18 years) hospitalized with severe COVID-19 illness. The trial was conducted from 6 February to 1 April 2020 at nine hospitals in Wuhan, Hubei Province, People's Republic of China (see Supplementary Appendix). Eligible patients were randomized 2:1 to either intravenous remdesivir (200 mg on day

1 followed by 100 mg on days 2-9 in single daily infusions) or placebo infusions for a total of 10 days (both provided by Gilead Sciences, Foster City, California). Randomization was stratified according to the level of respiratory support: (1) no oxygen support or oxygen support with nasal duct or mask; (2) high-flow oxygen, non-invasive ventilation, invasive ventilation, or extra-corporeal membrane oxygenation (ECMO). The permuted block (30 patients per block) randomization sequence, including stratification, was prepared by a statistician not involved in the trial using SAS software, version 9.4 (SAS Institute). Eligible patients were allocated to receive medication in individually numbered packs, according to the sequential order of the randomization centre (Jin Yin-Tan Hospital central pharmacy). Envelopes were prepared for emergency unbinding.

The trial was approved by the institutional review boards of each participating hospital. Written informed consent was obtained from all patients, or their legal representative if they were too unwell to provide consent. The trial was conducted in accordance with the principles of the Declaration of Helsinki and the International Conference on Harmonization–Good Clinical Practice guidelines.

Patients

Males and non-pregnant female patients aged ≥ 18 years were eligible if they were RT-PCR positive for SARS-CoV-2, had pneumonia confirmed by chest imaging, had a SaO_2 ≤94% on room air or a PaO_2/FiO_2 ratio ≤300mgHg, and were within 12 days of illness onset. Eligible subjects of child-bearing age (male or female) agreed to take effective contraceptive measures (including hormonal contraception, barrier methods or abstinence) during the study period and for at least 7 days following the last study drug administration. Exclusion criteria included pregnancy

or breast-feeding; hepatic cirrhosis or alanine aminotransferase (ALT)/aspartate aminotransferase (AST) elevated over 5 times the ULN; known severe renal impairment (estimated eGFR< 30 mL/min/1.73m^2), or having received continuous renal replacement therapy (CRRT), hemodialysis or peritoneal dialysis; possibility of transfer to a non-study hospital within 72h; and enrollment into an investigational treatment study for COVID-19 within 30 days prior to screening. The use of other treatments, including lopinavir-ritonavir, was permitted.

Clinical and laboratory monitoring

Patients were assessed once daily by trained nurses using diary cards that captured data on a 6-category ordinal scale and safety from day 0 to day 28, hospital discharge, or death. Other clinical data was recorded using the World Health organization (WHO) - International Severe Acute Respiratory and Emerging Infections Consortium (ISARIC) case record form [22]. The safety evaluation included daily monitoring for adverse events (AEs), clinical laboratory testing (days 1, 3, 7 and 10), 12-lead electrocardiogram (ECG)(days 1, 14), and daily vital signs measurements (see Protocol for details[23]). Clinical data were recorded on paper case record forms and then double entered into an electronic database and validated by trial staff. Nasopharyngeal or oropharyngeal swabs, lower respiratory tract samples (sputum/tracheal aspiration/alveolar lavage fluid) as available, and fecal/anal swab specimens were collected on days 1, 3, 5, 7, 10, 14, 21, and 28 for viral RNA detection and quantification.

The trial was monitored by a contract research organization (Hangzhou Tigermed Consulting Co., Ltd[24]). Virologic testing was done at Teddy Clinical Research Laboratory (Tigermed- DiAn Joint Venture) using quantitative real-time RT-PCR. RNA was extracted from clinical samples with the MagNA Pure 96 system, detected and quantified by Cobas z480 qPCR (Roche, switzerland), using LightMix Modular SARS-CoV-2 assays (TIB MOBIOL, Berlin, Germany). Baseline the upper

(nasopharyngeal, NP or Oropharyngeal swabs, OP) and lower respiratory tract specimens were tested for detection of E gene, RdRp gene and N gene, then samples on the subsequent visits were quantitatively and qualitative detected for E gene.

Outcome measures

The primary clinical endpoint was time to clinical improvement (TTCI) within 28 days after randomization. Clinical improvement was defined as a 2-point reduction in subjects' admission status on a 6-point ordinal scale, or live discharge from the hospital, whichever came first. The 6 point scale included death: 6; hospitalized for ECMO and/or mechanical ventilation: 5; hospitalized for noninvasive ventilation and/or high flow oxygen therapy: 4; hospitalized for oxygen therapy (but not requiring high flow or noninvasive ventilation): 3; hospitalization but not requiring oxygen therapy: 2; discharged or having reached discharge criteria (defined as clinical recovery, i.e., normalization of pyrexia, respiratory rate [< 24/minute], and SpO2 [>94% on room air], and relief of cough, all maintained for at least 72 hours): 1. The 6-point scale was modified from the 7-point scale used in our previous COVID-19 lopinavir-ritonavir treatment[11] by collapsing the two outpatient strata into one.

Secondary outcomes included the proportions of subjects in each category of the 6-point scale within 7, 14, and 28 days of randomization; all-cause mortality within 28 days; frequency of invasive mechanical ventilation; duration of oxygen therapy; duration of hospitalization; and incidence of nosocomial infection (see Supplementary Appendix). Virologic measures included the proportions with viral RNA detection over time and viral RNA titer area-under-the-curve (AUC) measurements. Safety outcomes included treatment-emergent adverse events (AEs), serious AEs, and premature discontinuations of study drug.

Statistical Analysis

The original design required a total of 325 events across both arms, since this would provide 80% power under a one-sided type I error of 2.5% if the hazard ratio comparing remdesivir to placebo is 1.4 which corresponds to a change in TTCI to 15 days assuming that TTCI is 21 days on placebo. One interim analysis using triangular boundaries[25] and a 2:1 allocation ratio between remdesivir and placebo has been accounted for in the original design. Assuming an 80% event rate within 28 days across both arms and a drop-out rate of 10% implies that approximately 453 patients were to be recruited for this trial (151 on placebo and 302 on remdesivir). The possibility for an interim analysis after enrollment of approximately 240 subjects was included in the design if requested by the independent data safety and monitoring board (DSMB). However, no subjects were enrolled after 12 March 2020 due to the control of the outbreak in Wuhan, and on 29 March the DSMB recommended that the study be terminated and analyzed. When all the other assumptions stayed the same, with the actual enrolment of 236 participants, the statistical power reduced from 80% to 58%.

The primary efficacy analysis was on an intention-to-treat (ITT) basis with all randomized patients. TTCI was assessed after all patients had reached Day 28; failure to reach clinical improvement or death before Day 28 were considered as right-censored at day 28. TTCI was portrayed by Kaplan-Meier plot and compared with a log-rank test. The hazard ratio (HR) 95% confidence intervals (CI) for clinical improvement and hazard ratio with 95% CI for clinical deterioration was calculated by Cox proportional-hazards model. Other analyses include subgroup analyses for those randomized $\leq$10 or >10 days after illness onset, time-to-clinical deterioration (defined as one category increase or death), and for viral RNA load at entry. We present adverse event data on the patients' actual treatment exposure, coded using Medical Dictionary for Regulatory Activities

(MedDRA). Statistical analyses were conducted using SAS software, version 9.4 (SAS Institute Inc.).

This trial is registered with ClinicalTrials.gov, number NCT04257656.

RESULTS

Patients

Among 255 patients who were screened, 237 patients were eligible, consented and were randomized, of whom 1 withdrew. 158 were assigned to receive remdesivir and 78 to receive placebo. In the remdesivir group, 155 (98.1%) received remdesivir as assigned and placebo was given to all patients in the control group (Figure 1). The median age of study patients was 65 years (interquartile range [IQR], 56 to 71 years) and 140 (59.3%) were males. The most common comorbidity was hypertension (43.2%), followed by diabetes (23.7%) and coronary heart disease (7.2%). Lopinavir-ritonavir was co-administered in 42 (17.8%) patients at day 1 (Table 1). Most patients (81.6% in the remdesivir and 83.3% in the control group) were in category 3 of the six-point ordinal scale of clinical status at baseline. There were more patients (60.3%) in the control group than in the remdesivir group (44.3%) who had been symptomatic for 10 days or less at the time of randomization. No other major differences in symptoms, signs, laboratory results, disease severity, or treatments were observed between groups at baseline.

The median days from illness onset to randomization was 10 days (IQR 9 to 12 days). No important differences were apparent between the groups in other treatments received (including lopinavir-ritonavir or corticosteroids) (Table 2). During the whole period of hospitalization, 155 (65.7%) patients received corticosteroids, with the median time from illness onset to corticosteroids therapy

being 8.5 days (IQR, 6.5 to 11.0 days), while 91 (38.6%) patients received corticosteroids before enrollment.

Primary outcome

In the intention-to-treat population, the time to clinical improvement in the remdesivir group was non-significantly shorter than the control group (median 21.0 days vs. 23 days; hazard ratio 1.23; 95% CI 0.87 to 1.75) (Table 3 and Figure 2). Results for TTCI were similar in the per-protocol population (median 21.0 days vs, 23.0 days, respectively hazard ratio 1.27; 95% CI 0.89 to 1.80) (Table S1 and Figure S1). Although not statistically significant, remdesivir was associated with a faster time to clinical improvement as compared to placebo among patients with symptom duration of 10 days or less in the intention-to-treat population (Figure S2). If clinical improvement was defined as a one, instead of two, category decline, the hazard ratio was 1.34 with 95% CI of 0.96 to 1.86 (Figure S3). Time-to-clinical deterioration, defined as a one category increase or death, the hazard ratio was 0.95 with 95% CI of 0.55 to 1.64 (Figure S4).

Secondary outcome

The 28-day mortality was similar between the two groups (13.9% in remdesivir vs. 12.8% in placebo; difference 1.1; 95% CI -8.1 to 10.3). Use of remdesivir within 10 days after symptom onset was associated with a non-significantly lower 28-day mortality (5.1% vs. 9.0%; difference -3.9; 95% CI -11.1 to 3.3), while late use was non-significantly associated with a higher 28-day mortality (7.6% vs. 3.8%; difference 3.7; 95% CI -2.2 to 9.7). The clinical improvement rates at days 14 and day 28 were higher in remdesivir group but this was non-significant (26.6% vs. 23.1% at day 14; 65.2% vs. 57.7% at day 28). For patients assigned to remdesivir group, the invasive mechanical ventilation (IMV) duration was numerically shorter than those assigned to control

group (median 7.0 days vs. 15.5 days; difference 4.0 days; 95% CI -2.0 to 14.0 days) but the number of patients was small. No significant differences were observed between the two groups in length of oxygen support, hospital length of stay, days from randomization to discharge, days from randomization to death and distribution of six-category scale at day 7, day 14 and day 28. (Table 3 and Figure S5)

Virology

Of 236 patients who were RT-PCR positive at enrollment, 37 (15.7%) had undetectable viral RNA on the NP/OP swab taken after consent. The mean baseline viral load of NP/OP swabs was 4.7 ± 2.8 log10 copies/mL in the remdesivir group and 4.7 ± 2.4 log10 copies/mL in the control group (Table 1). The viral load decreased over time equally in both groups (Figure 3A). No difference in viral load were observed when stratified by interval from illness onset to randomization (Figure S6 A&B). The findings of viral load reduction were similar by lower respiratory specimens (Figure 3B)

The cumulative rate of undetectable viral RNA of NP/OP swabs by day 28 was 64.8%, and the proportion negative was similar among patients receiving remdesivir and those receiving placebo (day 3, 23.4% to 24.4%; day 5, 33.5% to 32.1%; day 7, 41.8% to 41.0%; day 10, 51.9% to 57.7%; day 14, 58.9% to 62.8%; day 21, 62.0% to 67.9%; day 28, 62.7% to 69.2%) (Table S2).

Safety

Adverse events were reported in 102 (65.8%) patients in the remdesivir group and 50 (64.1%) in the control group. The most common adverse events in the remdesivir group were constipation (13.5%), hypoalbuminemia (12.9%), hypokalemia (11.6%), anaemia (11.6%), thrombocytopenia (10.3%), and increased total bilirubin (9.7%), and in control group were hypoalbuminemia (15.4%),

constipation (15.4%), anaemia (15.4%), hypokalemia (14.1%), increased aspartate aminotransferase (11.5%), elevated blood lipids (10.3%), and increased total bilirubin (9.0%). A total of 28 (18.1%) serious adverse events were reported in the remdesivir group and 20 (25.6%) in the control group. More patients in the remdesivir group discontinued drug for adverse events or serious adverse events (11.6% vs. 5.1%), among whom 7 (4.5%) were due to respiratory failure or ARDS in remdesivir group. All deaths during the observation period were judged by the site investigators to be unrelated to the intervention. (Table 4)

DISCUSSION

Our trial found that intravenous remdesivir did not significantly improve the time to clinical improvement (TTCI), mortality, or time to clearance of virus in patients with serious COVID-19 illness compared to placebo. Compared to a recent study of compassionate use remdesivir that suggested clinical benefit[20], our study population was not as ill (at time of enrollment 0.4% on invasive mechanical ventilation or ECMO versus 64%) and was treated somewhat earlier in their disease course (median, 10 days versus 12 days). Such differences might be expected to favor remdesivir providing greater effects in our study population, but we did not find this. However, our study did not reach its target enrollment because the stringent public health measures employed in Wuhan City led to marked reductions in new patient presentations in mid-March, and restrictions on hospital bed availability resulted in most patients being enrolled later in the course of disease. Consequently, we could not adequately assess whether earlier remdesivir treatment might have provided clinical benefit. In one murine model of SARS, remdesivir treatment starting at 2 days post infection, after virus replication and lung airway epithelial damage had already peaked, significantly reduced SARS-CoV lung titers but did not decrease disease severity or

mortality [13]. A need for early treatment has been found in nonhuman primate models of SARS and MERS in which virus replication is very short-lived and lung pathology appears to develop more rapidly than in human infections[13,16,17]. Such findings argue for testing of remdesivir earlier in COVID-19 illness.

Remdesivir did not result in significant reductions in SARS-CoV-2 RNA loads or detectability in upper respiratory tract or sputum specimens in this study despite showing strong antiviral effects in pre-clinical models of CoV infection. In African green monkey kidney Vero E6 cells remdesivir inhibited SARS-CoV-2 with a 50% effective concentration (EC_{50}) of 0.46 ug/ml and EC_{90} of 1.06 ug/ml [6]. In human nasal and bronchial airway epithelial (HAE) cells, a fixed 20 uM (12.1 ug/ml) concentration reduced estimated intracellular viral titers over 7.0 at 48 hours [18]. In human airway epithelial cells, remdesivir's EC_{50} was 0.042 ug/ml for SARS-CoV and 0.045 ug/ml for MERS-CoV [13]. In a murine model of MERS subcutaneous remdesivir demonstrated significant antiviral and clinical effects with a dose regimen that maintained plasma concentrations above 1 uM (0.60 ug/ml) throughout the dosing interval [13]. In rhesus macaques a 5 mg/kg dose, reported to be roughly equivalent to 100-mg daily dosing in humans, was effective for treatment of MERS-CoV infection and reduced pulmonary virus replication when started at 12 hours post infection [18]. Healthy adult volunteers receiving a doses similar to our trial (200-mg on day, 100-mg on days 2-4) had mean peak plasma concentrations of 5.4 ug/ml on day 1and 2.6 ug/ml on day 5. [26]. Doses of 150 mg/day for 14 days have been adequately tolerated in healthy adults, and a daily dose regimen of 150 mg for 3 days followed by 225 mg for 11 days appeared to be generally well-tolerated in one patient with Ebola meningo-encephalitis [27]. However, the pharmacokinetics of remdesivir in severely ill patients, and particularly the concentrations of the active nucleotide metabolite (GS-441524)

triphosphate in respiratory tract cells of treated patients, are unknown. Studies of higher dose regimens for which there are safety data (eg, 200 mg daily doses) warrant consideration.

Our study found that remdesivir was adequately tolerated and no new safety concerns were identified. The overall proportion of patients with serious adverse events tended to be lower in remdesivir recipients compared to placebo (Table 3). However, a higher proportion of remdesivir recipients had dosing prematurely stopped by the investigators for adverse events (11.6% versus 5.1% placebo) for various reasons including gastrointestinal symptoms (anorexia, nausea, vomiting), transaminase or bilirubin elevations, and worsened cardiopulmonary status.

In addition to its diminished power to detect differences in clinical outcomes and initiation of treatment relatively late in COVID-19, our trial provided limited data on lower respiratory tract virus detection and lacked data on infectious virus recovery or on possible emergence of reduced susceptibility to remdesivir. Coronaviruses partially resistant to inhibition by remdesivir (~6-fold increased EC_{50}) have been obtained following serial in vitro passage, but these viruses remain susceptible to higher remdesivir concentrations and show impaired fitness [28]. Another limitation of the trial was the high frequency of systemic corticosteroid use, which could have contributed to prolongation of viral replication, as observed in SARS [29] and MERS [30] and possibly diminished the likelihood of observing an antiviral effect with remdesivir.

In summary we found that this dose regimen of intravenous remdesivir was adequately tolerated but did not provide significant clinical or antiviral effects in seriously ill COVID-19 patients. Future studies with larger sample sizes will continue to inform on remdesivir's effect on COVID-19. Furthermore, strategies to enhance remdesivir's antiviral potency (e.g., higher dose regimens, combination with other antivirals or SARS-CoV-2 neutralizing antibodies) and to mitigate

immunopathologic host responses contributing to COVID-19 severity (e.g., inhibitors of IL-6, IL-1, TNF-a) require rigorous study.

Acknowledgements

The authors thank Gilead Sciences for providing the study drugs and Drs. Huyen Cao and Anu Osinusi for advice regarding safe use of remdesivir. We also thank members of the international DSMB (Jieming Qu (Chair), Weichung Joe Shih, Robert Fowler, Rory Collins, Chen Yao. Independent statisticians: Xiaoyan Yan, Bin Shan. Academic Secretaries: Lingling Gao, Junkai Lai. eDMC system provider: Tai Xie, Rong Ran, Peng Zhang, Emily Wang) for their service; Roche Diagnostics (Shanghai) provided instruments and SARS-CoV-2 assay detection; SMO assistance provided by Shanghai MedKey Med-Tech Development Co.,Ltd; Clinplus Co., Ltd; Hangzhou SIMO Co., Ltd; MEDPISON Co., Ltd.

Financial support and sponsorship

This work was supported by Chinese Academy of Medical Sciences (CAMS) Emergency Project of COVID-19 (2020HY320001); National Key Research and Development Program of China (2018YFC1200102); The Beijing Science and Technology Project (Z19110700660000). TJ is funded by a NIHR Senior Research Fellowship (2015-08-001). PH is funded by the Wellcome Trust, Bill and Melinda Gates Foundation, and the United Kingdom Department of Health and Social Care.

Conflicts of interest

The authors have no conflict of interest or financial relationships to disclose. FGH has served as non-compensated consultant to Gilead Sciences on its respiratory antiviral program. No form of payment was given to anyone to produce the manuscript. All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

Author Contributions:

Dr. Bin Cao, Dr. Chen Wang and Dr. Yeming Wang had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Dr. Chen Wang and Dr. Bin Cao decided to publish the paper.

Study concept and design: Bin Cao, Chen Wang, Yeming Wang, Peter W. Horby, Thomas Jaki and Frederick G. Hayden provide input on the trial design.

All authors contributed to the trial conduct.

Acquisition, analysis, and interpretation of data: Bin Cao, Chen Wang, Yeming Wang, Frederick Hayden and Peter Horby

Drafting of the manuscript: Yeming Wang, Frederick Hayden, Peter Horby, Guohui Fan.

Critical revision of the manuscript: Bin Cao, Chen Wang, Peter Horby, Frederick Hayden, Guohui Fan, Thomas Jaki, and Xiaoying Gu.

Statistical analysis: Yeming Wang and a statistician (Joe Yao) from Tigermed Consulting Co., Ltd. Guohui Fan gave valuable suggestions for data analysis.

1 COVID-19 Map. Johns Hopkins Coronavirus Resource. Center. https://coronavirus.jhu.edu/map.html (accessed April 12, 2020).

2 Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. *JAMA* 2020; published online Feb 24. DOI:10.1001/jama.2020.2648.

3 Chen N, Zhou M, Dong X, *et al.* Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet published online January 29, 2020. https://doi.org/10.1016/ S0140-6736(20)30211-7

4 Zhou F, Yu T, Du R, *et al.* Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet published online March 9, 2020. https://doi.org/10.1016/S0140-6736(20)30566-3.

5 Bhatraju PK, Ghassemieh BJ, Nichols M, *et al.* Covid-19 in Critically Ill Patients in the Seattle Region - Case Series. *N Engl J Med* 2020; published online March 30. DOI:10.1056/NEJMoa2004500.

6 Wang M, Cao R, Zhang L, *et al.* Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. *Cell Res* 2020; **30**: 269–71.

7 Liu J, Cao R, Xu M, *et al.* Hydroxychloroquine, a less toxic derivative of chloroquine, is effective in inhibiting SARS-CoV-2 infection in vitro. *Cell Discov* 2020; **6**: 16.

8 Gautret P, Lagier J-C, Parola P, *et al.* Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. *Int J Antimicrob Agents* In Press 17 March 2020.

9 Chen C, Huang J, Cheng Z, *et al.* Favipiravir versus Arbidol for COVID-19: A Randomized Clinical Trial. *medRxiv* preprint: https://doi.org/10.1101/2020.03.17.20037432.

10 Shen C, Wang Z, Zhao F, *et al.* Treatment of 5 Critically Ill Patients With COVID-19 With Convalescent Plasma. *JAMA* 2020; published online March 27. DOI:10.1001/jama.2020.4783.

11 Cao B, Wang Y, Wen D, *et al.* A Trial of Lopinavir–Ritonavir in Adults Hospitalized with Severe Covid-19. *N Engl J Med*; 2020, DOI: 10.1056/NEJMoa2001282

12 Lo MK, Jordan R, Arvey A, *et al.* GS-5734 and its parent nucleoside analog inhibit Filo-, Pneumo-, and Paramyxoviruses. *Sci Rep* 2017; **7**: 43395.

13 Sheahan TP, Sims AC, Graham RL, *et al.* Broad-spectrum antiviral GS-5734 inhibits both epidemic and zoonotic coronaviruses. *Sci Transl Med* 2017; **9**: eaal3653.

14 Warren TK, Jordan R, Lo MK, *et al.* Therapeutic efficacy of the small molecule GS-5734 against Ebola virus in rhesus monkeys. *Nature* 2016; **531**: 381–5.

15 Brown AJ, Won JJ, Graham RL, *et al.* Broad spectrum antiviral remdesivir inhibits human endemic and zoonotic deltacoronaviruses with a highly divergent RNA dependent RNA polymerase. *Antiviral Res* 2019; **169**: 104541.

16 Sheahan TP, Sims AC, Leist SR, *et al.* Comparative therapeutic efficacy of remdesivir and combination lopinavir, ritonavir, and interferon beta against MERS-CoV. *Nat Commun* 2020; **11**: 222.

17 de Wit E, Feldmann F, Cronin J, *et al.* Prophylactic and therapeutic remdesivir (GS-5734) treatment in the rhesus macaque model of MERS-CoV infection. *Proc Natl Acad Sci* 2020; : 201922083.

18 Pizzorno A, Padey B, Julien T, *et al.* Characterization and treatment of SARS-CoV-2 in nasal and bronchial human airway epithelia. *bioRxiv* 2020; : 2020.03.31.017889.

19 Mulangu S, Dodd LE, Davey RT, *et al.* A Randomized, Controlled Trial of Ebola Virus Disease Therapeutics. *N Engl J Med* 2019; **381**: 2293–303.

20 Grein J, Ohmagari N, Shin D, *et al.* Compassionate Use of Remdesivir for Patients with Severe Covid-19. *N Engl J Med* 2020; published online April 10. DOI:10.1056/NEJMoa2007016.

21 Holshue ML, DeBolt C, Lindquist S, *et al.* First Case of 2019 Novel Coronavirus in the United States. *N Engl J Med* 2020. DOI: 10.1056/NEJMoa200119

22 ISARIC • ISARIC. https://isaric.tghn.org/ (accessed April 12, 2020).

23 Evaluation of the Efficacy and Safety of Intravenous Remdesivir in Adult Patients with Severe Pneumonia caused by COVID-19 virus Infection: study protocol for a Phase 3 Randomized, Double-blind, Placebo-controlled, Multicentre trial. 2020; published online Feb 20. DOI:10.21203/rs.2.24058/v1.

24 Home. Tigermed. https://tigermedgrp.com/ (accessed April 12, 2020).

25 Whitehead J, Stratton I. Group sequential clinical trials with triangular continuation regions. *Biometrics* 1983; **39**: 227–36.

26 Investigator's brochure of remdesivir, Gilead science, Inc, 5th Edition, February 21, 2020.

27 Jacobs M, Rodger A, Bell DJ, *et al.* Late Ebola virus relapse causing meningoencephalitis: a case report. *The Lancet* 2016; **388**: 498–503.

28 Agostini ML, Andres EL, Sims AC, *et al.* Coronavirus Susceptibility to the Antiviral Remdesivir (GS-5734) Is Mediated by the Viral Polymerase and the Proofreading Exoribonuclease. *mBio* 2018; **9**: e00221-18, /mbio/9/2/mBio.00221-18.atom.

29 Lee N, Allen Chan KC, Hui DS, *et al.* Effects of early corticosteroid treatment on plasma SARS-associated Coronavirus RNA concentrations in adult patients. *J Clin Virol Off Publ Pan Am Soc Clin Virol* 2004; **31**: 304–9.

30 Arahi YM, Mandourah Y, Al-Hameed F, *et al.* Corticosteroid Therapy for Critically Ill Patients with Middle East Respiratory Syndrome. *Am J Respir Crit Care Med* 2018; **197**: 757–67.

Table 1. Baseline Demographic and Clinical Characteristics of the Patients

Characteristics	Total (n = 236)	Remdesivir group (n = 158)	Control group (n = 78)
Age, yr	65.0 (56.0-71.0)	66.0 (57.0-73.0)	64.0 (53.0-70.0)
Gender, male, n (%)	140 (59.3)	89 (56.3)	51 (65.4)
Any co-morbidities	167 (70.8)	112 (70.9)	55 (70.5)
Hypertension	102 (43.2)	72 (45.6)	30 (38.5)
Diabetes, n (%)	56 (23.7)	40 (25.3)	16 (20.5)
Coronary heart disease, n (%)	17 (7.2)	15 (9.5)	2 (2.6)
Body temperature, ℃	36.8 (36.5-37.2)	36.8 (36.5-37.2)	36.8 (36.5-37.2)
Fever, n (%)	87 (36.9)	56 (35.4)	31 (39.7)
Respiratory rate > 24 /min, n (%)	47 (19.9)	36 (22.8)	11 (14.1)
White blood cell count (× 109/L)	6.3 (4.5-8.3)	6.2 (4.4-8.3)	6.4 (4.5-8.3)
4-10, n (%)	166 (70.3)	108 (68.4)	58 (74.4)
<4, n (%)	39 (16.5)	27 (17.1)	12 (15.4)
>10, n (%)	28 (11.9)	20 (12.7)	8 (10.3)
Lymphocyte count (× 109/L)	0.8 (0.6-1.1)	0.8 (0.6-1.1)	0.7 (0.6-1.2)
⩾ 1.0, n (%)	72 (30.5)	49 (31.0)	23 (29.5)
< 1.0, n (%)	161 (68.2)	106 (67.1)	55 (70.5)
Platelet count (× 109/L)	187.0 (143.0-251.0)	183.0 (144.0-235.0)	194.5 (141.0-266.0)
⩾ 100, n (%)	223 (94.5)	148 (93.7)	75 (96.2)
< 100, n (%)	10 (4.2)	7 (4.4)	3 (3.8)
Serum creatinine (μmol/L)	69.4 (56.0-84.3)	68.0 (56.0-82.0)	71.3 (56.0-88.7)
⩽ 133, n (%)	227 (96.2)	151 (95.6)	76 (97.4)
> 133, n (%)	5 (2.1)	3 (1.9)	2 (2.6)
Aspartate aminotransferase (U/L)	32.0 (23.0-46.0)	31.0 (22.0-44.0)	33.0 (24.0-48.0)
⩽ 40, n (%)	158 (66.9)	109 (69.0)	49 (62.8)
> 40, n (%)	75 (31.8)	46 (29.1)	29 (37.2)
Alanine aminotransferase (U/L)	26.0 (18.0-43.0)	26.0 (18.0-42.0)	26.0 (20.0-43.0)
⩽ 50	196 (83.1)	130 (82.3)	66 (84.6)
> 50	37 (15.7)	25 (15.8)	12 (15.4)
Lactate dehydrogenase (U/L)	334.0 (248.0-437.0)	339.0 (247.0-441.5)	329.0 (249.0-411.0)
⩽ 245	53 (22.5)	36 (22.8)	17 (21.8)
> 245	170 (72.0)	112 (70.9)	58 (74.4)
Creatine kinase (U/L)	75.5 (47.0-145.0)	75.9 (47.0-131.1)	75.0 (47.0-158.0)
⩽ 185	172 (72.9)	118 (74.7)	54 (69.2)
> 185	36 (15.3)	23 (14.6)	13 (16.7)

NEWS2 score at day 1	5.0 (3.0, 7.0)	5.0 (3.0, 7.0)	4.0 (3.0, 6.0)
Six-category scale at day 1			
2 Hospitalization, not requiring supplemental oxygen, n (%)	3 (1.3)	0	3 (3.8)
3 Hospitalization, requiring supplemental oxygen, n (%)	194 (82.2)	129 (81.6)	65 (83.3)
4 Hospitalization, requiring HFNC and/or non-IMV, n (%)	37 (15.7)	28 (17.7)	9 (11.5)
5 Hospitalization, requiring ECMO and/or IMV, n (%)	1 (0.4)	0	1 (1.3)
6 Death	1 (0.4)	1 (0.6)	0
Mean baseline viral load of NP/OP swabs (SD), log10 copies/mL	4.7 ±2.6	4.7 ±2.8	4.7±2.4
Receiving injection of interferon α2b at day 1, n (%)	44 (18.6)	29 (18.4)	15 (19.2)
Receiving lopinavir-ritonavir at day 1, n (%)	42 (17.8)	27 (17.1)	15 (19.2)
Antibiotic at baseline, n (%)	184 (78.0)	121 (76.6)	63 (80.8)
Corticosteroids therapy at baseline, n (%)	91 (38.6)	60 (38.0)	31 (39.7)

Note. Numbers in parenthesis correspond to interquartile range observed value for continuous variables and to percentages for indicator variables as appropriate.

Table 2. Any Treatments Received before and after Enrollment.

Characteristics	Total (n = 236)	Remdesivir group (n = 158)	Control group (n = 78)
Days from illness onset to starting drug (days)	10.0 (9.0, 12.0)	11.0 (9.0, 12.0)	10.0 (8.0, 11.0)
Early (≤10 days of symptom onset), n (%)	117 (49.6)	70 (44.3)	47 (60.3)
Late (> 10 days of symptom onset), n (%)	111 (47.0)	83 (52.5)	28 (35.9)
Receiving injection of interferon α2b, n (%)	76 (32.2)	46 (29.1)	30 (38.5)
Receiving lopinavir-ritonavir, n (%)	67 (28.4)	44 (27.8)	23 (29.5)
Vasopressors, n (%)	38 (16.1)	25 (15.8)	13 (16.7)
Renal replacement therapy, n (%)	6 (2.5)	3 (1.9)	3 (3.8)
Highest oxygen therapy support			
Non-invasive mechanical ventilation, n (%)	17 (7.2)	14 (8.9)	3 (3.8)
Invasive mechanical ventilation, n (%)	21 (8.9)	11 (7.0)	10 (12.8)
IMV+ECMO, n (%)	2 (0.8)	2 (1.3)	0
Antibiotic, n (%)	215 (91.1)	142 (89.9)	73 (93.6)
Corticosteroids therapy, n (%)	155 (65.7)	102 (64.6)	53 (67.9)
Days from illness onset to corticosteroids therapy (days)	8.5 (6.5, 11.0)	9.0 (7.0, 11.0)	8.0 (6.0, 10.0)
Days of corticosteroids therapy (days)	10.0 (6.0, 15.0)	9.0 (5.0, 15.0)	10.0 (6.0, 16.0)

Note. Numbers in parenthesis correspond to interquartile range observed value for continuous variables and to percentages for indicator variables as appropriate. Abbreviation: NEWS2 = National Early Warning Score 2; HFNC = high-flow nasal cannula for oxygen therapy; IMV = invasive mechanical ventilation; ECMO = extracorporeal membrane oxygenation; SD = standard deviation.

Table 3. Outcomes in the intention-to-treat population.

Characteristics	Total (n = 236)	Remdesivir group (n = 158)	Control group (n = 78)	Difference §
TTCI	22.0 (13.5 to 28.0)	21.0 (13.0 to 28.0)	23.0 (15.0 to 28.0)	1.23 (0.87 to 1.75)†
Day 28 mortality, n (%)	32 (13.6)	22 (13.9)	10 (12.8)	1.1 (-8.1 to 10.3)
Early (≤10 days of symptom onset)	15 (6.4)	8 (5.1)	7 (9.0)	-3.9 (-11.1 to 3.3)
Late (> 10 days of symptom onset)	15 (6.4)	12 (7.6)	3 (3.8)	3.7 (-2.2 to 9.7)
Clinical improvement rates				
Day 7, n (%)	6 (2.5)	4 (2.5)	2 (2.6)	-0.0 (-4.3 to 4.2)
Day 14, n (%)	60 (25.4)	42 (26.6)	18 (23.1)	3.5 (-8.1 to 15.1)
Day 28, n (%)	148 (62.7)	103 (65.2)	45 (57.7)	7.5 (-5.7 to 20.7)
IMV duration (days)	8.0 (5.0 to 19.0)	7.0 (4.0 to 16.0)	15.5 (6.0 to 21.0)	4.0 (-2.0 to 14.0)
IMV duration in survivors (days) &	30.5 (17.0 to 42.0)	19.0 (5.0 to 42.0)	42.0 (17.0 to 46.0)	-12.0 (-41.0 to 25.0)
IMV duration in non-survivors (days) &	7.0 (4.0 to 15.0)	7.0 (2.0 to 11.0)	8.0 (5.0 to 16.0)	2.5 (-3.0 to 11.0)
Length of oxygen support (days)	20.0 (12.0 to 31.0)	19.0 (11.0 to 31.0)	21.0 (14.0 to 30.5)	2.0 (-1.0 to 6.0)
Hospital length of stay (days)	25.0 (16.5 to 37.0)	25.0 (16.0 to 38.0)	24.5 (18.0 to 36.0)	0.0 (-4.0 to 4.0)
Days from randomization to discharge (days)	21.0 (13.0 to 31.0)	21.0 (12.0 to 31.0)	21.0 (13.5 to 28.5)	0.0 (-3.0 to 3.0)
Days from randomization to death (days)	11.0 (6.0 to 18.0)	9.5 (6.0 to 18.5)	11.0 (7.0 to 18.0)	1.0 (-5.0 to 7.0)
Six-category scale at day 7				**0.69 (0.41 to 1.17)***
1 Discharge (alive)	6 (2.5)	4 (2.5)	2 (2.6)	
2 Hospitalization, not requiring supplemental oxygen, n (%)	37 (15.7)	21 (13.3)	16 (20.5)	
3 Hospitalization, requiring supplemental oxygen, n (%)	130 (55.1)	87 (55.1)	43 (55.1)	
4 Hospitalization, requiring HFNC and/or non-IMV, n (%)	34 (14.4)	26 (16.5)	8 (10.3)	
5 Hospitalization, requiring ECMO and/or IMV, n (%)	10 (4.2)	6 (3.8)	4 (5.1)	
6 Death	14 (5.9)	10 (6.3)	4 (5.1)	
Six-category scale at day 14				**1.25 (0.76 to 2.04)***
1 Discharge (alive)	57 (24.2)	39 (24.7)	18 (23.1)	
2 Hospitalization, not requiring supplemental oxygen, n (%)	31 (13.1)	21 (13.3)	10 (12.8)	
3 Hospitalization, requiring supplemental oxygen, n (%)	89 (37.7)	61 (38.6)	28 (35.9)	
4 Hospitalization, requiring HFNC and/or non-IMV, n (%)	21 (8.9)	13 (8.2)	8 (10.3)	

5 Hospitalization, requiring ECMO and/or IMV, n (%)	11 (4.7)	4 (2.5)	7 (9.0)	
6 Death	22 (9.3)	15 (9.5)	7 (9.0)	
Six-category scale at day 28				**1.14 (0.66 to 1.95)***
1 Discharge (alive)	136 (57.6)	91 (57.6)	45 (57.7)	
2 Hospitalization, not requiring supplemental oxygen, n (%)	18 (7.6)	14 (8.9)	4 (5.1)	
3 Hospitalization, requiring supplemental oxygen, n (%)	31 (13.1)	18 (11.4)	13 (16.7)	
4 Hospitalization, requiring HFNC and/or non-IMV, n (%)	4 (1.7)	2 (1.3)	2 (2.6)	
5 Hospitalization, requiring ECMO and/or IMV, n (%)	5 (2.1)	2 (1.3)	3 (3.8)	
6 Death	32 (13.6)	22 (13.9)	10 (12.8)	

Note. Number (percentage) or median (interquartile range) is summarized as appropriate. Abbreviation: ICU = intensive care unit; HFNC = high-flow nasal oxygen therapy; IMV = intensive mechanical ventilation; ECMO = extracorporeal membrane oxygenation; TTCI = time to clinical improvement. Clinical improvement (the event) was defined as a decline of two categories on the modified seven-category ordinal scale of clinical status, or hospital discharge.

* Calculated by ordinal logistic regression model.

& In survivors, 3 patients were in each group; In non-survivors, 10 patients were in remdesivir group, 7 cases in control group.

§ Differences were expressed as rate differences or Hodges-Lehmann estimator and 95% confidence intervals.

† The hazard ratio was estimated by COX proportional risk model.

Table 4. Summary of adverse events in safety population that occurred in more than one participant

Events	Remdesivir group (n = 155)		Control group (n = 78)	
	Any Grade	**Grade 3 or 4**	**Any Grade**	**Grade 3 or 4**
Any adverse event (in ⩾2% of patients in any treatment group) *	102 (65.8)	13 (8.4)	50 (64.1)	11 (14.1)
Hypoalbuminemia	20 (12.9)	0	12 (15.4)	1 (1.3)
Hypokalemia	18 (11.6)	2 (1.3)	11 (14.1)	1 (1.3)
Increased blood glucose	11 (7.1)	0	6 (7.7)	0
Anaemia	18 (11.6)	1 (0.6)	12 (15.4)	2 (2.6)
Rash	11 (7.1)	0	2 (2.6)	0
Thrombocytopenia	16 (10.3)	4 (2.6)	5 (6.4)	3 (3.8)
Increased total bilirubin	15 (9.7)	1 (0.6)	7 (9.0)	0
Elevated blood lipids	10 (6.5)	0	8 (10.3)	0
Elevated WBC	11 (7.1)	0	6 (7.7)	0
Hyperlipemia	10 (6.5)	0	8 (10.3)	0
Increased BUN	10 (6.5)	0	5 (6.4)	0
Elevated neutrophil	10 (6.5)	0	4 (5.1)	0
Aspartate aminotransferase increased	7 (4.5)	0	9 (11.5)	0
Constipation	21 (13.5)	0	12 (15.4)	0
Nausea	8 (5.2)	0	2 (2.6)	0
Diarrhoea	5 (3.2)	0	2 (2.6)	0
Vomiting	4 (2.6)	0	2 (2.6)	0
Reduced serum sodium	4 (2.6)	0	2 (2.6)	0
Increased serum potassium	4 (2.6)	2 (1.3)	1 (1.3)	0
Any serious adverse event*	28 (18.1)	9 (5.8)	20 (25.6)	10 (12.8)
Respiratory failure or acute respiratory distress syndrome	16 (10.1)	4 (2.6)	6 (7.7)	4 (5.1)
Cardiopulmonary failure	8 (5.2)	0	7 (9.0)	1 (1.3)
Pulmonary embolism	1 (0.6)	1 (0.6)	1 (1.3)	1 (1.3)
Recurrence of COVID-19	1 (0.6)	0	0	0
Cardiac arrest	1 (0.6)	0	0	0
Acute coronary syndrome	0	0	1 (1.3)	1 (1.3)
Tachycardia	0	0	1 (1.3)	0

Septic shock	1 (0.6)	0	1 (1.3)	1 (1.3)
Lung abscess	0	0	1 (1.3)	1 (1.3)
Sepsis	0	0	1 (1.3)	1 (1.3)
Bronchitis	0	0	1 (1.3)	1 (1.3)
Thrombocytopenia	1 (0.6)	1 (0.6)	0	0
Increased D-dimer	0	0	1 (1.3)	1 (1.3)
Hemorrhage of lower digestive tract	1 (0.6)	1 (0.6)	0	0
Ileus	0	0	1 (1.3)	0
Deep vein thrombosis	1 (0.6)	1 (0.6)	1 (1.3)	1 (1.3)
Acute kidney injury	1 (0.6)	0	0	0
Diabetic keto-acidosis	0	0	1 (1.3)	1 (1.3)
Multiple organ dysfunction syndrome	1 (0.6)	0	2 (2.6)	0
Any AE/SAE leading to discontinued drug	18 (11.6)	3 (1.9)	4 (5.1)	1 (1.3)
Respiratory failure or acute respiratory distress syndrome	7 (4.5)	1 (0.6)	1 (1.3)	0
Cardiopulmonary failure	3 (1.9)	0	1 (1.3)	0
Nausea	1 (0.6)	0	0	0
Vomiting	1 (0.6)	0	0	0
Ileus	0	0	1 (1.3)	0
Elevated ALT	2 (1.3)	1 (0.6)	0	0
Rash	2 (1.3)	0	0	0
Poor appetite	1 (0.6)	0	0	0
Increased total bilirubin	1 (0.6)	0	0	0
Acute kidney injury	1 (0.6)	1 (0.6)	0	0
Seizure	0	0	1 (1.3)	0
Aggravated schizophrenia	0	0	1 (1.3)	1 (1.3)
Aggravated depression	0	0	1 (1.3)	1 (1.3)

Data are n (%) and include all events reported after antiviral treatment.

*Some patients had more than one adverse event.

§ Totally,36 patients discontinued the drug, 22 cases for AE/SAE, 14 patients for other reason (such as hospital discharge or early death). Detailed individual reasons for drug discontinuing was listed in appendix.

Figure 1. Trial profile

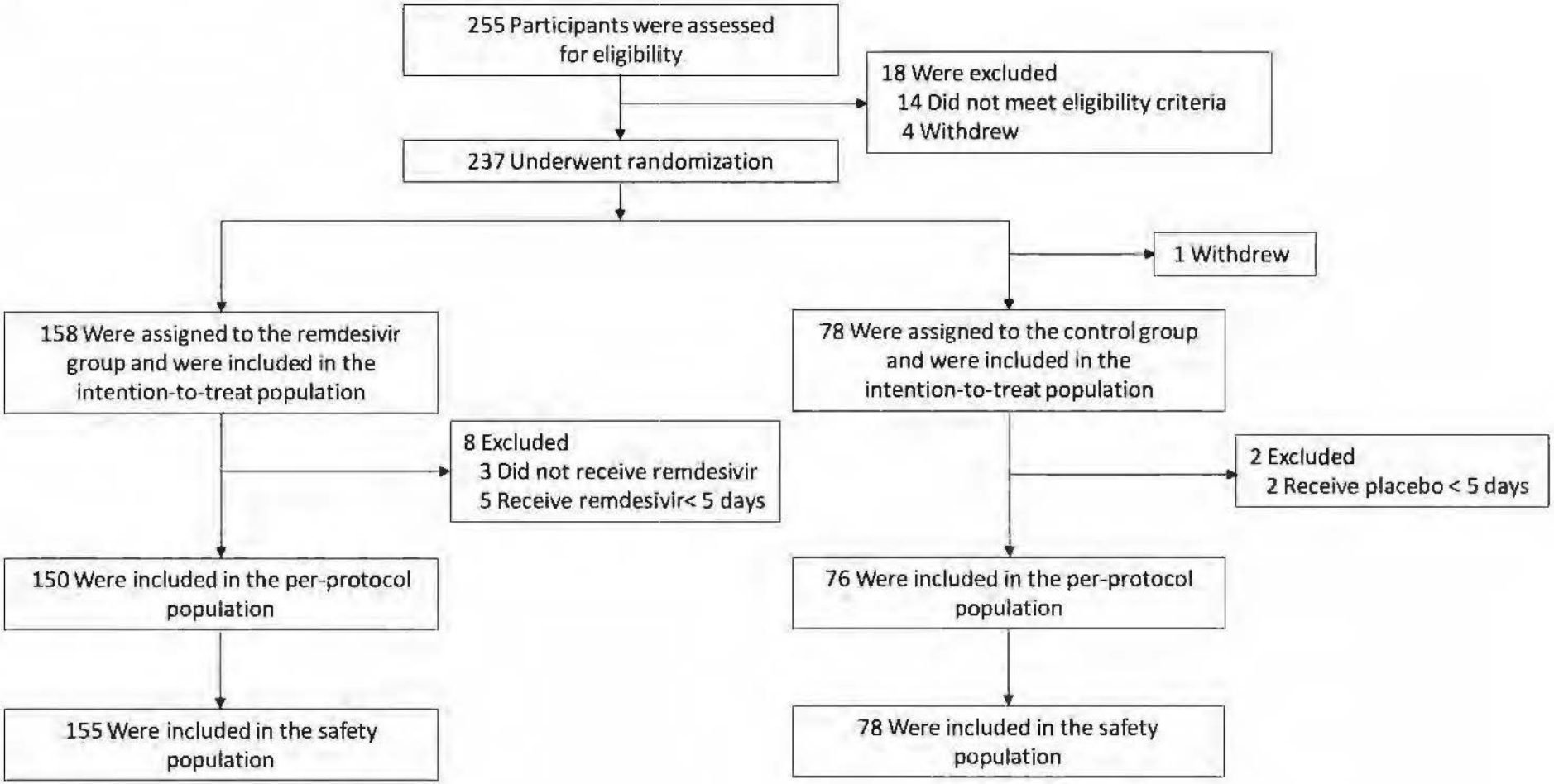
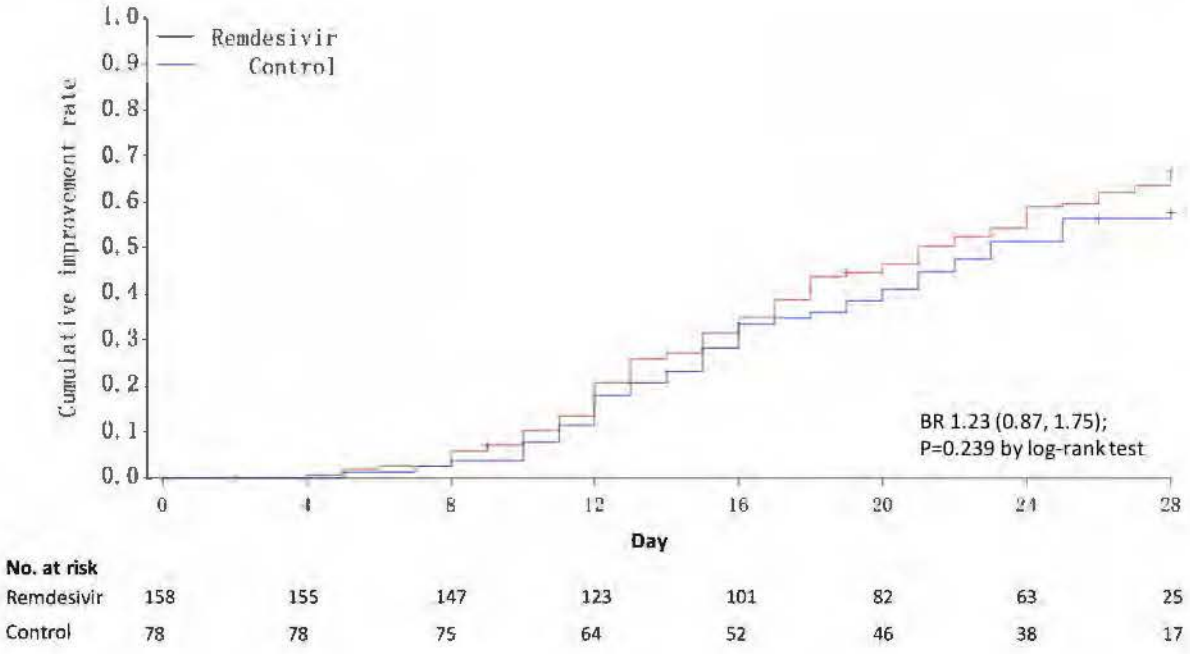
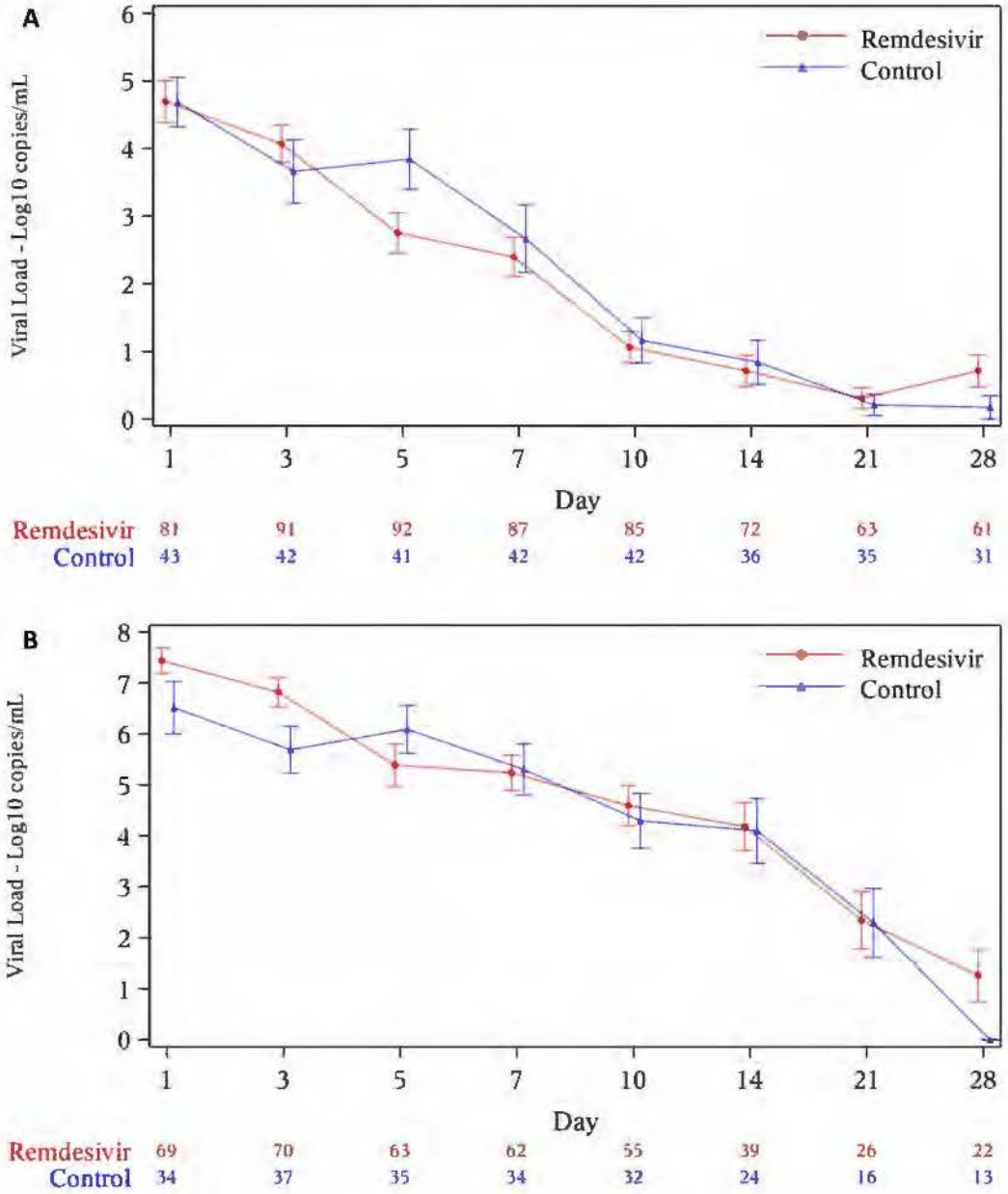


Figure 2. Kaplan Meier of time-to-clinical improvement in the Intention-to-Treat Population during the 28 days.



Note. Benefit ratio (BR) for clinical improvement was 1.23; 95% confidence interval [CI], 0.87 to 1.75; The adjusted BR for randomization stratification was 1.25; 95% CI 0.88 to 1.78.

Figure 3. SARS-CoV-2 load by qPCR on the upper (nasopharyngeal or oropharyngeal swabs) (Panel A) /lower (Panel B) respiratory tract specimens (data only from viral positive population).



Data were presented mean (±SE). Results less than the lower limit of quantification of PCR assay and greater than the limit of qualitative detection are imputed with half of actual value log10 copies/mL; results of patients with viral negative RNA are imputed with 0 $\log_{10}$ copies/mL.

Click here to access/download
Supplementary Material
2020.4.13 Appendix_V4.0.docx

From:	Disbrow, Gary (OS/ASPR/BARDA) </O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=0FD5845DEFDA4DC0BB45F8FAC629CF09-DISBROW, GA>
To:	Farley, John (FDA/CDER) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=13fc405c444b402bb26f5f43b8b0eee6-john.farley <John.Farley@fda.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>; Woodcock, Janet (FDA/CDER) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5f925e9a0f9147b186d40072d474d13d-janet.woodc <Janet.Woodcock@fda.hhs.gov>; Cavazzoni, Patrizia (FDA/CDER) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=41bd389298db4965bf2443225fb2a4ae-patrizia.ca <Patrizia.Cavazzoni@fda.hhs.gov>; Stein, Peter (FDA/CDER) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ba4e62d31cc84202a58fbc8f56879067-peter.stein <Peter.Stein@fda.hhs.gov>
Subject:	RE: Important Update - FOUO INFORMATION
Date:	2020/04/28 18:28:47
Priority:	Normal
Type:	Note

This information is being provided under the PHEMCE MOU and contains information that must be protected from unauthorized use and disclosure as per the PHEMCE MOU.

Thanks, John.

Good news.

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

Sent Date:	2020/04/28 18:28:46
Delivered Date:	2020/04/28 18:28:47

Courses of Action (COAs) to Increase the Availability and Access to Remdesivir for Trials and Potential Treatment of COVID-19

(b)(5)

(b)(5)

(b)(5)

DRAFT, PREDECISIONAL, DELIBERATIVE

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Witnesses appearing before the
Senate Appropriations Committee
Subcommittee on Labor, Health and Human Services, Education, and Related Agencies

Hearing on
Operation Warp Speed, vaccines, diagnostics, and therapeutics

Francis Collins, M.D., P.h.D., Director, National Institutes of Health

Robert R. Redfield, M.D., Director, Centers for Disease Control and Prevention

Gary Disbrow, Ph.D., Acting Director Biomedical Advanced Research and Development Authority

July 2, 2020

(b)(5)

(b)(5)

(b)(5)

(b)(5)

(b)(5)

(b)(5)

(b)(5)

(b)(5)

(b)(5)

(b)(5)

(b)(5)

(b)(5)

(b)(5)

(b)(5)

(b)(5)

(b)(5)

(b)(5)

Assistant Secretary for Preparedness and Response, Biomedical Advanced Research and Development Authority

(b)(5)

(b)(5)

(b)(5)

(b)(5)

(b)(5)

A Multi-site, Randomized, Double-Blind, Comparative Trial of the Safety and Efficacy of Standard of Care (SOC) plus Famotidine vs SOC plus Placebo for the Treatment of Non-Hospitalized symptomatic Adults with COVID-19

Northwell Health HRPP:

IND Exempt: PIND #149307

PROTOCOL VERSION: May 19, 2020

Proprietary and Confidential

TABLE OF CONTENTS

PROTOCOL SYNOPSIS

1. INTRODUCTION

The outbreak of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection was first reported in Wuhan, China, on 31 December 2019. The World Health Organization (WHO) declared the outbreak a global health emergency on 30 January 2020. Based on current epidemiological investigations, the post-exposure incubation period prior to onset of COVID-19 symptoms is one to 14 days, and typically ranges from three to seven days. In 80% of patients, COVID-19 presents as mild disease, but is still associated with significant "silent" viral shedding and infectivity.[1] 20% of cases develop severe (13%) or critical (6%) illness.[2] More severe forms of COVID-19 present as clinical severe acute respiratory syndrome, but include a T-predominant lymphopenia, high circulating levels of proinflammatory cytokines and chemokines, accumulation of macrophages and neutrophils in lungs, and immune dysregulation including immunosuppression.[3] SARS-CoV-2 is highly infectious, and a minimal infectious dose has been estimated at 10 to 1000 viral particles. Infection can be transmitted by direct interpersonal contact, fomites, respiratory secretions, and direct viral shedding into the air via normal respiration. SARS-CoV-2 has been isolated from both feces and urine. As of May 18, 2020 the US has reported over 1.6 million cases and over 92,000 dead. In New York State there are over 352,000 confirmed cases with nearly 23,000 deaths.

The treatment for COVID-19 remains unclear. There are no definitive vaccine, therapeutic antibody, or antiviral drug medical countermeasures currently authorized by the FDA for prevention or treatment of COVID-19 disease. General treatment is supportive care supplemented by oxygen therapy as needed, progressing to active ventilatory support for critical cases. Experimental antiviral treatments have included Alpha-interferon, Remdesivir, Ribavirin, and chloroquine phosphate.[4,5]

There are currently no clear treatment options early on in the ambulatory setting. Famotidine may be a candidate medication for this setting. Famotidine is a histamine-2 receptor antagonist, widely available over-the-counter and at low cost, does not interact with other medications, and is safely used for suppression of gastric acid production over a wide range of doses from 20mg once daily to 160mg four times daily.[6] In computer-based simulations, Famotidine has been identified as a potential inhibitor of the 3-chymotrypsin-like protease ($3CL^{pro}$).[7]With regard to clinical studies a propensity score matched retrospective cohort study a significantly reduced risk for death or intubation (adjusted hazard ratio 0.43, 95% confidence interval 0.21-0.88) was identified for patients with COVID-19 who were taking Famotidine before or at the point of hospital admission.[8] In addition, a case series of 10 patients with COVID-19 who self-medicated with oral famotidine, significant improvement of symptoms was associated with famotidine use after 24-48 hours .[9]

1.1. Background

Clinical presentation: COVID-19 presentation may include fever, but most frequently includes a range of symptoms such as fatigue, dry cough, shortness of breath, headaches, and loss of smell or taste. Nasal congestion, runny nose, sore throat, myalgia and diarrhea are found in a few cases. Severe cases often develop dyspnea and/or hypoxemia after one week. In severe cases, patients may progress rapidly to acute respiratory distress syndrome (with classic ground glass radiographic findings), septic shock, metabolic acidosis that is difficult to correct, coagulopathy, cytokine storm and multiple organ failure. Severe and critically ill patients may present with moderate to low fever or may even be afebrile.[10]

Symptom severity scores have been used in other clinical syndromes. Janowitz and colleagues developed a symptom score based on the Eastern Collaborative Oncology Group performance status scale, which was initially developed for patients with cancer diagnoses.[11] In a case series[9] symptom scores for general unwellness, cough, shortness of breath, fatigue, headaches, and loss of taste or smell (anosmia) were retrospectively reported by patients on an ordinal scale: 1 = not affected, 2 = little affected, 3 = affected, 4 = severely affected. The symptoms were chosen from a list of NIH endorsed symptoms for COVID-19 patient reported outcome[12]. When the changes of the normalized total symptom score across all patients were analyzed, the authors found that a significant improvement in the symptom score was reported within 24 hours of starting Famotidine and that symptoms continued to improve and nearly normalized to pre-illness levels at 14 days after the first Famotidine use. The improvement of symptoms was across all categories, but airway related symptoms such as cough and shortness of breath were reported to improve more rapidly than systemic symptoms such as fatigue.

Laboratory tests: In the early stages of the disease, peripheral WBC count is normal or decreased with decreased lymphocyte count. Some patients develop elevated liver enzymes, lactate dehydrogenase (LDH), ferritin, muscle enzymes and myoglobin. Elevated troponin is seen in some critically ill patients, while most patients have elevated C-reactive protein, erythrocyte sedimentation rate and normal procalcitonin. In severe cases, D-dimer increases and peripheral blood lymphocytes progressively decrease. Severe and critically ill patients often have elevated inflammatory factors and cytokine levels, but the degree of elevation in mildly to moderately ill patients is not known. Development of lymphopenia (pan T) often corresponds with deteriorating respiratory function requiring ventilatory support, and a trend towards resolution of lymphopenia may predict recovery and transfer from ICU to more traditional inpatient supportive care. The value of laboratory tests for management of non-hospitalized patients is not known and an important research question.

Viral detection: SARS-CoV-2 nucleic acid can be detected in nasopharyngeal swabs, sputum, lower respiratory tract secretions, blood, feces and other specimens using RT-PCR methods. Detection of viral nucleic acid may be more accurate if specimens from lower respiratory tract (sputum or air tract extraction) are tested. The specimens should be submitted for testing as soon as possible after collection. The value of viral detection tests for management of non-hospitalized patients is not known and an important research question.

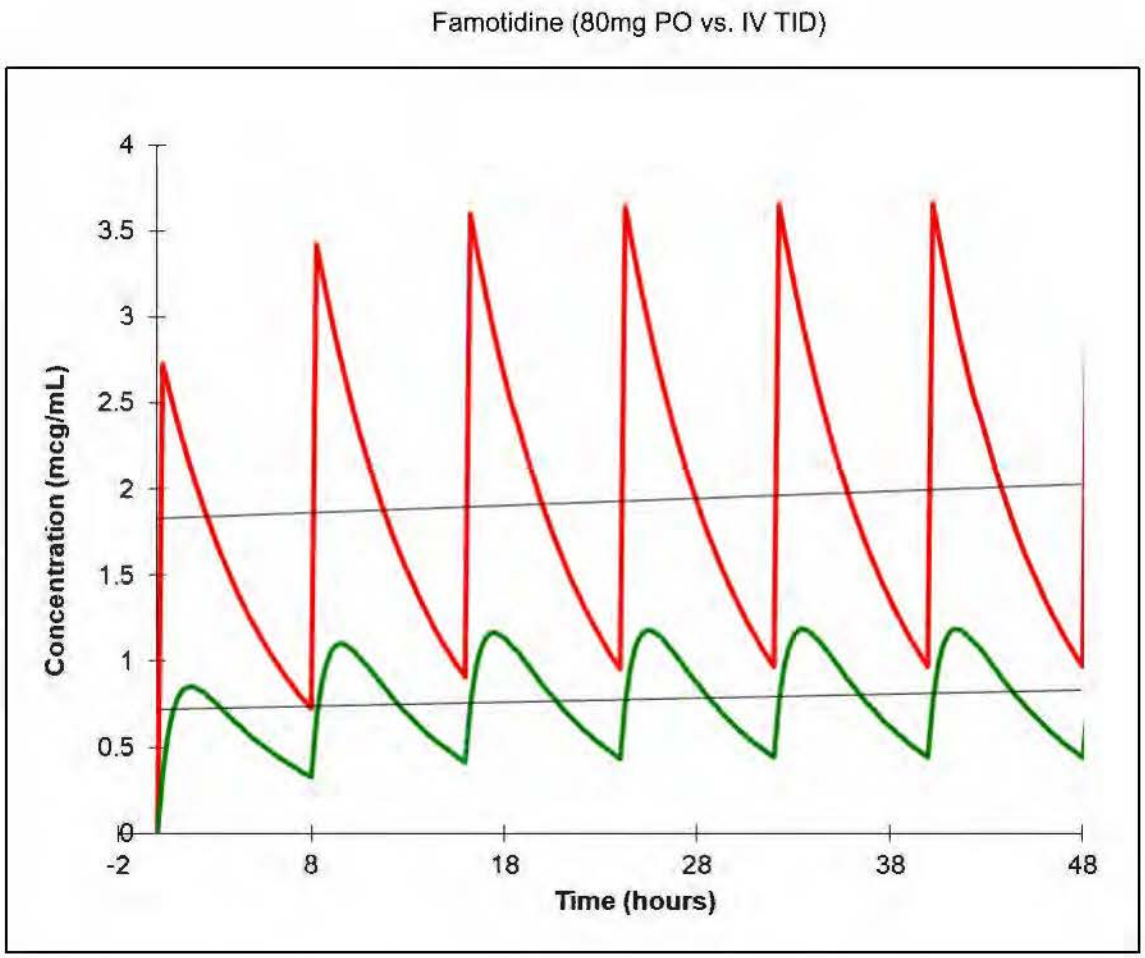
Physiological and activity monitoring: Fever, hypoxia, and reduced activity levels are associated with mild to moderate COVID-19. These can be monitored and recorded in an outpatient setting

using standard thermometers, peripheral oxygen saturation measurements, and activity monitoring devices.

1.1.1. Pharmaceutical and Therapeutic Background

There is an urgent need for an effective treatment to treat symptomatic patients but also to decrease the duration of virus transmission in the community. Among candidate drugs to treat COVID-19, repurposing of FDA-approved drugs for use as antiviral treatments is proposed because knowledge on safety profile, side effects, and drug interactions are well known.

In silico screening of FDA licensed compound libraries against the SARS CoV 2 protease Plpro catalytic site was performed using solved crystal structures of the protein. Plpro (Papain-like protease) is an early acting protease responsible for initial processing of tbe SARS CoV2 polyprotein into active subunits.[13] Plpro also has ubiquitinase activity, and is implicated in early infection phase inhibition of innate (interferon) immune responses which otherwise would suppress viral replication. A ranked list of licensed compounds with predicted binding activity in the Plpro catalytic site was computationally generated, and the Plpro catalytic site binding pose of each of the top compounds was examined and ranked by a team of pharmaceutical chemists. Package inserts or product monographs for the licensed compounds which generated high computational binding scores and passed inspection were then reviewed and used to rank compounds based on adverse events, warnings, drug interactions on-target mechanisms, pharmacokinetic and absorption, metabolism, excretion and toxicity (ADMET), protein binding and available therapeutic window considerations. Famotidine (Pepcid), a histamine H2 antagonist widely available over-the-counter, was repeatedly computationally scored among the highest of the compounds tested, and was associated with the most favorable pharmacokinetic and safety profile. A series of analogs of famotidine were generated using PubChem, and many of these scored even higher as potential candidates. This control compound set further confirmed the predicted binding of the molecular backbone chemotype at the Plpro protease/ubiquitinase site. Currently available as oral and IV products, famotidine has a very attractive proven safety, drug interaction, and therapeutic window profile. Samples of famotidine have been submitted at Southern Research and IITRI for in vitro testing in COVID-19 cultures. Famotidine is known to possess linear pharmacokinetics. Figure 1 shows the pharmacokinetic simulations based on IV and oral product prescribing information pharmacokinetic parameters at 80 mg dosing. Unpublished anecdotal case studies suggest clinical benefits associated with administration of famotidine 40 mg PO TID in mild COVID-19 infection. More recently, retrospective data released out of Columbia University Medical Center showed that use of famotidine was associated with reduced risk for death or intubation (adjusted hazard ratio (aHR) 0.42, 95% CI 0.21-0.85) and also with reduced risk for death alone (aHR 0.30, 95% CI 0.11-0.80). After balancing baseline patient characteristics using propensity score matching, these relationships were unchanged (HR for famotidine and death or intubation: 0.43, 95% CI 0.21-0.88).[8] Additionally, a case series of 10 patients who self-administered Famotidine, most frequently at a dose of 80 mg po TID, demonstrated an association of Famotidine use with an improvement in symptoms scores [Figure 2]. [9]



80mg PO dose TID	IV	Oral
Peak steady-state (mcg/mL)	3.83	1.19
Trough steady-state (mcg/mL)	0.97	0.44
Tmax steady-state [h]	0.00	1.48
Cave (mcg/mL)	2.08	**0.83**
ke [1/h]	0.171	0.171
ka [1/h]	6931	1.386
t1/2(el) [h]	4.04	4.04
Fluct. [%]	137.1	89

Figure 1: Simulated pharmacokinetics of Famotidine. Famotidine is known to possess linear pharmacokinetics. The information above are pharmacokinetic simulations based on the IV and oral product prescribing information pharmacokinetic parameters at 80 mg dosing. The information above is not data from human studies.

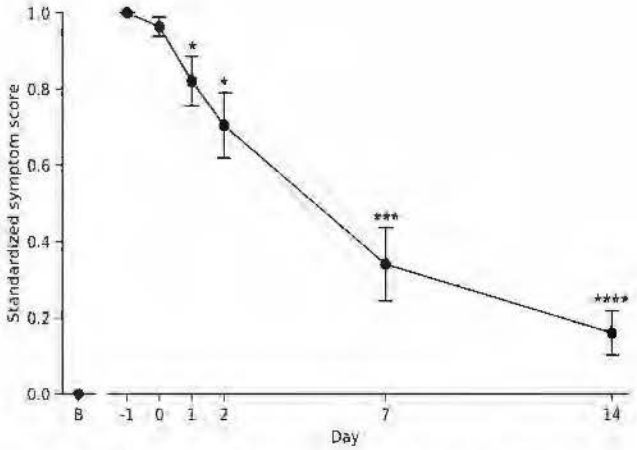


Figure 2. Normalized symptom scores of all patients. The mean longitudinal normalized symptom score for all patients is shown. The standard error of the mean is indicated. Statistical comparisons by t-test in comparison to day 0, the day of starting Famotidine. *, $p<0.05$; ***, $p<0.001$; ****, $p<0.0001$

1.2. Study Rationale

To reduce global morbidity and mortality effective treatment strategies for non-hospitalized patients are required. Famotidine widely available over-the-counter at low cost, does not interact with other medications, and has been safely used for suppression of gastric acid production over a wide range of oral doses from 20mg once daily to 160mg four times daily. In computer simulations, Famotidine was identified as a potential inhibitor of the 3-chymotrypsin-like protease ($3CL^{pro}$). In a retrospective propensity scored cohort study, famotidine use coincided with reduced mortality and morbidity in hospitalized patients. In a case series of non-hospitalized patients with COVID-19, famotidine was well tolerated when taken orally at doses up to 80mg TID and was associated with rapid symptomatic improvement. These findings support the implementation of a randomized double blinded study that investigates efficacy of famotidine in the treatment of non-hospitalized patients with COVID-19.

2. STUDY OBJECTIVES AND HYPOTHESIS

2.1. Study Objectives

2.1.1. Primary Objective

The overall objective of the study is to evaluate the clinical efficacy of COVID-19 treatments consisting of standard of care (SOC), vs SOC with oral famotidine in symptomatic non-hospitalized patients with confirmed COVID-19 disease using a longitudinal comparison of a graded symptom score. The symptom score questionnaire is designed based on and NIH endorsed guideline and has been utilized as a scoring system in the case series by Janowitz et al. Six symptoms (fatigue, shortness of breath, general unwellness, loss of taste or smell, headache, cough) will be graded daily on an ordinal scale from 1 to 4. The score will be referred to as "COVID-19 symptom score" hereafter.

Primary Clinical Endpoint: The primary endpoint is the relative change in the COVID-19 symptom score from baseline (Day 0 before taking any medication) to Day 7, defined as the

difference of Day 7 total symptom score and baseline symptom score (Day 0 total symptom score) divided by baseline symptom score.

2.1.2. Secondary Objectives

Evaluate the safety and clinical efficacy of famotidine in addition to SOC compared to SOC as assessed by:

1. Clinical Progression as measured by any increase in the ordinal scale (seven-point scale- see section 2.3.2) from Day 0 bay Day 14.
2. Evaluate the safety of the intervention through the 14 days of treatment as compared to the control arm as assessed by:
    - Cumulative incidence of serious adverse events (SAEs)
    - Cumulative incidence of Grade 3 and 4 adverse events (AEs).

2. Comparing severity of inflammatory response measured by Ferritin concentrations on Day 7
3. Comparing Oxygenation on Day 7:
    - Oxygen saturation measured daily

2.1.3. Exploratory Objectives

Comparisons across the two treatment arms with respect to the following list of measurements will be made:

1. Pulmonary function using peak flow rates
2. Change on Days 7, 14, 28 compared to Day 0 of:
    a. hematological markers (including but not restricted to Immune cell activation, of WBC fractions, i.e. neutrophils, monocytes, macrophages, B- and T – lymphocytes, eosinophils, platelets)
    b. Organ function, including estimated glomerular filtration rate, AST, ALT, bilirubin, albumin, and coagulation panel
    c. Plasma cytokine levels (including but not restricted to to IL-1B, IL-4, IL-6, IL-10, IL-12, IL-18, TNF alpha, IFN-gamma)
    d. Plasma chemokine levels (including but not restricted to CXCL8, CXCL10, CCL2)
    e. Inflammatory markers (including but not restricted to CRP)
    f. micronutrient levels (including but not restricted to bivalent zinc ions)
    g. Organ function, including estimated glomerular filtration rate, AST, ALT, bilirubin, albumin, and coagulation panel
    h. d-dimer
    i. Plasma Famotidine Levels
3. Longitudinal change in body weight
4. Longitudinal change in body temperature: Body temperature measured daily from Day 0 to Day 14 or, if fever (≥98.6°F = 37°C) persists after Day 14, until afebrile
5. Symptoms other than those listed under the main objective, including, but not restricted to: myalgia, nausea, diarrhea, chest tightness, runny nose, loss of appetite/skipping of meals.

6. Virologic Response. Evaluate virologic response as measured by significant changes in PCR copy number at Day 7 and optionally Day 14 and 28 compared to enrollment Day 0. Presence of SARS-CoV-2 Viral RNA in Nasopharyngeal swab OR sputum OR lower respiratory secretions (airway suction) will be considered evidence of current viral infection. SARS-CoV-2 RNA will be assessed by real-time reverse transcription-PCR using a standardized diagnostic test method
7. Production of Antibodies against SARS-CoV 2: Measurement of Antibodies on Day 28
8. Change in activity measures including but not restricted to resting heart rate, walking distance equivalence, estimated energy expenditure.
9. Length of Stay (LOS) if patient becomes hospitalized
10. Difference in 28-day Mortality

2.2. Hypothesis

The working hypothesis is that SOC+ famotidine will he superior to SOC alone in reducing disease related symptoms in non-hospitalized COVID19 patients with mild or moderate disease.

2.3. Study Endpoints

2.3.1. Primary Efficacy Endpoint

The primary endpoint is the relative change in the COVID-19 symptom score from baseline (Day 0 before taking any medication) to Day 7, defined as the difference of Day 7 total symptom score and baseline symptom score (Day 0 total symptom score) divided by baseline symptom score.

2.3.2. Secondary Efficacy Endpoint

1. Clinical status of subject (7-point ordinal scale):
   - 1. Death;
   - 2. Hospitalized, on invasive mechanical ventilation or ECMO;
   - 3. Hospitalized, on non-invasive ventilation or high flow oxygen devices;
   - 4. Hospitalized, requiring supplemental oxygen;
   - 5. Hospitalized, not requiring supplemental oxygen;
   - 6. Not hospitalized, limitation on activities;
   - 7. Not hospitalized, no limitations on activities.
2. Serious Adverse Events
3. Ferritin level on Day 7
4. Peripheral oxygen saturation on Day 7

2.3.3. Exploratory Efficacy Endpoint

1. Peak flow rates
2. Change on Days 7, 14, 28 compared to Day 0 of:
   a. hematological markers (including but not restricted to Immune cell activation, of WBC fractions, i.e. neutrophils, monocytes, macrophages, B- and T – lymphocytes, eosinophils, platelets)
   b. Organ function, including estimated glomerular filtration rate, AST, ALT, bilirubin, albumin, and coagulation panel

c. Plasma cytokine levels (including but not restricted to IL-1B, IL-4, IL-6, IL-10, IL-12, IL-18, TNF alpha, IFN-gamma)
d. Plasma chemokine levels (including but not restricted to CXCL8, CXCL10, CCL2)
e. Inflammatory markers (including but not restricted to CRP, Ferritin)
f. micronutrient levels (including but not restricted to bivalent zinc ions)
g. Organ function, including estimated glomerular filtration rate, AST, ALT, bilirubin, albumin, and coagulation panel
h. Change in d-dimer
i. Plasma Famotidine Levels

3. Change in body weight on Days 7, 14, 28 compared to Day 0
4. Longitudinal body temperature
5. Reduction of score in symptoms other than those included in the current COVID-19 symptom score used to assess the main endpoint, including, but not restricted to: myalgia, nausea, diarrhea, chest tightness, runny nose, loss of appetite/skipping of meals.
6. Virologic response as measured by percent change in PCR copy number at Day 7 and optionally Day 14 and 28 relative to enrollment Day 0.
7. Production of Antibodies against SARS-CoV 2: Measurement of Antibodies on Day 28
8. Change in activity measurements including but not restricted to resting heart rate, walking distance equivalence and estimated energy expenditure.
9. Length of Stay (LOS) if patient becomes hospitalized (number of days from admission to discharge)
10. 28-Day Mortality

3. STUDY DESIGN

3.1. Overall Design

Phase 2 Randomized Double-Blind Comparative Trial

3.1.1. Study Duration

The study is expected to last for up to six months.

3.1.2. Duration of Study Participation

An individual subject will complete the study in about 28 days, from screening at Day -1 to the visit on Day 28.

4. STUDY POPULATION

4.1.1.2. Inclusion Criteria

1. Subject (or legally authorized representative) provides written informed consent prior to initiation of any study procedures.
2. Understands and agrees to comply with planned study procedures.
3. Male or non-pregnant female adult ≥18 years of age at time of enrollment.
4. Subject consents to randomization.

5. Has PCR confirmed COVID-19 disease < 72 hours prior to randomization.
6. Has been experiencing mild to moderate symptoms as defined by a total score of > 10 in the COVID-19 symptom score for >1 day but ≤7 days

4.1.2. Exclusion Criteria

- Recent history of or any in-hospital exposure to investigational medications targeting COVID-19.
- Self-medicating with famotidine.
- Severe COVID-19 disease at time of enrollment requiring admission to hospital
- History of Stage 3 severe chronic kidney disease, i.e. eGFR of < 40ml/min
- Pregnancy
- History of hepatic disease, Hepatitis C infection, or alcoholism
- Allergy to famotidine
- Known to be immunocompromised by disease or treatment for existing disease
- Inability to perform the tasks required for the patient reported outcome measure recordings

4.1.2.1. Rationale for Selected Exclusion Criteria

There are no adequate or well-controlled studies of famotidine in pregnant women. Since the safe use of famotidine in pregnant women has not been established, the benefits of treatment with famotidine should be weighed against potential risks. Treatment of pregnant women on a compassionate use basis may be considered by the treating physician. Famotidine is overall well tolerated but in the case of renal insufficiency the risk of prolongation of the QT interval is increased. Subjects treated per protocol on a compassionate use basis will not be included in data analysis, due to their unique characteristics and the anticipated small sample size.

5. STUDY TREATMENTS

5.1. Stratification, Randomization, and Blinding

5.1.1. Stratification

Prior to randomization, subjects will be stratified by Gender (M/F), age group (<60/≥60) in addition to study site (Northwell COVID Clinic; Maimonides Medical Center Practice Site).

5.1.2. Randomization

This study is a Phase II randomized, double blinded, controlled trial to evaluate the safety and efficacy of standard of care (SOC) plus 80 mg of oral famotidine three times daily in comparison to SOC plus placebo in non-hospitalized adult patients diagnosed with COVID-19. The study is a multi-site trial that will be conducted in neighborhoods of hospitals within the Northwell Health system in New York, United States.

Randomization will be carried out using a balanced 1:1 permuted block design with block sizes 2,4,6.

The Biostatistics Unit will develop and implement the randomization procedure using the Biostatistics Randomization Management System (BRMS). The Biostatistics Randomization Management System (BRMS) is a secure, HIPAA-compliant, web-based application that allows investigators to randomize subjects into randomized clinical trials (RCTs) using their personal computer. The BRMS allows for multi-center, stratified, and single/double blinded RCTs, using permuted blocks. Randomization notifications (respectful of blinding status) are automatically sent to the PI and other authorized personnel. BRMS includes a feature that allows for medically indicated breaking of the blind, with requirement for justification. BRMS includes an audit trail of all transactions.

5.1.3. Blinding

Upon determining eligibility, the assigned study coordinator will utilize the BRMS randomization system to randomize the subject. The research pharmacist will be automatically notified by BRMS via email that a subject has been randomized and the identity of the treatment arm will be made known to the pharmacist.

Qualified study personnel will deliver the famotidine for oral self-administration. Specific instructions for managing the investigational products will be provided in the pharmacy manual. There will be a placebo tablet. Participants randomized to the placebo famotidine arm will receive placebo tablets, hence all participants will receive medication regardless of what arm of the study they are being enrolled in. The drug must be provided in identical form for active and placebo treatments, so that they remain indistinguishable to both study personnel and subjects. Study subjects, the principal investigators, and study site personnel will remain blinded to all randomization assignments throughout the study. The Study Director, Study Monitor, and any other study personnel who are in regular contact with the study site will remain blinded to all subject randomization assignments. The study team members directly involved with study conduct will be blinded. Selected individuals not involved in the conduct of the study may have access to unblinded data as needed for safety review or other data review. An independent pharmacist will be unblinded and in communication with the DSMB to make decisions for adaptations to the study.

5.1.4. Emergency Unblinding Procedure

BRMS includes a feature that allows for medically indicated breaking of the blind, with requirement for justification. User logs onto BRMS and clicks the "break the blind" icon and follows instructions.

5.2. Study Drug

Famotidine Tablets, 80mg
Specific instructions for managing investigational products will be provided in the Pharmacy Manual.

5.2.1. Description

Famotidine is a competitive inhibitor of histamine H2-receptors. The primary clinically important pharmacologic activity of famotidine is inhibition of gastric juice secretion. Famotidine reduces the acid and pepsin content, as well as the volume of basal, nocturnal and

stimulated gastric secretions. Famotidine and other H2 antagonists, including cimetidine and ranitidine, have been documented as having potent antiviral activity against Human Immunodeficiency Virus. Using advanced computational tools, including in silico docking, we identified famotidine as a potential candidate to block SARS-CoV-2 PLpro (papain-like protease) coronavirus protease required for viral replication.

5.2.2. Preparation

Each tablet contains either 20 mg or 40 mg of famotidine. Both the 20 and 40 mg tablets contain the following non-medicinal ingredients: microcrystalline cellulose, pregelatinized starch, talc, magnesium stearate, titanium dioxide, polyethylene glycol 400, yellow iron oxide and red iron oxide. The 20 mg tablets also contain hydroxypropyl methylcellulose, while the 40 mg tablets also contain hydroxypropyl methylcellulose and black iron oxide.

5.2.3. Administration

The study will investigate oral doses of famotidine given at 2-4x increments above the typical daily oral dose. The Prescribing Information for oral famotidine suggests 20 or 40mg tablets TID. The total daily dose proposed is 240 mg/day famotidine po for a maximum of 14 days, or until hospital admission, whichever comes first.

5.2.4. Storage

Store famotidine at room temperature 15-30°C. Protect from light.

5.2.5. Pregnancy

There are no adequate or well-controlled studies in pregnant women. Since the safe use of famotidine in pregnant women has not been established, the benefits of treatment with famotidine should be weighed against potential risks by the health care team on a compassionate use basis.

5.2.6. Contraception

Women of childbearing age must agree to use contraception for the duration of study treatment prior to providing consent.

5.2.7 Adverse Reactions

Famotidine is usually well tolerated; most adverse reactions have been mild and transient. The following adverse reactions have been reported at a rate greater than 1% in patients on therapy with famotidine in controlled clinical trials, and may be causally related to the drug: headache (4.6%), dizziness (1.2%), constipation (1.2%) and diarrhea (1.6%). The following additional adverse reactions have been reported since the drug was marketed: urticaria, liver enzyme abnormalities, cholestatic jaundice, anaphylaxis, angioedema. Toxic epidermal necrolysis has been reported very rarely with H2-receptor antagonists. As with other H2-receptor antagonists, cases of bradycardia, A-V block and other arrhythmias have been reported rarely in patients treated with famotidine. Gynecomastia has been reported rarely. In most cases that were followed up, it was reversible after treatment was discontinued. Famotidine in some case studies is QT prolonging (most in renal failure) and has been noted to prolong QT at usual dose.

Decreased kidney function: Famotidine is unlikely to be causal, but we recognize that in COVID-19 patients the development of renal insufficiency is not uncommon and can lead to an increase in other AEs. Risk of delirium with H2 blockers especially high dosage is most associated in the setting of renal dysfunction.[6]

5.4. Drug Accountability

All drug accountability records will be kept current and contain the dates, quantity, and study medication dispensed to each subject. The PI must be able to account for all opened and unopened study drug. All unused study drug must be disposed of at the site or returned to the sponsor or designee. All drug accountability records will be made available for inspection by regulatory agencies and kept on file onsite as per Northwell Health institutional policy.

5.5. Guidelines for Delay, Reduction and/or Discontinuation of Study Medications

Dose modification for an individual subject is described in Section 5.2.7.

5.6. Prior and Concomitant Medications

Concomitant use of hepatotoxic medications, immunosuppressive therapy and/or investigational study drugs for the treatment of COVID-19 are an exclusion criterion for participation. Any other treatment administered from the first dose of study drug to the final study assessment will be considered concomitant medication and recorded per subject.

5.7. Method of Assessing Treatment Compliance

Study drugs will be administered per protocol while subjects are hospitalized. Medication records will be made available for inspection by the sponsor and/or regulatory agencies, and kept on file onsite as per Northwell Health institutional policy.

5.8. Subject Withdrawal/Discontinuation

A subject has the right to withdraw from the study at any time. The investigator and/or sponsor have the right to withdraw a subject from the study if it is no longer in the best interest of the subject to continue, or if the subject's continuation in the study places the scientific outcome of the study at risk.

5.8.1. Subject Replacement

Withdrawn subjects will be replaced.

6. STUDY PROCEDURES

6.1. Screening

The research coordinator will be notified about potentially eligible patients who require screening. The lab parameters required to determine eligibility are part of standard of care and will be available to the research coordinator shortly after admission.

6.2. Enrollment

Upon meeting the inclusion/exclusion criteria including consent, the research coordinator will officially enroll the subject and implement the randomization procedure.

6.3. Treatment Period

Famotidine will be prescribed at 80 mg TID for a maximum of 14 days, or until hospital admission, whichever comes first. Subjects will be monitored per standard of care for the duration of the study. The patients will be asked to report medication intake, occurrence of possible adverse events, and their symptoms, O2 saturation and body temperature daily from day 1 to day 14 and on Days 21 and 28. If O2 saturation is ≤ 98% on day 14, patients are asked to report O2 saturation daily until O2 saturation is ≥98% for three consecutive days. If the body temperature ≥ 98.6°F (37°C) on day 14, the patient is asked to report body temperature daily until body temperature is ≤98.6°F (37°C) for three consecutive days. Subjects will wear a Fitness tracker that monitors heart rate, movement, energy expenditure for the duration of the study. Patients will be asked to provide daily weight measurements or synchronize the fitness tracker with their scale if possible. Research labs will be drawn, peak flow measurements and clinical exams will be performed, and Nasal Swabs/Sputum sample will be taken on Days 0, 7, 14, and 28 after enrollment. Weight will be measured on Day 0, Day 7, Day 14, and Day 28. A serological test for Anti Sars-Cov 2 antibodies will be performed on Day 28.

6.4. Follow-up

Subjects will be followed for 28 ±3 days. If a patient gets hospitalized, they will be followed up till discharge, which may be longer than 28±3 days. There should be very few of such patients.

7. EFFICACY ASSESSMENTS

See Section 2.

8. SAFETY EVALUATION AND REPORTING

8.1. Assessment of Safety Endpoints

Subject safety will be assessed continuously while in study as per standard of care. Subject safety will be assessed in the questionnaires on Days 1-14, 21 and 28 and at visits on Days 1,7,14 and 28.

8.2. Adverse Events and Serious Adverse Events

8.2.1 Definition of Adverse Event (AE)

Adverse event is defined as any untoward medical occurrence associated with the use of an intervention in humans, whether or not considered intervention-related (21 CFR 312.32 (a)).

8.2.2. Definition of Serious Adverse Event (SAE)

An adverse event (AE) or suspected adverse reaction is considered "serious" if, in the view of either the investigator or sponsor, it results in any of the following outcomes: death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the participant and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

8.2.3. Classification of Adverse Event

8.2.3.1. Severity of Event

The following guidelines will be used to describe severity of Adverse Events (AE):

- **Mild** – Events require minimal or no treatment and do not interfere with the participant's daily activities.
- **Moderate** – Events result in a low level of inconvenience or concern with the therapeutic measures. Moderate events may cause some interference with functioning.
- **Severe** – Events interrupt a participant's usual daily activity and may require systemic drug therapy or other treatment. Severe events are usually potentially life-threatening or incapacitating. Of note, the term "severe" does not necessarily equate to "serious".

8.2.3.2. Relationship to Study Intervention

All adverse events (AEs) must have their relationship to study intervention assessed by the clinician who examines and evaluates the participant based on temporal relationship and his/her clinical judgment. The degree of certainty about causality will be graded using the categories below. In a clinical trial, the study product must always be suspect.

- **Definitely Related** – There is clear evidence to suggest a causal relationship, and other possible contributing factors can be ruled out. The clinical event, including an abnormal laboratory test result, occurs in a plausible time relationsbip to study intervention administration and cannot be explained by concurrent disease or other drugs or chemicals. The response to withdrawal of the study intervention (dechallenge) should be clinically plausible. The event must be pharmacologically or phenomenologically definitive, with use of a satisfactory rechallenge procedure if necessary.
- **Probably Related** – There is evidence to suggest a causal relationship, and the influence of other factors is unlikely. The clinical event, including an abnormal laboratory test result, occurs within a reasonable time after administration of the study intervention, is unlikely to be attributed to concurrent disease or other drugs or chemicals, and follows a clinically reasonable response on withdrawal (dechallenge). Rechallenge information is not required to fulfill this definition.

- **Possibly Related** – There is some evidence to suggest a causal relationship (e.g., the event occurred within a reasonable time after administration of the trial medication). However, other factors may have contributed to the event (e.g., the participant's clinical condition, other concomitant events). Although an AE may rate only as "possibly related" soon after discovery, it can be flagged as requiring more information and later be upgraded to "probably related" or "definitely related", as appropriate.
- **Unlikely to be related** – A clinical event, including an abnormal laboratory test result, whose temporal relationship to study intervention administration makes a causal relationship improbable (e.g., the event did not occur within a reasonable time after administration of the study intervention) and in which other drugs or chemicals or underlying disease provides plausible explanations (e.g., the participant's clinical condition, other concomitant treatments).
- **Not Related** – The AE is completely independent of study intervention administration, and/or evidence exists that the event is definitely related to another etiology. There must he an alternative, definitive etiology documented by the clinician.

8.2.3.3. Expectedness

The DSMB will be responsible for determining whether an adverse event (AE) is expected or unexpected. An AE will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information previously described for the study intervention.

8.2.4. Time Period and Frequency for Event Assessment and Follow-Up

The occurrence of an adverse event (AE) or serious adverse event (SAE) may come to the attention of study personnel, or upon review by a study monitor.

All AEs including local and systemic reactions not meeting the criteria for SAEs will be captured on the appropriate case report form (CRF). Information to be collected includes event description, time of onset, clinician's assessment of severity, relationship to study product (assessed only by those with the training and authority to make a diagnosis), and time of resolution/stabilization of the event.

All AEs occurring while on study must be documented appropriately regardless of relationship. All AEs will be followed to adequate resolution.

Any medical condition that is present at the time that the participant is screened will be considered as baseline and not reported as an AE. However, if the study participant's condition deteriorates at any time during the study, it will be recorded as an AE.

Changes in the severity of an AE will be documented to allow an assessment of the duration of the event at each level of severity to be performed. AEs characterized as intermittent require documentation of onset and duration of each episode.

All reportable events with start dates occurring any time after informed consent is obtained until 7 (for non-serious AEs) or 30 days (for SAEs) after the last day of study participation will be recorded. Events will be followed for outcome information until resolution or stabilization.

8.2.5. Adverse Event Reporting

Adverse events (AE) will be reported immediately to the PI, the co-investigators, and the Safety Officer/Medical Monitor. It will also he reported to the Northwell IRB and to all members of the research team.

8.2.6. Serious Adverse Event Reporting

The study clinician will immediately report any serious adverse event (SAE), whether or not considered study intervention related, including those listed in the protocol and must include an assessment of whether there is a reasonable possibility that the study intervention caused the event.

All serious adverse events (SAEs) will be followed until satisfactory resolution or until the site investigator deems the event to be chronic or the participant is stable. Other supporting documentation of the event will be recorded.

The Principal Investigator (PI) will be responsible for notifying the Food and Drug Administration (FDA) of any unexpected fatal or life-threatening suspected adverse reaction as soon as possible, but in no case later than 7 calendar days after initial receipt of the information.

8.2.7. Reporting Events to Participants

Participants will not be informed of AEs and SAEs unless the AE or SAE happened to them.

8.2.8. Events of Special Interest

N/A

8.2.9. Reporting of Pregnancy

N/A

8.3. Unanticipated Problems

8.3.1. Definition of Unanticipated Problems (UP)

The Office for Human Research Protections (OHRP) considers unanticipated problems involving risks to participants or others to include, in general, any incident, experience, or outcome that meets **all** of the following criteria:

- Unexpected in terms of nature, severity, or frequency given (a) the research procedures that are described in the protocol-related documents, such as the Institutional Review Board (IRB)-approved research protocol and informed consent document; and (b) the characteristics of the participant population being studied;
- Related or possibly related to participation in the research ("possibly related" means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- Suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

8.3.2. Unanticipated Problem Reporting

The investigator or study team member who becomes aware will report unanticipated problems (UPs) to the reviewing Institutional Review Board (IRB) and to the Principal Investigator (PI). The UP report will include the following information:

- Protocol identifying information: protocol title and number, PI's name, and the IRB project number;
- A detailed description of the event, incident, experience, or outcome;
- An explanation of the basis for determining that the event, incident, experience, or outcome represents an UP;
- A description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the UP.

To satisfy the requirement for prompt reporting, UPs will be reported using the following timeline:

- UPs that are serious adverse events (SAEs) will be reported within 5 business days of the investigator becoming aware of the event.
- Any other UP will be reported within 5 business days of the investigator becoming aware of the problem.

8.4. Other Safety

8.4.1. Clinical Laboratory Evaluations

Laboratory values will be obtained by venipuncture and evaluated for white blood cell count, hemoglobin, platelets, creatinine, glucose, total bilirubin, ALT, and AST on Days 0, 1, 7, 14, 28. The PI will be made aware of abnormal lab values.

8.4.2. Vital Signs

Vital signs will be collected daily via Bluetooth linked monitors (BP, Pulse, O2 Sat, Temp).

8.4.3. Physical Examination

Changes in clinical severity will be assessed via structured survey.

8.4.4. Other Examinations

9. STATISTICAL METHODS

9.1 Primary endpoint

The primary endpoint is the relative change in the total symptom score over 6 symptoms from baseline (Day 0 before taking any medication) to Day 7, defined as the difference of Day 7 total symptom score and baseline symptom score (Day 0 total symptom score) divided by baseline symptom score.

9.2 Sample size consideration

In our previous case series with 10 patients, their total symptom scores ranged from 11 to 23 at Day -1 and Day 0, but dropped to 6-12 by Day 7. From Day 0 to Day 7, the relative change from these 10 patients had a mean value at 38.4% with SD=18.4%. Using 1000 bootstrapping samples, the relative change at Day 7 from baseline after taking famotidine for 7 days has a median of 37.8% (Q1=34.2%, Q3=41.8%) with a median SD=17.3%. We used the relative change from day -1 to day 0 among these 10 patients to estimate the relative change at Day 7 from baseline in the placebo group conservatively assuming the relative change per day is constant until Day 7. Using 1000 bootstrapping samples, the relative change at Day 7 from baseline in the placebo group has a median of 15.2% (Q1=8.9%, Q3=23%). Table * below shows the sample size needed per arm under different assumptions to detect the difference in the primary end point between two arms with 80% power and using a two-sided two-sample t-test with type I error being 0.05 (PASS 12). The SD of the primary end point in both arms is conservatively assumed to be 18%.

Table *: sample size needed under different assumed relative changes at Day 7 from baseline within each study arm. Sample size calculation is based on using a two-sided two-sample t-test with type I error being 0.05 and power being 80%.[14] The SD of the primary end point in both arms is conservatively assumed to be 18%.

Relative change at Day 7 from baseline in the placebo arm	Relative change at Day 7 from baseline in the treatment arm		
	34.2%	37.8%	41.8%
8.9%	10	8	6
15.2%	16	12	9
23%	**42**	25	16

Even though we expect few patients to withdraw from the study or get hospitalized within the first 7 days after treatment, we conservatively set our target sample size at 50 per arm (total patients enrolled = 100) in order to take into account other possible reasons for missing data. In addition, we plan to use a linear mixed model for longitudinal data to compare the relative change at Day 7 between two arms by using all available data observed daily till Day 14 and then Day 21 and Day 28. By using all available data, this theoretically will improve our model's detection power.

9.2. Statistical Analysis Plan for Primary Hypothesis

In general, patient baseline characteristics will be summarized with appropriate descriptive statistics. All baseline demographics and clinical data will be summarized by treatment arm using frequencies, rates, means, medians, standard deviations and quartiles appropriate to the dataset. There will be no inferential comparison of treatment arms with respect to baseline and demographic clinical data; such comparisons will be descriptive only. Unless otherwise specified, all results will be considered significant if $p<0.05$. All data analysis will be performed using SAS 9.4 (SAS institute Inc., Cary, NC).

All model assumptions will be diagnosed and data transformation may be needed to make the model assumption met. All analysis will employ the intent-to-treat (ITT) principle and results will be reported according to CONSORT guideline. All randomized patients in the groups to

which they are randomly assigned, regardless of the intervention they actually receive and regardless of subsequent withdrawal from treatment or deviation from the protocol for any cause will be included in the final analysis.

Our primary hypothesis is that patients on the treatment arm will have a significantly bigger change/drop in the total symptom score than patients on the placebo arm. Since the data are longitudinal and have hierarchical structure, we will use a linear mixed effects model for the analysis. The fixed effects of the model will include group (treatment and placebo), visit (Day 0-7, Day 14 and Day 28) and an interaction between group and visit. Baseline total symptom core, will be used as covariate. Due to the lack of preliminary information hy age, gender and study site, these stratification factors were not used in the sample size calculation. However, these three stratification factors will be adjusted for in the linear mixed model. This model will include a random intercept at the patient level to account for correlations due to the repeated measurements from the same patients. The dependence structure for longitudinal data from the same patient will be selected with the Akaike Information Criterion. More specifically, the model will take the following mathematical form,

$$Y_{it} = \alpha_t + \beta_t X_i + \gamma_i Z_i + b_i + e_{it} \qquad (A1)$$

Where Y_{it} is the percent change of BD for subject i=1,…, n at Day t; X_i is a binary indicator for treatment (1 for subjects in the treatment arm and 0 otherwise), $Z_i$stand for covariates including baseline symptom score, gender, age, and site;α_t,β_t,γ_i are unknown coefficients; $b_i \sim N(0, \sigma_b^2)$ is a Gaussian random effect to reflect the correlation of BD measurement from the same subject and the residual vector $e_{it} \sim MVN(0,\Sigma_e)$. The form of Σ_e will he selected with the Akaike Information Criterion (AIC). The regression coefficients should satisfy appropriate constraints for model identifiability. Under this model, β_7 represents the symptom score reduction at Day 7 in the treatment arm compared to placebo group. Testing the hypothesis H_0:$\beta_7 = 0$ will provide the primary analysis results. This model (A1) allows for estimating the symptom score changes at different time point within each arm and their differences at any time point, which will be performed as secondary analysis. This model also allow us to later adjust for other possible confounding factors such as patients' comorbidity. Model assumption such as normality will be diagnosed and data transformation may be applied if needed.

Similar analysis will be carried out by using the *per protocol* (PP) data set which will include all ITT patients who did not have any relevant major protocol deviations and have taken at least 70% of prescribed Famotidine. The PP data will be used for sensitivity analysis of the primary efficacy endpoint. For the purposes of the PP definition, the use of REM on or prior to Day 7 will constitute a major protocol violation. Accordingly, data on subjects who receive REM on or prior to Day 7 will be excluded from the PP dataset. Subjects who begin REM dosing on Day 7 or later will be included in the PP dataset using their data up to Day 7. In addition, all symptom scores collected after patients got hospitalized will be set as missing in the PP data analysis as they would get other interventions once hospitalized.

9.3. Missing Data

The missing data pattern for longitudinal studies is typically complicated. In our study, we will make daily phone calls to remind study participates to minimize missing data. The linear mixed

effect model (A1) account for missing data by implicitly assuming data at random. Missing data in our study is highly like to be intermittently missing pattern and we don't expect any death during 30 days. Therefore, missing at random is high likely to be the missing data mechanism in our study. Nonetheless, as a sensitivity analysis, we will also use multiple imputations by chained equation to impute missing primary endpoint,[15,16] use complete cases only for analysis and pattern mixture approach[17,18] which is useful in the case of informative dropout.

9.4. Statistical Analysis Plan for Secondary Objectives

There are four planned secondary endpoints: clinical status ordinal score; Serious Adverse Events; Ferritin level on Day 7; Peripheral oxygen saturation on Day 7. The comparison between all longitudinal measurements such as clinical status ordinal scores, ferritin level and peripheral oxygen saturation will be first illustrated using spaghetti plots.

Clinical progression status: Clinical status ordinal scores will be measured on a 7 point ordinal scale as shown in section 2.3.2. As the expected death or hospitalization is expected to be rare (<5%) in our study population, we will compare the proportion of patients who had clinical progression (defined as ever having an increase in the clinical status ordinal score by day 14) between two study arms. Estimated clinical progression rates and corresponding 95% Casella-Blyth-Still confidence intervals will be reported within each arm. Fisher's exact test will be used for the comparison. Because death and hospitalization are rare, our study may not have enough power to detect such difference.

Serious adverse events (SAE): For each specific type of SAE in addition to overall SAE, the estimated event rates and corresponding 95% Casella-Blyth-Still confidence intervals will be reported within each arm. The cumulative incidence of overall SAE will be estimated within each arm and compared between two study arms by using Pepe and Mori's test.[19] Discontinuation or temporary interruption of famotidine use (for any reason) in the treatment arm will be described.

Ferritin level: Ferritin levels will be measured on Days 0, 7, 14 and 28. We hypothesize that patients in the treatment arm will have a significantly lower ferritin levels than those in the placebo arm. Based on literature we assume mean and SD at day 0 and d7 for placebo arm of 600ng/ml +/- 100 ng/ml and mean and SD on day 7 for treatment arm of 400ng/ml +/- 100 ng/ml, 50 patients per arm will have more than 90% power using a two-sided two-sample t-test with alpha 0.05 (PASS 12). We will further use a linear mixed model for longitudinal data to further compare ferritin levels between two arms on Day 7 in addition to other time points (Day 14 and 28). Such comparison will be performed as both ITT analysis and PP analysis. Age, gender and study sites will be used as covariates.

Peripheral Oxygen Saturation Peripheral oxygen saturation will be measured daily from Day 0 to Day 14, Day 21 and 28. Days with oxygen saturation ≤ 98% before reaching over 98% for patients within each arm will be first described using appropriate statistics such as mean and SD. We expect that the placebo group would not have any increase by Day 7 but the treatment group would have an increase of 4-6% from 90-94% to 96-98% within 7 days. Assuming a conservative SD being 2%, 50 patients per arm will have more than 90% power to detect such

difference on Day 7 using a two-sided two-sample t-test with alpha 0.05 (PASS 12). Analysis for peripheral oxygen saturation on Days 7 will be compared using similar analysis methods for comparing ferritin levels.

9.5. Statistical Analysis Plan for Exploratory Objectives

All longitudinal continuous measurements such as peak flow rates, all lab test results, body weight, body temperature, symptom scores for other symptoms, drop in the PCR copy numbers, activity measurements from all participants will be first illustrated using spaghetti plots within each arm. Linear mixed models for longitudinal measurements will be performed to explore the difference between two study arms after adjusting for stratification factors (age, gender and site). Model assumptions will be diagnosed and dependence structure will be selected using AIC. Such model will use all available data and provide estimated differences between any two time points or between two arms at each specific time point. Because of the exploratory nature of these analysis, multiple testing adjustment is not planned (20). However, for the comparison of all lab test results, we are planning to use false discovery rate at 10% to find candidates for further investigation. Antibody presence/positive rate at Day 28, 28-day mortality rate and hospitalization rate will be estimated within each arm and reported with corresponding 95% Casella-Blyth-Still confidence intervals. Fisher's exact test will be used to explore the possible difference between two study arms. For patients who get hospitalized, their LOS as measured as days from admission to discharge will be reported with descriptive statistics such as median and interquartile range by study arm. We will also explore the correlation between virologic response as measured by the drop in the PCR copy numbers over time and other longitudinal measures such as symptom scores, ferritin levels through linear mixed models and explore if there is a cutoff value in the drop rate of PCR copy number that could be used to predict positive treatment response or disease recovery.

9.6. Safety Analysis

Safety population: The safety population includes all randomized patients who received at least one dose of the study drug. Analysis of the safety population will be done according to the treatment received (as treated).

9.7. Data Safety Monitoring Board

An independent data safety monitoring board (DSMB) will actively monitor interim data to review the ongoing safety of patients and can make recommendations about early study closure or changes to the protocol. The DSMB members will include 2 to 4 physicians with relevant medical specialty training and 1 statistician. The DSMB will convene bi-weekly, with additional meetings or conference calls scheduled as needed. The detailed operation of the DSMB is governed by a charter (see Appendix C.) describing further details such as frequency of meeting, procedures (including but not limited to periodic safety monitoring) and requirements for reporting.

10. DATA INTEGRITY AND QUALITY ASSURANCE

10.1. Monitoring

The PI or designee will visit each site prior to enrollment and throughout the study duration to ensure safety and adherence to study protocols. The number of visits for any given site may vary based on site risk indicators. Study-related monitoring may also be done by internal and external regulatory agencies, including the IRB and OHRP. Study monitors will perform ongoing source data review to verify that data recorded in the CRF by authorized site personnel are accurate, complete, and verifiable from source documents, that the safety and rights of patients are being protected, and that the study is being conducted in accordance with the current approved protocol version and any other study agreements, ICH GCP, and all applicable regulatory requirements.

10.2. Data Collection

Subjects enrolled in this study will undergo laboratory testing as per protocol. The results of these tests will be collected, as indicated. Subjects will be made aware of and will be required to consent to additional procedures during the Informed Consent process. Detailed instructions for blood/NP swab sample collections will be in the laboratory manual provided to study sites.

10.3. Data Management

A data management plan specifying all relevant aspects of data processing for the study will be maintained with the regulatory documentation for this protocol. All data coding (SAEs, baseline findings, medication, medical history, etc.) will be done using internationally recognized and accepted abbreviations. Northwell Health has designed and implemented a HIPAA compliant COVID-19 Datamart data collection tool (see Appendix D.) which will be utilized to obtain clinical data for COVID-19 patients witbin the health system in addition to the medical record.

10.4. Electronic Systems

Electronic systems that may be used to process data in this study will include:

- Biostatistics Randomization Management System (BRMS) –randomization
- RedCap – data collection CRF
- Statistical Analysis System (SAS) – statistical review and analysis

Data will be collected on Android based tablets using HIPAA compliant software (VitalTecb). Biometric sensors including pulse oximetry, temperature sensors, blood pressure cuffs and activity monitors via blue tooth will be connected to the tablet. Patient reported outcomes using the symptom-based scale developed by Janowitz et al will also be collected. Other patient reported symptoms and outcomes will also be recorded through the tablet computer. In the even that patients do not possess interest access for immediate upload study personnel will arrange a visit to directly download stored date from the tablet

Data

10.5. Study Documentation

10.5.1. Case Report Form Requirements

Study data obtained in the course of the clinical study will be recorded onsite on paper Case Report Forms (CRFs), and then transferred to RedCap by trained study staff. All required CRFs must be completed for every study subject. The PI will ensure the accuracy, completeness, and timeliness of the data and will provide his electronic signature upon review.
Copies of paper CRFs will be retained as part of the study record and available for inspection by regulatory authorities. The electronic systems used for data management all employ an audit trail that will reflect any changes made to study records.

10.5.2 Record Retention and Storage

All essential study documents, including ICFs, source documents, CRFs, drug accountability records, and regulatory documentation will be stored in a locked office at the Center for Health Innovations and Outcomes Research at Northwell Health with access limited to approved study personnel only. All documents will be retained for at least 15 years following the completion or discontinuation of the study.

10.6. Operational Procedures

A 'Meta-Site' will be established to coordinate study personnel working remotely to perform study tasks that do not need to be completed on-site. These will include but are not limited to the following: 1) track all data, 2) coordinate meetings, 3) maintain regulatory documentation, 4) oversee study personnel and address staffing needs. A Meta-Site Principal Investigator will be identified to oversee this team.

11. PUBLICATION POLICY

11.1. Publication and Public Disclosure of Clinical Trial Information

This study and results will be made publicly available on ClinicalTrials.gov. Processes for publications resulting from this study will be outlined separately.

12. ETHICS AND ADMINISTRATIVE INFORMATION

12.1. Good Clinical Practice Statement

It is the responsibility of the PI and all study personnel to ensure that this clinical study will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with the ICH guidelines for GCP and applicable regulatory requirements.

12.2. Confidentiality

All appropriate measures will be taken to ensure that the anonymity of each subject is maintained. Subjects will be identified by an alphanumeric code only on CRFs and other related documentation. Source documentation that may not be coded will be kept confidential.

12.3. Informed Consent

It is the responsibility of the PI or other IRB-approved study personnel to obtain informed consent from each subject or a legally authorized representative (LAR) prior to his/her participation in the study and after the aims, methods, objectives, and potential hazards of the study have been explained to the potential subject in language that he/she can understand.

(Patients with Limited English Proficiency (LEP) that are fluent in Spanish will not be excluded from this study. Informed Consent will be obtained in this case following the procedures detailed above, using an impartial interpreter and a short form translated into Spanish, and in accordance with Northwell Health policy GR089 for obtaining informed consent for patients with Limited English Proficiency. Patients with Limited English Proficiency without sufficient Spanish Proficiency will be excluded from the study, as this excludes the patient from accurately answering the questionnaire with the COVID-19 symptom score.)

12.4. Regulatory Compliance

The Northwell Health Institutional Review Board (IRB), as described in ICH guidelines for GCP, will provide regulatory oversight of this clinical study. The IRB will review and approve:

- The protocol, Informed Consent Form, and advertising materials,
- Amendments or modifications to the protocol or ICF before implementation,

In addition, the IRB will be informed of any event likely to affect the safety of patients or the conduct of the study. Records of the IRB review and approval of all study documents will be kept on file by the PI.

12.5. Protocol Deviations

Major and minor protocol deviations will be reported according to institutional policy.

12.6. New Information Affecting the Conduct of the Study

If new information affecting either the conduct of the study or the initial risk/benefit assessment becomes available, this protocol will be amended as needed and submitted for IRB review. Subjects will be informed and required to provide informed consent.

12.7. Protocol Amendments

All amendments or modifications to this protocol will be reviewed and approved by the IRB prior to implementation. In the event that a modification is required in an emergency situation, the IRB will be notified immediately.

12.8. Study Termination

The sponsor, investigator, and/or regulatory agencies have the right to terminate the study prematurely on the basis of safety, efficacy or futility.

13. REFERENCES

1. To KK-W, Tsang OT-Y, Leung W-S, et al. Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. *Lancet Infect Dis*. 2020;20(5):565-574. doi:10.1016/S1473-3099(20)30196-1
2. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China. *JAMA*. 2020;323(13):1239. doi:10.1001/jama.2020.2648
3. Catanzaro M, Fagiani F, Racchi M, Corsini E, Govoni S, Lanni C. Immune response in COVID-19: addressing a pharmacological challenge by targeting pathways triggered by SARS-CoV-2. *Signal Transduct Target Ther*. 2020;5(1):84. doi:10.1038/s41392-020-0191-1
4. Wang Y, Zhang D, Du G, et al. Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial. *Lancet*. 2020;395(10236):1569-1578. doi:10.1016/S0140-6736(20)31022-9
5. Geleris J, Sun Y, Platt J, et al. Observational Study of Hydroxychloroquine in Hospitalized Patients with Covid-19. *N Engl J Med*. Published online May 7, 2020:NEJMoa2012410. doi:10.1056/NEJMoa2012410
6. Food and Drug Agency Information Sheet on Famotidine, Reference ID: 4280861. 1986. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/019462s039lbl.pdf.
7. Wu C, Liu Y, Yang Y, et al. Analysis of therapeutic targets for SARS-CoV-2 and discovery of potential drugs by computational methods. *Acta Pharm Sin B*. 2020;10(5):766-788. doi:10.1016/j.apsb.2020.02.008
8. Freedberg DE, Conigliaro J, Wang TC, et al. Famotidine Use is Associated with Improved Clinical Outcomes in Hospitalized COVID-19 Patients: A Propensity Score Matched Retrospective Cohort Study. *Gastroenterology*. Published online May 2020. doi:10.1053/j.gastro.2020.05.053
9. Janowitz T, Gablenz E, Pattinson D, et al. Famotidine use and quantitative symptom tracking for COVID-19 in non-hospitalised patients: a case series. *Gut*. Published online June 4, 2020:gutjnl-2020-321852. doi:10.1136/gutjnl-2020-321852
10. Richardson S, Hirsch JS, Narasimhan M, et al. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. *JAMA*. 2020;323(20):2052. doi:10.1001/jama.2020.6775
11. Oken MM, Creech RH, Tormey DC, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. *Am J Clin Oncol*. 1982;5(6):649-655. http://www.ncbi.nlm.nih.gov/pubmed/7165009
12. Harris P. All of Us Research Program Covid-19 Participant Experience (COPE) Survey (PPI). 2020. https://www.phenxtoolkit.org/toolkit_content/PDF/NIH_COPE.pdf.
13. Wu C, Liu Y, Yang Y, et al. Analysis of therapeutic targets for SARS-CoV-2 and discovery of potential drugs by computational methods. *Acta Pharm Sin B*. 2020;(xxx). doi:10.1016/j.apsb.2020.02.008

14. Hintze, J. (2013). PASS 12. NCSS, LLC. Kaysville, Utah, USA. www.ncss.com.
15. van Buuren S. Multiple imputation of discrete and continuous data by fully conditional specification. *Stat Methods Med Res*. 2007;16(3):219-242. doi:10.1177/0962280206074463
16. White IR, Royston P, Wood AM. Multiple imputation using chained equations: Issues and guidance for practice. *Stat Med*. 2011;30(4):377-399. doi:10.1002/sim.4067
17. Little R. Modeling the drop-out mechanism in repeated-measures studies. JASA.1995; 90:1112-21.
18. Little R. Pattern-mixture models for multivariate incomplete data. JASA. 1995; 88:125-34.
19. Pepe MS, Mori M . Kaplan–Meier, marginal or conditional probability curves in summarizing competing risks failure time data? Stat Med 1993; 12: 737–751.
20. Bender R and Lange S. (2001) " Adjusting for Multiple Testing – When and How?". Journal of Clinical Epidemiology. 54:343-9

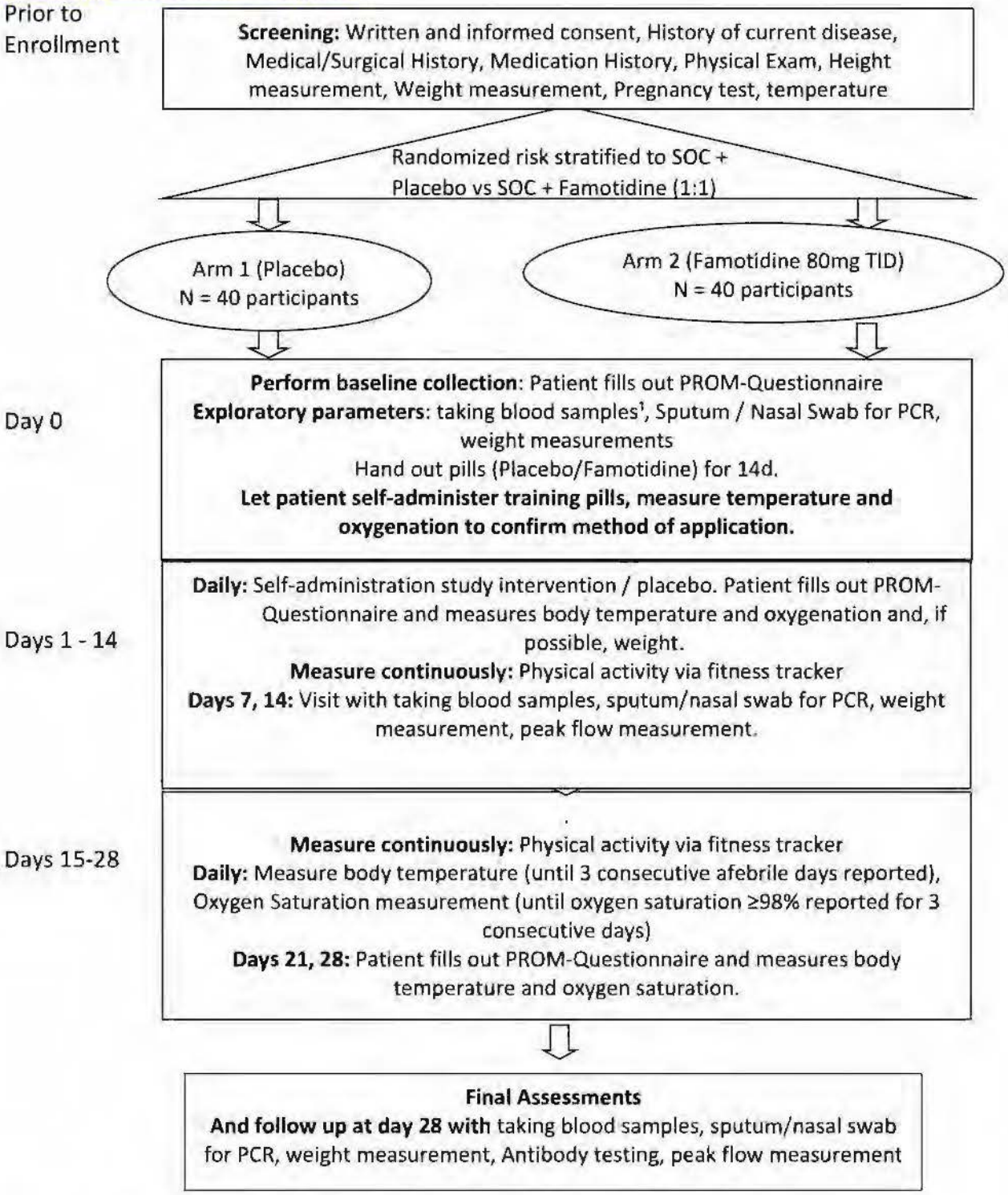
14. APPENDICES

14.2. Appendix A Schedule of Events

Procedures	Screening: Day -1	Enrollment/Baseline: Day 0	Study Days 1—14	Study Days 21, 28	Visits 7, 14, 28	Study days 0 - 28
Informed Consent	X					
Demographics	X					
History of Present Illness	X					
Medical/Surgical History	X					
Medication History (Outpatient and Inpatient)	X				X	
Pregnancy Test[a]	X					
Randomization	X					
Hand out drug		X				
Physical Exam	X				X	
Height	X					
Nasal Swab / Sputum for PCR		x			X	
Antibody testing					Day 28	
Weight	X	X			X	If possible
PROM Questionnaire	X	X	X	X		
Temperature Measurement	X	X	X	X	X	X[b]
Oxygen Saturation Measurement	X	X	X	X		X[c]
Vital Signs	X	X			X	
Physical Activity Monitoring						X
Self-administration Study Intervention			X			
Peak flow measurement		X			X	
Hematological markers		X		X		
Serum Chemistry		X		X		
Inflammatory Markers		X		X		
Chemokine Panel		X		X		
Cytokine Panel		X		X		
Micronutrient levels		X		X		
D-Dimer levels		X		X		
Plasma Famotidine levels		X		X		
Adverse Event Review and Evaluation	X					X
Complete Case Report Forms (CRFs)	X				X	

a: Serum or urine pregnancy test (women of childbearing potential) if not already performed.
b: Temperature measurements continue until patient reports 3 consecutive afebrile days
c: Oxygen saturation measurements continue until patient reports 3 consecutive days with saturation ≥98%

14.2. Appendix B Flow Diagram



[1] tests specified in Table X.

14.2. Appendix C

Data Safety and Monitoring Board (DSMB) Charter

1. Introduction

This Charter is for the Data and Safety Monitoring Board (DSMB) for the study entitled: A Multi-site, Randomized, Double-Blind, Multi-Arm Historical Control, Comparative Trial of the Safety and Efficacy of Hydroxychloroquine, Famotidine, and the Combination of Hydroxychloroquine and Famotidine for the Treatment of COVID-19 in Hospitalized Adults

The Charter is intended to be a living document. The DSMB may wish to review it at regular intervals to determine whether any changes in procedure are needed.

2. Responsibilities of the DSMB

The DSMB is responsible for safeguarding the interests of study participants, assessing the safety and efficacy of study procedures, and for monitoring the overall conduct of the study.

THE DSMB IS AN INDEPENDENT ADVISORY GROUP, AND IS REQUIRED TO PROVIDE RECOMMENDATIONS ABOUT STARTING, CONTINUING, AND STOPPING THE STUDY. IN ADDITION, THE DSMB IS ASKED TO MAKE RECOMMENDATIONS, AS APPROPRIATE, ABOUT:

- Efficacy of the study intervention
- Benefit/risk ratio of procedures and participant burden
- Selection, recruitment, and retention of participants
- Adherence to protocol requirements
- Completeness, quality, and analysis of measurements
- Amendments to the study protocol and consent forms
- Performance of individual centers and core labs
- Participant safety, and
- Notification of and referral for abnormal findings

3. Organization and Interactions

Communication with DSMB members will be primarily through the Principal Investigator (PI), Office of the Vice President for Research and the HHS Program Office. It is expected that other study investigators will not communicate with DSMB members about the study directly, except when making presentations or responding to questions at DSMB meetings or during conference calls.

4. DSMB Members and Program Staff

DSMB will be comprised of 2-4 physicians with relevant medical experience, at least one biostatistician, and others as needed The DSMB will have a Chair and Executive Secretary (ES) proposed by the Vice President for Research at Northwell Health and elected by the board members. The ES will provide an

unbiased staff interface for the DSMB, especially during executive sessions. The ES is responsible for assuring the accuracy and timely transmission of the final recommendations and DSMB minutes.

5. Scheduling, Timing, and Organization of Meetings

DSMB meetings are usually held by remote connections. The purpose of the first meeting is to review and discuss this Charter, to provide an overview of study activities, to review and make recommendations about the protocol, and to determine the frequency of interim analyses and whether data will or will not be masked to identity of randomized groups. Enrollment in this study cannot begin until the DSMB Charter has received IRB approval.

Given the extraordinary circumstance of this study, meetings will be held biweekly, with additional meetings or conference calls scheduled as needed.

- For this DSMB, meetings and calls will be held: Every 2nd Friday

- Review of interim data analyses will occur:

  Two interim analyses will be performed, one after 1/3 of the subjects have been followed for 30 days, and, if applicable, after 2/3 of the subjects have been followed for 30 days. An O'Brien Fleming stopping rule for efficacy or futility will be carried out.

The agenda for DSMB meetings and calls will be drafted by the ES, in consultation with HHS staff. The ES will finalize the agenda after consultation with the DSMB Chair. The agenda and meeting materials will be distributed by the ES 2 days before each meeting or call.

Before each meeting, when the agenda is sent out, the ES will ask all DSMB members to state whether they have developed any new conflicts of interest. If a new conflict is reported, the Chair and other members will determine if the conflict limits the ability of the DSMB member to participate in the discussion, and whether further evaluation of the conflict by the awardee institution for extramural studies, or Northwell ethics officer, is warranted. The DSMB also will review adverse event data, other safety data, enrollment data, and quality and completeness of study data at each meeting to ensure proper trial conduct. At intervals, as noted above, the DSMB will also review formal interim analyses of the primary end point.

It is expected that all DSMB members will attend every meeting and call. However, it is recognized that this may not always be possible. Quorum for voting is considered to be half the number of standing members plus one. The Board may wish to decide if particular expertise is needed within the quorum for the meeting to be valid. All standing Monitoring Board members are voting members. The Board may also wish to decide in advance whether *ad hoc* members can vote.

6. Discussion of Confidential Material

DSMB meetings and calls will be organized into open, closed, and executive sessions.

- During the **open sessions**, information will be presented to the DSMB by the study investigators and HHS staff as appropriate, with time for discussion.

- During the **closed sessions**, the DSMB, and HHS staff, if appropriate and approved by the Chair, will discuss confidential data from the study, including information on efficacy and safety by treatment arm. The DSMB will decide whether to remain masked to the treatment assignments at each meeting.
- The DSMB may elect to hold an **executive session** in which generally only the DSMB members and Executive Secretary are present in order to discuss study issues independently.

Voting on recommendations will follow Robert's Rules of Order **(Robert's Rules of Order Newly Revised (10th Edition) RONR** by Henry M. Robert III, William J. Evans (Editor), Daniel H. Honemann (Editor), Thomas J. Balch (Editor), Sarah Corbin Robert, Henry M. Robert III, General Henry M. Robert).

If the **closed or executive session** occurs on a conference call or video connection, steps will be taken to ensure that only the appropriate participants are on the call, and to invite others to re-join the call only at the conclusion of the executive session.

At the conclusion of the **closed or executive** sessions, the participants will be re-convened so that the DSMB Chair can provide a summary of the DSMB's recommendations. This provides an opportunity for study investigators, and HHS staff to ask questions to clarify the recommendations. The meeting is then adjourned.

7. Reports of DSMB Deliberations

- Formal minutes: The ES is responsible for the accuracy and transmission of the formal DSMB minutes. These minutes are prepared to summarize the key points of the discussion and debate, requests for additional information, response of the investigators to previous recommendations, and the recommendations from the current meeting. If concerns are identified, the report will outline the concerns, the board's discussion of the concerns, and the basis for any recommendations that the DSMB has made in response to the concerns.
- The DSMB Chair may sign the minutes or indicate approval electronically via email. If there are no concerns or major issues raised, signed minutes will be sent to the HHS Program Office or Vice President for Research, and the PI within 5 days of each meeting or call. If concerns or major issues are raised during the meeting, signed minutes will be sent to the HHS Program Office Vice President for Research, and the PI within 2 days of the meeting or call. The PI will forward the minutes to the IRB as soon as possible. Subsequently, minutes are included in the materials for the subsequent DSMB meeting to be approved by voice vote at that meeting. Once they have been voted and approved by the Board, they are considered final.

8. Reports to the DSMB

For each meeting, the DCC, with input from HHS staff if needed, will prepare summary reports and tables to facilitate the oversight role of the DSMB. The DSMB should discuss at the first or subsequent meetings what data they wish to review and how it should be presented.

9. Statistical Monitoring Guidelines

At the first meeting, review of the protocol will include review of the statistical analysis plan. The DSMB should discuss the adequacy of that plan. The final plan, whether part of a research protocol or separate document, will be maintained as Appendix C to this charter. The DSMB should discuss the statistical

monitoring procedures they propose to follow to guide their recommendations about termination or continuation of the trial. These procedures could include guidelines for early termination for benefit, termination for futility, and termination for safety reason.