Questions for the Honorable Alex M. Azar II Secretary Department of Health and Human Services Questions from Rep. Foster (IL-11)

October 2, 2020 Hearing with Secretary of Health and Human Services Alex M. Azar II

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1. On a Thursday, October 1, 2020, call between Congressman Foster and Secretary Azar, the Secretary conveyed that Operation Warp Speed (OWS) had reserved adequate production capacity of COVID mAb's to meet expected demand, and offered to provide more information.
    a. What is the anticipated or contracted production capacity, on a month-by- month basis over the next year, for different types of mAb's?

HHS Response: For AstraZeneca, Operation Warp Speed (OWS) has reserved 100,000 doses to be delivered in January 2021. Separately, the Department of Defense (DoD) has reserved 100,000 doses to be delivered in March 2021. For Regeneron, OWS has purchased 300,000 doses to be delivered by January 2021. For Eli Lilly, OWS has purchased 300,000 doses to be delivered by December, with the option to purchase 650,000 additional doses through the end of June 2021. This information is current as of December 9, 2020.

    b. How does this translate into number of patients who can be treated, under optimistic and pessimistic assumptions about the required doses, for both therapeutic and prophylactic use?

HHS Response: For AstraZeneca, 200,000 prophylaxis doses have been purchased by OWS and DoD. The treatment dose for AstraZeneca has not been determined. This purchase could treat between 20,000 and 200,000 patients with coronavirus disease (COVID-19). Regeneron is investigating two doses for prophylaxis; the purchased product could be used to prevent SARS-CoV-2 in 650,000 to 1.3M people. For treatment, the purchased product could be used to treat 100,000 to 300,000 patients with COVID-19. Eli Lilly submitted an emergency use authorization (EUA) package for treatment using a 700mg dose, which if authorized, would translate to a minimum of 300,000 patients who could be treated and the potential to treat up to 950,000 patients. Clinical trials and discussions with the Food and Drug Administration (FDA) will determine the final doses for these products.

    c. What is the anticipated demand for therapeutic and prophylactic use, on a month-by-month basis, assuming that current pandemic conditions persist and that positive clinical trial results lead to an EUA issued in November?

HHS Response: It is difficult to predict the demand for therapeutic and prophylactic use without knowing how the FDA will authorize these products for use and in what specific

populations.

d. If a shortfall is anticipated, what plans are in place for allocating mAb therapeutic and prophylactic treatments?

HHS Response: Under conditions of scarcity, therapeutics (whether mAb or others and whether therapeutic or prophylactic) will be allocated based upon nationwide confirmed case data. Specifically, HHS's Office of the Assistant Secretary for Preparedness and Response (ASPR) will look at confirmed hospitalizations and confirmed total cases by state in HHS Protect. Confirmed hospitalizations and confirmed total cases will be combined into a single, weighted case count. States and territories will be allocated their portion of the available weekly supply in proportion to their share of this case count.

2. On the October 1 call, Secretary Azar agreed with Congressman Foster that more effort should be put into repurposing existing drugs, and that there was a particular role for the government in supporting clinical trials for drugs which are off-patent and thus do not benefit from financial support from the patent holder. The recently announced promising result from an inexpensive, privately funded, placebo-controlled outpatient trial of fluvoxamine was discussed. Does the HHS have plans to expand efforts like these, either by directly funding similar trials or by supporting nonprofit funds that do?

HHS Response: This Administration has left no stone unturned when it comes to identifying treatments for COVID-19. The National Institutes of Health (NIH) funded a study that screened a chemical "library" that contained nearly 12,000 existing drug compounds for their potential activity against COVID-19. Twenty-one of these existing drugs showed potential for repurposing to thwart COVID-19 —13 of these drugs at doses that likely could be safely given to people. Remdesivir was one of the 21 existing drugs and is now approved for treatment of adult and pediatric patients 12 years of age and older and weighing at least 40 kilograms (approximately 88 pounds) for the treatment of COVID-19 requiring hospitalization.

HHS is now testing the other drugs in dose-response studies to see if they work well in combination with Remdesivir to block SARS-CoV-2.

NIH is also in the process of soliciting applications (NOT-TR-20-012 and RFA-TR-20-003) from research institutions to conduct clinical testing on the repurposing of existing drugs to treat COVID-19. Applications that have been received thus far are going through an accelerated review process.

3. Does (or will) HHS provide the White House access to non-public information from the results from ongoing clinical trials for treatments such as the Regeneron mAb cocktail give to POTUS, or from other ongoing COVID clinical trials?

HHS Response: OWS receives data on therapies and vaccines under development only after the relevant Data Safety Monitoring Board (DSMB) conducts analysis per established protocols, and the sponsor or company releases the data to OWS. A DSMB is a group of individuals with pertinent expertise that reviews, data on a regular basis from one or more ongoing clinical trials.

Interim monitoring of accumulating study data is essential to ensure the safety of trial participants. Individuals closely involved with the design and conduct of a trial may not be able to be fully objective in reviewing the interim data for emerging concerns. The involvement of the DSMB, a group of expert advisors who are external to the trial organizers, sponsors, and investigators is critical to ensure that such problems are addressed in an unbiased way. Interim study data are generally kept confidential and not available to those conducting the trial to minimize potential bias.

In some cases, such as the case of antibody treatments under development by Eli Lilly and Company and Regeneron Pharmaceuticals, the companies proactively and publicly shared their data before it was shared with OWS. HHS components follow applicable law regarding disclosure of non-public information.

4. Does (or will) HHS provide the White House with non-public access to preliminary results from partially completed vaccine trials, or will the preliminary results remain restricted to the Data Safety Monitoring Board as per normal practice?

HHS Response: Please see the response above.

5. There are many vaccines in development, and there is a very good likelihood that several vaccines will cross the finish-line at roughly the same time. Since each vaccine candidate will have its pro's and con's, how do you plan to manage and provide recommendations to the public about which vaccine to take? In the case that multiple EUA's are granted while vaccine trials are ongoing, will all underlying preliminary data be released so that the public can make an informed choice about which vaccine to take?

HHS Response: Our goal is to safely, effectively, and efficiently implement a COVID-19 vaccination program immediately after FDA authorizes or licenses and the Advisory Committee on Immunization Practices (ACIP) recommends a vaccine, and the Centers for Disease Control and Prevention (CDC) Director adopts that recommendation.

6. Operation Warp Speed has a time frame limitation that is approaching. How does BARDA, FDA, NIH, DOD, and others plan to continue cross agency collaboration post OWS?

HHS Response: The MOU between HHS and DoD that established OWS is effective through January 31, 2021, and may be extended as necessary. The Federal partners that are involved in OWS collaborate and communicate regularly. If the MOU is not extended because OWS has met its goal, then these federal partners will continue to collaborate to address any residual concerns or issues.

7. On September 10, 2020, HHS posted a very quick turn-around Request for Information soliciting interest from labs that could scale up with additional qPCR and extraction instrumentation. Responses for this RFI were due on September 21, 2020. Please

provide an update on this, specifically what the strategy is to continue to build lab capacity?

HHS Response: HHS received over 260 responses to the request for information (RFI). We are in the process of evaluating the responses and determining requirements/recommendations from this RFI.

Questions for the Honorable Alex M. Azar II Secretary Department of Health and Human Services Questions from Rep. Raskin (MD-08)

October 2, 2020 Hearing with Secretary of Health and Human Services Alex M. Azar II

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1. Scaling-up COVID-19 testing capabilities at labs across the country continues to be an important issue, particularly as we head into flu season. On September 10, 2020 HHS posted a Request for Information (RFI) soliciting interest from labs that could scale-up testing with additional equipment from Thermo Fisher Scientific—a company with multiple sites in my district. Responses for this RFI were due on September 21, 2020. The company says it has not been able to get any additional information from HHS that would help it to adequately prepare for any significant increase in demand. Can you please tell us how many labs were interested in participating, based on the RFI responses? How many does HHS plan to support, and at what levels? What is the ultimate strategy to help scale-up testing for the fall?

HHS Response: HHS received over 260 responses to the request for information (RFI). We are in the process of evaluating the responses and determining requirements/recommendations from this RFI. We are routinely connecting laboratories and states with companies that have informed us that they have available inventory and equipment.

2. Last month 243 Members of Congress sent a letter to Secretary Azar outlining our opposition to recent actions taken by several pharmaceutical companies that seek to no longer provide 340B discounts to safety net providers for drugs dispensed through contract pharmacies. We were pleased to see the HHS General Counsel send a letter that shared our concerns and outlined sharp criticisms over the actions of Eli Lilly, but the letter stopped short of telling these drug companies to stop their new policies, citing an ongoing investigation by your department. Please provide us with an update on the status of the department's review and explain what actions you will be taking to stop manufacturers from denying 340B pricing discounts, in violation of the law, moving forward.

HHS Response: The Health Resources and Services Administration (HRSA) continues to review certain drug makers' recent actions limiting access to 340B drugs. This includes Eli Lilly's plan to no longer provide 340B discounts on several of its drug products to covered entities through contract pharmacy arrangements. Several other manufacturers have similar plans, while others are limiting sales by imposing specific data requirements or selling drugs only after a covered entity has demonstrated 340B compliance.

Some covered entities have reached out to HRSA expressing concern that they are unable to receive the 340B ceiling price on certain drug products due to these recent actions. HRSA is working closely with each impacted covered entity and is actively investigating the matter in order to make a final determination as to any potential action.

As background, the 340B statute does not specify the mode by which 340B drugs may be dispensed. HRSA believes contract pharmacies serve a vital function in covered entities' ability to serve underserved and vulnerable populations, particularly as many covered entities do not operate in-house pharmacies. Without comprehensive regulatory authority, however, HRSA has only limited ability to issue regulations to ensure clarity in program requirements across all the interdependent aspects of the 340B Program. HRSA has requested regulatory authority in the President's Budget Proposal each year since fiscal year (FY) 2017 and has again requested this in the FY 2021 President's Budget. Binding and enforceable regulations for all aspects of the 340B Program would provide HRSA the ability to more clearly define and enforce policy and would significantly strengthen HRSA's oversight of the 340B Program.

HRSA believes that manufacturers that refuse to honor contract pharmacy orders could limit access to 340B-discounted drugs for many underserved and vulnerable populations who may be located in geographically isolated areas and rely on contract pharmacies as a critical point of access for obtaining their prescriptions. To this end, HRSA continues to strongly encourage all manufacturers to sell 340B priced drugs to covered entities directly and through contract pharmacy arrangements.

Questions for the Honorable Alex M. Azar II Secretary Department of Health and Human Services Questions from Rep. Kim (NJ-03)

October 2, 2020 Hearing with Secretary of Health and Human Services Alex M. Azar II

Vaccine Distribution

The vaccine distribution strategy, *From the Factory to the Frontlines*, outlines a three-phased distribution structure. In the first phase, 100 million doses will be available, followed by a larger number of doses in phase two, approximately 660 million cumulative doses, and finally a surplus of doses in phase 3 as vaccination transitions to Routine Immunization. Although the strategy recognizes that the timeline of vaccine distribution throughout these phases is contingent upon FDA regulatory decision-making, HHS has contracted McKesson to deliver 100 million doses in the first phase, followed by an increased number of doses thereafter.

1. What is the anticipated timeline of the first phase of deliveries?

HHS Response: Operation Warp Speed (OWS) has been laying the groundwork for months to distribute and administer a safe and effective COVID-19 vaccine as soon as it is granted an Emergency Use Authorization (EUA) or a Biologic License Application (BLA) approval. The COVID-19 vaccine(s) and ancillary supplies (needles, alcohol pads) will be procured and distributed by the Federal Government at no cost to individuals receiving the vaccine. During phase 1, the anticipated delivery timeline of the vaccines is within 24 hours of BLA approval or EUA by the Food and Drug Administration (FDA). The Centers for Disease Control and Prevention (CDC) will use its centralized distribution contract to fulfill orders for most vaccine products and associated ancillary supplies. Some of the vaccine candidates, specifically those with ultra-cold temperature requirements, will be shipped directly from the manufacturer to the vaccination provider site. Thus, it is essential that jurisdictions ensure accurate and complete shipping information for fast and effective distribution efforts. Americans can trust that our country's best public health and logistics experts are working together to get COVID-19 vaccines to them safe and effective vaccines as soon as possible.

2. Once a larger number of doses becomes available and the program enters Phase 2, approximately how long do you anticipate that that phase will last?

HHS Response: All of the companies who have partnered with OWS are actively engaged in large scale manufacturing demonstrations. The length of time it will take to produce enough doses for every American who wants one, and to distribute and administer such doses, depends on when, which, and how many vaccine candidates are granted EUA or receive BLA approval from the FDA. Five of the six OWS vaccine candidates require two doses for vaccination, with

21-28 days in between the first and second dose. The Janssen vaccine is the only potential single-dose candidate. OWS anticipates vaccines will generally be available to the general public at the end of Quarter 1 or beginning of Quarter 2 of 2021.

Vaccine Approval Process

In the hearing on October 2, you stated "The vaccine approval process, as I said in my opening, will be determined by career officials at FDA, Dr. Peter Marks, who is the center director for The Center for Biologics…[He] is going to make the decision, whether a vaccine is safe and effective."

1. What exactly is the EUA approval process? Who are the individuals, in addition to Dr. Marks, responsible for making the final decision for approval?

HHS Response: For an overview of FDA's EUA processes, see FDA's guidance *Emergency Use Authorization of Medical Products and Related Authorities* (EUA guidance) at: https://www.fda.gov/media/97321/download. Additional information specific to EUAs for COVID-19 vaccines can be found in FDA's October guidance, *Emergency Use Authorizations for Vaccines to Prevent COVID-19*, which is available at: https://www.fda.gov/media/142749/download. The recommendations in this guidance describe key information and data that would support issuance of an EUA, including chemistry, manufacturing and controls information, nonclinical and clinical data, and regulatory and administrative information. In addition, the guidance provides recommendations regarding key information and data that should be submitted to a relevant investigational new drug application or cross-referenced master file prior to submission of an EUA request in order to facilitate FDA's complete and timely review of such a submission, including convening the Vaccines and Related Biological Products Advisory Committee.

Generally, FDA's review and recommendation processes for EUA requests, including those for vaccines, mirror those for product approvals within the applicable medical product center. As is the case for these types of applications, FDA's Center for Biologics Evaluation and Research (CBER) assembles cross-disciplinary review teams of experts as appropriate to the specific submission. The teams that CBER assembles to review EUAs are composed of the same highly qualified scientists and physicians who specialize in vaccines and routinely advise sponsors on development programs, manufacturing considerations, and assessment of safety and effectiveness for these products.

The issuance of an EUA will follow the Agency's evaluation of the totality of the available evidence regarding the safety and the efficacy of the product and the Agency's finding that the product met the criteria for issuance of an EUA. Under the Federal Food, Drug, and Cosmetic Act (FD&C Act), FDA may issue an EUA during a declared public health emergency if certain statutory criteria are met. FDA may issue an EUA for a product if it concludes that the product may be effective in diagnosing, treating, or preventing a serious or life-threatening disease or condition; that the known and potential benefits of the product, when used to diagnose, prevent, or treat such disease or condition, outweigh the known and potential risks of the product; and that there are no adequate, approved, and available alternatives to the product for preventing or

treating the disease or condition. If after reviewing the EUA request, CBER staff, including Dr. Marks, conclude that the statutory standard has been met, they will provide a recommendation to the Agency's Chief Scientist, who is delegated the legal authority to issue the EUA.

2. What safety and efficacy standards will need to be met before a vaccine is approved?

HHS Response: FDA will only approve a BLA or issue an EUA for a COVID-19 vaccine after FDA has determined that the vaccine meets the relevant statutory standard.

When making decisions about licensure or authorization of COVID-19 vaccines, FDA will apply the relevant statutory and regulatory requirements that help ensure the safety and effectiveness of vaccines.

As with all vaccines, FDA will require that COVID-19 vaccine developers provide FDA sufficient data for the Agency to evaluate the safety and effectiveness of vaccines for their intended population. FDA is working with vaccine developers to ensure that ongoing and planned clinical trials will provide sufficient data to support deployment of safe and effective vaccines in the United States.

On June 30, 2020, FDA took additional action to facilitate the development of safe and effective vaccines to prevent COVID-19 by releasing a guidance document with recommendations for those developing COVID-19 vaccines for the ultimate purpose of licensure. The guidance, titled *Development and Licensure of Vaccines to Prevent COVID-19* (June 2020 guidance), reflects the advice and assistance that FDA has been providing over the past several months to companies, researchers, and others, and describes the Agency's current recommendations regarding the data needed to facilitate the manufacturing, nonclinical and clinical development, and approval of COVID-19 vaccines. The guidance can be accessed here: https://www.fda.gov/media/139638/download

Due to the current public health emergency, the June 2020 guidance addresses considerations regarding the issuance of an EUA for an unapproved (i.e. unlicensed) vaccine and makes clear that an assessment regarding any potential EUA for a COVID-19 vaccine would be made on a case-by-case basis considering the target population, the characteristics of the product, and the totality of the relevant, available scientific evidence, including preclinical and human clinical study data on the safety and effectiveness of the product. An EUA can be issued to facilitate the availability of an unapproved product only after several statutory requirements are met. Among these requirements is a determination by FDA that the known and potential benefits of an unapproved product, when used to diagnose, prevent, or treat a serious or life-threatening disease or condition, outweigh the known and potential risks of the unapproved product.

To expand upon the recommendations provided in the June guidance regarding EUAs for COVID-19 vaccines, FDA's October 2020 guidance document, *Emergency Use Authorizations for Vaccines to Prevent COVID-19* (available at: https://www.fda.gov/media/142749/download), provides FDA's recommendations regarding the scientific data and information that would be necessary to support the issuance of an EUA for a COVID-19 vaccine. This guidance makes

clear that, for a COVID-19 vaccine for which there is adequate manufacturing information to ensure its quality and consistency, issuance of an EUA would require a determination by FDA that the vaccine's benefits outweigh its risks based on data from at least one well-designed Phase 3 clinical trial that demonstrates the vaccine's safety and efficacy in a clear and compelling manner.

Both guidances also note that after approval of a BLA or issuance of an EUA by FDA, the safety of COVID-19 vaccines will continue to be closely monitored using various existing surveillance systems. In certain cases, FDA may require the manufacturer to conduct post-marketing studies to further assess known or potential serious risks.

As described in the June and October guidance documents, FDA would expect that a COVID-19 vaccine would be at least 50 percent more effective than placebo in preventing COVID-19 or SARS-CoV-2 infection among the clinical trial participants. COVID-19 is a new disease that is causing a pandemic, infecting millions of people in the United States and globally and has caused the death of over 225,000 people in the United States. Furthermore, current data indicate that infection and death rates are continuing to rise. Given the gravity of the public health situation and the fact that there are no FDA-approved treatments yet, 50 percent efficacy is a reasonable expectation. Although the scientific community is working towards more effective vaccines, a vaccine with at least 50 percent efficacy would have a significant impact on the disease, both at the individual and societal level. Any vaccine made available under EUA will be an interim step. Additional data, including data with relevance to duration of efficacy, will continue to be collected. The global scientific community is working to combat this disease, including understanding how long protection will last after vaccination and how long after natural infection.