FRANK PALLONE, JR., NEW JERSEY
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CATHY McMORRIS RODGERS, WASHINGTON
RANKING MEMBER

ONE HUNDRED SEVENTEENTH CONGRESS

Congress of the United States

House of Representatives

COMMITTEE ON ENERGY AND COMMERCE

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March 16, 2021

Ruud Dobber, Ph.D.
Executive Vice President and President, BioPharmaceuticals Business Unit
AstraZeneca
1800 Concord Pike
Wilmington, DE 19803

Dear Dr. Dobber:

Thank you for appearing before the Subcommittee on Oversight and Investigations on Tuesday, February 23, 2021, at the hearing entitled "Pathway to Protection: Expanding Availability of COVID-19 Vaccines." I appreciate the time and effort you gave as a witness before the Committee on Energy and Commerce.

Pursuant to Rule 3 of the Committee on Energy and Commerce, members are permitted to submit additional questions to the witnesses for their responses, which will be included in the hearing record. Attached are questions directed to you from certain members of the Committee. In preparing your answers to these questions, please address your response to the member who has submitted the questions in the space provided.

To facilitate the printing of the hearing record, please submit your responses to these questions no later than the close of business on Monday, March 30, 2021. As previously noted, this transmittal letter and your responses, as well as the responses from the other witnesses appearing at the hearing, will all be included in the hearing record. Your written responses should be transmitted by e-mail in the Word document provided to Austin Flack, Policy Analyst, at austin.flack@mail.house.gov. To help in maintaining the proper format for hearing records, please use the document provided to complete your responses.

Thank you for your prompt attention to this request. If you need additional information or have other questions, please contact Austin Flack with the Committee staff at (202) 225-2927.

Sincerely,

Frank Pallone, Jr.
Chairman

Attachment

cc: The Honorable Cathy McMorris Rodgers Ranking Member
Committee on Energy and Commerce

The Honorable Diana DeGette Chair
Subcommittee on Oversight and Investigations

The Honorable Morgan Griffith Ranking Member
Subcommittee on Oversight and Investigations

Attachment—Additional Questions for the Record

Subcommittee on Oversight and Investigations Hearing on
"Pathway to Protection: Expanding Availability of COVID-19 Vaccines"
February 23, 2021

Ruud Dobber, Ph.D., Executive Vice President and President,
BioPharmaceuticals Business Unit, Astrazeneca

The Honorable Anne McLane Kuster (D-NH)

1. Can you speak to your reliance, if any, on foreign sources for vaccine manufacturing supplies?
   We source some of the vaccine components globally but we manufacture all vaccine supply for the US government in the US.

2. Considering the federal government's actions to date, what gaps or restrictions still exist across the domestic manufacturing supply chain and the export/import landscape that influence your decision to use foreign over domestic sources?
   Domestic availability of some supplies make it necessary for us to source certain components globally.

3. What changes should be made for you to prioritize using domestic sources?
   For our vaccine, we have had to source some components globally to ensure adequate access and speed in manufacturing.

4. Can you speak to what constraints, including with respect to specific products within the supply chain (e.g., APIs, bioreactors, glass vials, stoppers, fills/finishers, etc.), are currently preventing the production of more vaccines?
   We are not currently experiencing significant material or equipment constraints that affect our ability to manufacture.

5. Can you speak to how making the investments called for in the American Rescue Plan, like the investment in new factories, may optimize vaccine fill lines to ensure maximum efficiency to meet future demands?
   Access to more large scale manufacturing capacity and capabilities on the scale needed for a pandemic would be helpful. It can be challenging when multiple companies are trying to access the same space/service and supplies.

The Honorable Lori Trahan (D-MA)

1. Since October 2020 you have refused to extend mandatory 340B program discounts to the safety-net providers that we are relying on to distribute and administer COVID-19 vaccines – including publicly funded community health centers. Community health centers rely on 340B discounts to stretch scarce federal resources to medically underfunded communities, which is exactly what Congress intended when it established the program. Will you commit to resuming 340B drug sales to qualified safety-net providers and their contracted pharmacies and commit to refunding overcharges to those providers on qualifying outpatient drugs purchased since October 1, 2020 as a condition of receiving additional public funding?
AstraZeneca is strongly committed to the 340B Program and to ensuring that any patient prescribed an AstraZeneca product has access to that medicine. AstraZeneca continues to offer its products to all covered entities at the 340B price or better, and under its policy also makes 340B drugs available through a designated contract pharmacy for any covered entity that lacks an in-house pharmacy. In 2020, we changed our approach to help mitigate the significant compliance issues that have been well documented in audits performed by GAO regarding contract pharmacy arrangements. AstraZeneca's policy is not directed at cutting the costs of complying with the program. Rather, it was adopted in response to serious, documented abuses of the program by contract pharmacies.[1] AstraZeneca's approach to contract pharmacy arrangements fully complies with all operative requirements and continues to support the mission of the program to provide a healthcare safety net for the most vulnerable patients in our country. It is important to note that our policy change should not impact a patient's ability to access our medications. Indeed, AstraZeneca remains committed to ensuring that all patients have access to our medications, regardless of their ability to pay. Through our various patient assistance programs, we offer free medicines and other assistance to eligible patients in need.

2. T cells and antibodies are two arms of the immune system that provide insights into disease activity and an individual's personal immunity. Serology is more commonly used to measure immune responses to infections. Since antibody responses wane within 2 – 3 months of COVID-19 infection, serology alone is not enough to assess personal immunity or "herd immunity" against SARS-CoV-2. We have seen that other countries have approached vaccine approval differently than the U.S. For example, the United Kingdom established a "vaccine task force" to objectively compare the T-Cell and antibody immune response of each vaccine approved for usage in the country. Based on published reports, the UK government felt this was important to enable objective comparison across vaccine modalities. Did any of your company study T-Cell responses during the development of your vaccines?
Two papers have been published in the same issue of Nature Medicine (December 17, 2020) from additional analysis conducted from the Phase I/II COV001 trial. T-cell responses were induced, peaking by day 14 after the first dose and were maintained two months after injection, regardless of dose level and number of doses.

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[1] *See, e.g.*, HRSA, *Program Integrity: FY19 Audit Results*, https://www.hrsa.gov/opa/program-integrity/audit-results/fy-19-results; Berkeley Research Group, *For-Profit Pharmacy Participation in the 340B Program* (Oct. 2020), https://bit.ly/3owtUwa; Gov. Accountability Office, *Drug Discount Program: Federal Oversight of Compliance at 340B Contract Pharmacies Needs Improvement*, GAO-18-480 (June 2018), https://www.gao.gov/assets/700/692697.pdf; Stuart Wright, Deputy Inspector General for Evaluation and Inspections, Office of the Inspector Gen., Dep't of Health and Human Servs., *Memorandum Report: Contract Pharmacy Arrangements in the 340B Program*, OEI-05-13-00431 (Feb. 4, 2014), https://oig.hhs.gov/oei/reports/oei-05-13-00431.pdf; Letter from Sen. Chuck Grassley, S. Comm. on the Judiciary, to Mary K. Wakefield, Administrator, Health Resources and Servs. Admin. (March 27, 2013), https://bit.ly/3kFquVS; Gov. Accountability Office, *Drug Pricing: Manufacturer Discounts in the 340B Program Offer Benefits, but Federal Oversight Needs Improvement*, GAO-11-836 (Sept. 23, 2011), https://www.gao.gov/assets/330/323702.pdf.

3. When thinking about expanding the availability of vaccines, one thing that is extremely important is that vaccine distribution is done in an equitable manner. Many state leaders, including those in my state of Massachusetts, tried to approach plans for vaccine distribution early on in an equitable way—they consulted with public health leaders to develop a tiered plan to equitably prioritize distribution. Due to the limited supply of vaccines and slow distribution to the state, the implementation has heavily relied upon mass vaccination sites. While mass vaccination sites may work well for some patients, others will be best served by their own physicians, in their own communities. Physicians are a trusted source of medical information, and they can proactively reach out to their patients who need the vaccines most, including the elderly, the sick, and specifically communities of color who have been disproportionately affected by this pandemic. Mass vaccination sites, while getting the vaccine out quickly, prioritize those with access to transportation to get to the site, as well as resources to navigate the process to register for a vaccine. What role can manufacturers play in helping states get vaccines distributed to physician practices— whether by allowing smaller shipment sizes tailored to physician offices (that may only need ~50-100 vaccine doses) or creative solutions to aid in vaccine storage?
   We would be willing to work with the government on this issue. Currently, we have agreed to deliver to government distribution centers and the government handles deliveries beyond that point.

   a. What assistance would you need from the government for this, in terms of ramping up production/manufacturing and packaging shipments in a manner tailored to physician offices?
      If it was determined that this was the most efficient way to distribute the vaccines, AstraZeneca would work with the government to move forward a mutually agreed upon plan.

The Honorable Morgan Griffith (R-VA)

1. What types of process improvements and innovation can lead to boosting vaccine production?
   Ensuring access to large scale manufacturing during a pandemic would be helpful. We are not currently experiencing problems but it can get difficult when multiple companies are trying to access the same space/service.

2. Given the variants that are circulating across the world and that we may need a booster or annual shot similar to the influenza vaccine, how quickly can your vaccine manufacturing platform be adapted to scale up and manufacture a new or altered vaccine formula?
   Because viral-vectored vaccines can be engineered in the laboratory, as the virus mutates, we can adapt the platform technology to keep at pace with the new variants, if needed.
   Oxford University have already started developing the next generation adenoviral vector vaccines incorporating the genetic changes to spike protein found in the new variants.
   The adenoviral vectored vaccine genetic code can be alerted to match new variants of coronavirus spike protein in a matter of days in the laboratory. It is important to remember though that additional steps will be required to ensure the quality and effectiveness of the new vaccine.
   Following the molecular changes to the spike protein, there are crucial manufacturing processes needed to ensure the vaccine can be produced in mass quantities. This is a biological process and it takes time to create the virus seed stock and host cell banks to ensure the vaccine can be made efficiently. Host cells are grown in a series of bioreactors of increasing scale and act as

mini-factories to produce the final vaccine. This step cannot be speeded as the host cells take a finite time to grow and divide, and our experience from production and scale up of the vaccine in 2020 suggests it will likely take 3-4 months.
In parallel, as vaccine stocks increase it will be important to test the effectiveness of the new vaccine against the new variants in a clinical trial. Given we will have a wealth of safety data on the vaccine platform, it is likely a smaller Phase 2/3 efficacy study could be designed to primarily assess efficacy within a few months. This approach would require discussion and approval by regulators.
We currently estimate the whole process from start to finished product would take about 6-8 months to complete.
Of course, we need to consider and assess how best to address the global need going forward. Establishing a potential pipeline of future vaccines, on the assumption that will we need them in either this ongoing pandemic or an endemic setting, as we do with flu, will be essential. Careful ongoing safety monitoring over the longer term, efficient clinical evaluation with immunology and early safety assessment will be critical.
Effective collaboration between global regulatory authorities on requirements and government investment in advanced manufacturing capabilities to enable an efficient global rollout will also be important.

3. Has your company developed partnerships with other companies to provide your company with assistance in the vaccine manufacturing process?
   Yes, we are partnered with other companies that assist in certain steps of the drug manufacturing process.

   a. Is your company looking to develop additional partnerships?
      Not at this time.

4. Is your company utilizing, or has explored utilizing, the Department of Health and Human Services' (HHS) Centers for Innovation in Advanced Development and Manufacturing (CIADM) program to expand existing manufacturing capacity? Why or why not?
   We are not currently experiencing significant material or equipment constraints that affect our ability to manufacture.

5. As time passes, the virus continues to mutate causing new variants to emerge. Can you explain the level of difficulty involved in creating a booster shot to provide protection against these new variants, specifically in an mRNA vaccine?
   AZD1222 is a viral-vectored vaccine, not an mRNA. As stated above, viral-vectored vaccines can be engineered in the laboratory; this means as the virus mutates we can adapt the platform technology to keep at pace with the new variants, if needed.

6. As you clinically evaluate the dosage for a booster shot to provide protection against new variants, do you have any projections for the necessary dose in these booster shots? How will this estimated dosage affect production capacity?
   Not at this time, but we are working on that question.

The Honorable Neal P. Dunn, M.D. (R-FL)

1. In addition to your heroic efforts in vaccine development, are your companies also engaged in research and development of therapeutics? That is to say anti-virals that could potentially have a broader spectrum of activity across the coronavirus variants?
   Yes, we are at the early stages of research with our long acting monoclonal antibody candidate and our focus currently is to prove its efficacy and tolerability as a potential prevention and treatment against COVID-19. We started Phase IIII clinical trials in December 2020 and look forward to working with regulators as we move forward.