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21 Jan 2021

Mr. Peter Fox
Office of Regulatory Affairs
Food and Drug Administration
12420 Parklawn Dr. Rm. 4146
Rockville MD 20857

Re: Development and Licensure of Vaccines to Prevent COVID-19 (Docket No. FDA-2020-D-1137)

Dear Mr. Fox:

PDA appreciates the opportunity to comment on FDA's Guidance for Industry and Staff regarding the Development and Licensure of Vaccines to Prevent COVID-19. In general, the draft guidance provides useful information. In our attached comments, PDA offers specific suggestions that may provide clarity for agency staff and regulated industry, as well as accelerate bringing the products to market.

PDA is a non-profit international professional association of more than 10,000 individual member scientists having an interest in the fields of pharmaceutical, biological, and device manufacturing and quality. Our comments have been prepared by a committee of volunteers with expertise in pharmaceutical and biopharmaceutical manufacturing on behalf of PDA's Biopharmaceutical Advisory Board and Board of Directors.

If you have any questions, please do not hesitate to contact me via email at johnson@pda.org.

Sincerely,

Richard Johnson
President and CEO

cc: Glenn Wright, PDA; Josh Eaton, PDA

U.S. Food and Drug Administration
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General Comments

General Comments	Rationale
The Guideline includes some potential negotiation points in the CMC space, including: • Re-use of platform knowledge • Acknowledgement of product- specific specs, that would be discussed ad hoc with the Agency (implying room for dialogue on evolving content) • Post-approval commitment to provide full shelf-life data • Encouragement of early and continuous dialogue with manufacturers • Deferral of process validation of formulation and filling post approval (note: sterile filtration, equipment qualification, media fills would need to be validated prior to file). • FDA using additional tools, where available, to determine the need for an on-site inspection and to support the application assessment, such as reviewing a firm's previous compliance history, and requesting records in advance of or in lieu of on-site inspections or voluntarily from facilities and sites. However, in general the CMC section seem to be quite conservative and not taking into consideration several options discussed at EMA/FDA workshop on early access in 2018 (https://www.ema.europa.eu/en/events/stakeholder-workshop-support-quality-development-early-access-approaches-such-prime-breakthrough) and subsequently discussed within EFPIA/MAPPs team for COVID-19. • We would like to explore the potential to develop alternative CMC approaches and therefore appropriate data packages for such products, that will enable companies to be agile in bringing acceptable quality products, which are safe and efficacious to the global population as soon as possible. An example of this would be in applying some of the accelerated approaches agreed at the workshop in 2018 with the FDA and EMA and issued in the EMA report, with input from the FDA.	Given the unique and complex nature of vaccines, it is important to integrate product understanding, process control strategies and analytical control strategies, and ensure a structured approach for evolving knowledge in pandemic situation. For instance, the possibility to utilize risk-based approaches (based on ICH Q9) could be considered for defining the appropriate levels of validation for equipment, process and analytical methods at time of submission, applying thinking in terms of benefit to patient. In the context of COVID emergency, risks associated with process validation could be mitigated through provision of protocols, the reliable product control strategy, concurrent validation and/or continuous process verification, particularly where there is extensive prior and platform knowledge. It could be acceptable to waive requirements for actual process validation data to be included in the application or variation where justified by risk assessment and where a suitable process validation protocol is supplied. More detail can be found in the EFPIA White Paper on CMC development, manufacture and supply of pandemic COVID-19 therapies and vaccines.

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General Comments	Rationale
• Further, the use of prior knowledge from early data should also be considered, to support agility of product development and time to submission and prevent aspects of commercialization becoming an unnecessary burden on timing for launch and access for patients. • Finally, we are keen to explore the application of scientific benefit / risk approaches during assessment of COVID vaccines to ensure that patients can be treated as soon as an appropriate. • When reviewing sponsor data, we further encourage FDA to prioritize rapid and robust scientific advice for COVID-19 candidates through virtual meetings and teleconferences with sponsors. Timely, interactive scientific communication via email and telephone with senior-level review leadership should be prioritized over formal meetings with longer scheduling times. • PDA recommends that FDA apply the concept of real-time review applied to Module 5 (clinical) to Module 3 (CMC) of the submission. This will ensure that CMC/quality activities do not become a bottleneck and therefore delay patient access to critically needed COVID-19 vaccines.	

Specific Comments to the Text

Page No.	Current Text	Proposed Change	Rationale
7	Data to support the consistency of the manufacturing process should be provided, including process validation protocols and study reports, data from engineering lots, and drug substance process performance qualification.	Issue interim guidance describing alternate process validation approaches that can be used. For example: • Defer submission of certain process validation information to post-approval o Provide guidance on: How much data can be deferred? What types of data can be deferred?	Current requirement of process validation information to be submitted in BLA is a bottle neck issue for accelerate process and product development. Alternate process validation approaches should be considered. FDA could provide their current thinking on alternative approaches for an expedited process validation lifecycle management.

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		• The guidance should describe the extent to which Prior/Platform Knowledge can compensate for a deferral of certain process validation data • Concurrent validation o Provide guidance on: How can protocols for concurrent validation be most efficiently presented in regulatory submissions? The interim guidance should also discuss the mechanism(s) (e.g., regulatory commitment, PACMP, handled via the PQS and made available during inspection) sponsors can use to provide validation data to FDA post-approval	
7	For vaccine licensure, the stability and expiry date of the vaccine in its final container, when maintained at the recommended storage temperature, should be demonstrated using final containers from at least three final lots made from different vaccine bulks	"For vaccine licensure, the stability and expiry date of the vaccine in its final container, when maintained at the recommended storage temperature, should be demonstrated using final containers from at least three final lots made from different vaccine bulks **or, if appropriate, using development data, modeling and extrapolation.**"	Additional language is recommended to allow for a risk-based, alternative approach to providing sufficient scientific justification of product stability labeling information so as not to be a bottleneck to timely distribution.
8 - 9	Pre-license inspections of manufacturing sites are considered part of the review of a BLA and are generally conducted following	Please spell out currently available tools in this paragraph, e.g., inspection waiver, information request under FDASIA, virtual	This would aid in the understanding of how the agency is making its decisions.

Page No.	Current Text	Proposed Change	Rationale
	the acceptance of a BLA filing (21 CFR 601.20). During the COVID-19 public health emergency, FDA is utilizing all available tools and sources of information to support regulatory decisions on applications that include sites impacted by FDA's ability to inspect due to COVID-19. During this interim period, we are using additional tools, where available, to determine the need for an on-site inspection and to support the application assessment, such as reviewing a firm's previous compliance history, and requesting records in advance of or in lieu of on-site inspections or voluntarily from facilities and sites.	inspections as recommended by the regulated industry.	