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May 23, 2016

Division of Docket Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Reference: FDA Draft Guidance for Industry Implementation of the
“Deemed to be a License” Provision of the Biologics Price Competition
and Innovation Act of 2009 Docket ID: FDA-2015-D-4750

Dear Sir/Madam:

PDA appreciates the FDA developing such a short and straightforward guidance document on this subject and has the following comments and recommendations to enhance the clarity and content.

PDA recommends that FDA explicitly state in this or future guidance its intent to consider the transition as an administrative process (as opposed to one that requires data or a substantive review). An FDA mandate for sponsors to address differences in technical requirements as part of the transition is an unnecessary utilization of both FDA and authorization holder resources. Biological products approved under section 505 of the FD&C Act are demonstrated to be safe and effective and have a long history of quality.

FDA’s current interpretation creates, as a practical matter, the potential for at least a 6 month black out period for the submission of post-approval supplements for approved 505 biological products. This black out period may, for example, delay the implementation of critical manufacturing changes needed to meet the increasing demand for life savings medicines. This is especially problematic for Changes Being Effected supplements that are effective but not yet approved as of the 23 March 2020 transition date. PDA recommends that FDA develop a mechanism whereby a pending NDA supplement would not have to be withdrawn and resubmitted as a BLA supplement.

PDA recommends that FDA provide a more specific definition of what products are covered by this change in status other than those greater than 40 amino acids and made in or naturally derived from cells. No information is included on whether recombinant products and natural products are treated differently.





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In the attached response, PDA has indicated which of its recommended changes to the draft we believe will have the most critical impact based on the following criteria:

- Comment has a major impact on patient safety or product quality
- Not adopting the comment will have a large/major impact on the industry or process (i.e. greater than 1 year to become compliant; financially greater than 1M \$/Euros to implement)
- Not adopting the comment will lead to difficult or complex to implement changes that may impact multiple quality and/or operating systems.

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 were prepared by a committee of experts with experience in pharmaceutical and biological manufacturing including members representing the Regulatory Affairs and Quality Advisory Board, and Board of Directors.

If there are any questions, please do not hesitate to contact me.

Sincerely,

A handwritten signature in black ink that reads "Richard M. Johnson". The signature is written in a cursive style with a large, prominent "R" and "J".

Richard Johnson

Cc: Denyse Baker, PDA; Richard Levy, PDA.

**Food and Drug Administration Draft Guidance
Implementation of the “Deemed to be a License” Provision
of the Biologics Price Competition and Innovation Act of 2009
February 20, 2015**

General Comments	Rationale	Critical Comment Y/N
<p>In lines 30-32 the FDA is not very specific on the types of products other than the examples which are all greater than 40 amino acids and made in or naturally derived from cells. There should be a more specific definition of what these products are such as a product produced from a cell or naturally derived from a cell. In addition no information is included on whether recombinant products and natural products are treated differently.</p>	<p>The current definition is vague and should be revised to account for factors other than an arbitrary number of amino acids.</p>	<p>Yes</p>
<p>The draft guidance does not address how proteins approved under 505(j) prior to 23 March 2020 will transition to a BLA.</p>	<p>PDA recommends that FDA clearly state these products will transition to 351(k) status and that, on 23 March 2020, they will not be considered interchangeable unless they comply with the requirements for interchangeability as defined in section 7002(a) of the BPCI Act.</p>	<p>Yes</p>
<p>The BPCI Act is silent regarding any new or different technical requirements for the transition products associated with the 23 March 2020 transition. Accordingly, the draft guidance is also silent regarding this matter. Therefore, footnote 7 as referenced in line 151 is interpreted to apply only to approaches FDA may develop for determining whether an approved application for a biological product under section 505 of the FD&C Act will be deemed an approved license for the biological product under either section 351(a) or 351(k) of the PHS Act.</p>	<p>PDA recommends that FDA explicitly state in this or future guidance its intent to consider the transition as an administrative process (as opposed to one that requires data or a substantive review). Footnote 12 as referenced in line 239 acknowledges FDA’s continued intent to minimize differences in the review and approval of products required to have approved BLAs under section 351 of the PHS Act and products required to have approved NDAs under section 505 of the FD&C Act. An FDA mandate for sponsors to address differences in technical requirements as part of the transition is an unnecessary utilization of both FDA and sponsor resources. Biological products approved under section 505 of the FD&C Act are demonstrated to be safe and effective and have a long history of quality.</p>	<p>Yes</p>

**Food and Drug Administration Draft Guidance
Implementation of the “Deemed to be a License” Provision
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February 20, 2015**

General Comments	Rationale	Critical Comment Y/N
<p>Section III of the draft guidance is focused on the impact of the 23 March 2020 transition on the submission of new 505 applications. The document does not provide guidance on FDA’s interpretation on the “deemed to be a license” provision as it relates to planned and pending NDA supplements.</p>	<p>FDA’s current interpretation of the provision creates, as a practical matter, the potential for at least a 6 month black out period for the submission of post-approval supplements for approved 505 biological products. This black out period may, for example, delay the implementation of critical manufacturing changes needed to meet the increasing demand for life savings medicines. This is especially problematic for Changes Being Effected supplements that are effective but not yet approved as of the 23 March 2020 transition date. PDA recommends that FDA develop a mechanism whereby a pending NDA supplement would not have to be withdrawn and resubmitted as a BLA supplement. FDA’s flexibility in the interpretation of the “deemed to be a license” provision is noted in footnote 12 as referenced in line 239.</p>	<p>Yes</p>
<p>As written this guidance would seem to imply that no additional submissions under the 505(b) mechanism should be made prior to March 2020 to completely avoid the risk of being under review on that date. PDA requests that FDA clarify the mechanism or outcome if a submission has been made and is still under review as of the transition date.</p>	<p>PDA recommends FDA explain more strongly that it is not recommended to submit under 505(b) if you can’t achieve approval before the March 2020 deadline. Alternatively, PDA recommends FDA should deem a pending NDA as of the deadline to be a pending BLA. It is not clear under the 351 route what the exclusivity would be.</p>	

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Specific Comments to the Text

Line No.	Current Text	Proposed Change	Rationale	Critical Comment? Y/N
151 and Foot note 7; from line 164	As noted in footnote 7, FDA intends to provide additional guidance regarding its approach for determining whether an approved application for a biological product under section 505 of the FD&C Act will be deemed a license for the biological product under section 351(a) or 351(k) of the PHS Act, and for handling administrative issues associated with the transition (including BLA numbers and user fee questions).		It is important that industry have sufficient time to evaluate the impact of FDA proposals for determining whether an approved application for a biological product under section 505 of the FD&C Act will be deemed a license for the biological product under section 351(a) or 351(k) of the PHS Act. PDA requests this additional guidance be developed and issued as soon as possible. This document should include specific guidance on labeling as FDA’s current interpretation of the provision creates the potential need to submit supplements for labeling changes in advance of the 23 March 2020 transition date.	Yes
197	Any post-approval requirements or post-approval commitments, including any pediatric assessments necessary to comply with the Pediatric Research Equity Act (PREA) (Public Law 108-155), also would transfer to the BLA.	Any approved supplements , post-approval requirements or post-approval commitments, including any pediatric assessments necessary to comply ...	The draft guidance does not address the regulatory status of approved supplements following transition to the BLA.	Yes