Parenteral Drug Association

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June 30, 2016

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

Reference: FDA Draft Guidance Comparability Protocols for Human Drugs and Biologics: Chemistry, Manufacturing, and Controls Information
Docket ID: FDA-2016-D-0973

Dear Sir/Madam:

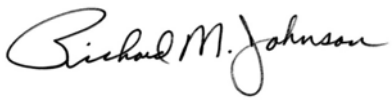
PDA applauds this new draft and feels this guidance is an improvement on what was previously available and appreciates the options provided. It clearly portrays FDAs intent to work, and partner, with applicants to achieve positive outcomes for patients. It is very helpful to have details on what information to submit. The acknowledgement and opportunity to utilize risk assessments to provide sound scientific justification to discuss post-approval changes with the agency introduces needed flexibility to the review process and is considered very helpful.

PDA encourages FDA to work towards alignment of this guidance and the ICH Q12 document. In addition PDA recommends that combination products should be included in this scope. Please also clarify if there are any special considerations for Comparability Protocols (CPs) for biosimilar products. .

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, Post Approval Change Task Force, and Board of Directors.

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

Sincerely,



Richard Johnson
President and CEO,PDA

Cc: Denyse Baker, PDA; Richard Levy,

General Comments

General Comments	**Rationale**	**Critical Comment Y/N?**
PDA applauds this new draft and feels this guidance is an improvement on what was previously available and appreciates the options provided. It clearly portrays FDAs intent to work, and partner, with applicants to achieve positive outcomes for patients. It is very helpful to have details on what information to submit. The acknowledgement and opportunity to utilize risk assessments to provide sound scientific justification to discuss post-approval changes with the agency introduces needed flexibility to the review process and considered very helpful.		
PDA recommends that combination products should be included in this scope. Please also clarify if there are any special considerations for Comparability Protocols (CPs) for biosimilar products.	With the growth of these types of products, firms will likely have questions as to how the CP concepts apply.	Yes
This guidance as written does not provide clarity on the applicability of CPs in special circumstances like orphan products or accelerated review pathways. . In some of these cases, standard batch information may not be available at time of submission and FDA has made allowances to accept additional batch information following approval. As such, the Established Conditions may not be determined at the time of licensure, making the development of CP for potential or known future changes a challenge.	PDA recommends that FDA clarify the guidance to acknowledge these review pathways in the scope of the document and to clarify if FDA feels there are any special considerations that might apply to products that do not yet have defined established conditions.	
FDA is asking for planning information (timelines, status updates before changes are implemented).	PDA notes that this type of information for potential changes is not required by 601.12 and could be burdensome on industry and to FDA reviewers. Industry sometimes files a CP proactively for anticipated changes or emergency use and not all the information is available.	
PDA notes the guidance doesn't address how proactive	PDA recommends allowances in situations in which there may be	

General Comments	Rationale	Critical Comment Y/N?
changes could be integrated with a Continuous Process Verification (CPV) protocol. Many CPV conditions are not Established Conditions.	minor failures to meet CP acceptance criteria that would accommodate maintaining the reduced reporting category described in the CP if such a failure can be justified as having no impact on the product quality or patient. One example is a failure of sub-visible particulate criteria due to a heavier than expected silicone level in a pre-filled syringe lot. It would also be useful to apply risk assessment to separate measures of consistency from product quality measures. Low risk measures for consistency perhaps would not need acceptance criteria in the CP.	
PDA recommends the term "comparability protocol" be changed to match the ICH term "post approval change management protocol." PDA also encourages FDA to work towards alignment of this guidance and the ICH Q12 document.	"Comparability "is used in other ICH documents for a slightly different meaning looking at the change itself and not including all the validation and supporting data. (Q5E focuses on process changes). CFR uses the term "protocol" and so this would allow for such an adjustment in guidance [i.e. 21CRF314.70(e) and 21CRF601.12(e)].	

Specific Comments to the Text

Line No.	Current Text	Proposed Change	Rationale	Critical Comment Y/N?
269	The CP should use a combination of both routine quality controls (eg. specifications, process controls) and non-routine tests and studies (e.g., characterization tests and studies, stability studies.)	**Depending on the nature of the proposed change and potential risks to product quality**, the CP ~~should~~ **may** use a combination of both routine quality controls (eg. **release** specifications, process control **limits**) and non-routine tests and studies (e.g., characterization tests and studies, stability studies.)	Clarify the CP will use specifications from both release tests and routine in-process control tests and not necessarily newly defined or other in-process measures or characterization tests unless otherwise warranted due to the nature of the proposed change, Characterization tests may be very helpful and informative, but should not be required for every CP.	
353	After approval of the submission containing the CP, any modification to the CP must be submitted as a new PAS.	After approval of the submission containing the CP, any modification to the CP **that is not a minor change** must be submitted as a new PAS.	Suggest adding a qualifier to the types of modification that would be permissible. Minor amendments to the CP should not automatically require a new PAS submission. Examples provided in next paragraph address moderate potential changes but not minor changes such as substituting a lot etc.	
398	Finally, we expect that the change outlined in the approved CP will be implemented within your change management system as part of your overall pharmaceutical quality system.	Finally, we expect that the change outlined in the approved CP will be implemented within your change management system **at the time the change is initiated** as part of your overall pharmaceutical quality system.	Clarification that not all CPs are intended for immediate implementation. Some CPs are developed in advance of a change or in case of an emergency loss of supplier.	