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October 8, 2013

European Commission
Health and Consumers Directorate –General, Brussels
sanco-pharmaceuticals-d6@ec.europa.eu

Ref: EU Guideline on the use of porcine trypsin used in the manufacture of human biological medicinal products

To the Health and Consumers Directorate-General:

PDA appreciates the opportunity to provide comments on this guideline submitted for public consultation. 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 review was completed by an international group of expert volunteers with experience in virology, regulatory affairs and GMPs on behalf of our Regulatory Affairs and Quality Advisory Board.

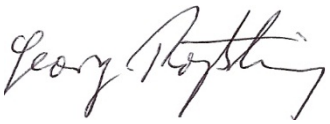
PDA recognizes this guideline provides a scientific approach to assess the virus safety of trypsin produced from porcine pancreatic tissue. It contains both, guidance for the acceptance of trypsin used as a reagent for production of medicinal products and it provides, in addition, current knowledge. PDA supports inclusion of both areas but suggests clearly separating the two within the document for enhanced clarity.

The guideline requires a high level of documentation of sourcing, testing and manufacturing including adventitious agent inactivation of trypsin that may be difficult to implement in a short time frame and might possibly lead to potential supply issues. PDA therefore suggests an extended implementation timeframe.

There are other topics which need some clarification. PDA therefore respectfully suggests this guideline should be revised to reflect our attached recommendations.

If you have any questions, please contact me.

With very best regards,



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EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

31 August 2013

Guideline on the use of porcine trypsin used in the manufacture of human biological medicinal products Name of Document

Comments from:

Name of organisation or individual
PDA (The Parenteral Drug Association)

Please note that these comments and the identity of the sender will be published unless a specific justified objection is received.

When completed, this form should be sent to the European Medicines Agency electronically, in Word format (not PDF).

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1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment (if any)	Outcome (if applicable) *(To be completed by the Agency)*
Name	Comment	Decision to Submit/ withdraw comment
	PDA recognizes this guideline provides a scientific approach to assess the virus safety of trypsin produced from porcine pancreatic tissue. It contains both, guidance for the acceptance of trypsin used as a reagent for production of medicinal products and it provides, in addition, current knowledge. PDA supports inclusion of both areas but suggests to clearly separate the two within the document for enhanced clarity. The requirements for the documentation of sourcing, testing and manufacturing including inactivation of trypsin are very high. It is important to remember that the business objective of the trypsin supplier and the manufacturer of the medicinal product are not necessarily the same. In general, the trypsin produced is not exclusively for medicinal product manufacturing. If requirements become too specific some firms may reduce production of this material or increase costs for this speciality of a trypsin product possibly leading to potential supply issues. PDA recommends that rather than citing specific literature or inactivation methods, manufacturers be allowed to design their own and justify them based on robustness and effectiveness for their particular process.	

Stakeholder number *(To be completed by the Agency)*	General comment (if any)	Outcome (if applicable) *(To be completed by the Agency)*
	PDA suggests to make it clear that inactivation methods listed are examples and that other methods could be used if shown that they are effective in inactivating a broad range of viruses or specific virus(es) of concern. The request to implement two complementary virus reduction steps, which are controlled according to the CPMP/BWP/268/95 guideline, may be difficult to implement in a short time frame. PDA therefore suggests allowing for an extended implementation timeframe.	

Specific comments on text

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
Line 39	Name (First & Last)	Comment: PDA recommends modifying the text by adding some specific examples. Proposed change (if any): This may especially be the case for certain viruses **for example porcine parvovirus and porcine circovirus I and II….**	
Lines 114-115		Comment: The sentence should be revised to be more specific as to whether the concern is about virus contamination detected pre or post inactivation. Circovirus will be detected in the majority of pre inactivation tissues therefore PDA recommends the following change to the text:	

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
		Proposed change (if any): if virus contamination is detected **post inactivation** the trypsin batch should not be used…	
Line 144		The specific risk of contamination with PPV and PCV should be highlighted. This can be realized by the addition of the sentence as shown below. Proposed change (if any): … Therefore selected process steps should be carefully validated with respect to pathogen reduction. **Highly resistant viruses like PPV and PCV type I and II should especially be considered.** Reference is made …	

Please add more rows if needed.