PDA Global Headquarters
Bethesda Towers
4350 East West Highway
Suite 150
Bethesda, MD 20814 USA
Tel: +1 (301) 656-5900
Fax: +1 (301) 986-0296
www.pda.org

July 25, 2013

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

Ref: EU Guidelines for GMP for Medicinal Products; Chapter 5: Production

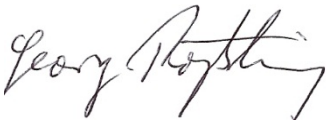
To the Health and Consumers Directorate-General:

PDA is pleased to provide comments on this chapter 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 investigational medicinal products, regulatory affairs and GMP on behalf of our Regulatory Affairs and Quality Advisory Board.

In general PDA believes that it is the role of GMPs to describe what to do rather than a prescriptive description of how to do it. In this context, PDA recommends removing the overly detailed lists in section 5.20 and placing these in a separate guidance document if warranted. In addition, PDA suggests clarifying the meaning of the term "starting material." In other contexts, the term commonly refers to materials for the manufacture of active substances. Within the context of this chapter, it appears to be used to mean the active substance and / or excipients incorporated into medicinal products.

If you have any questions, please contact me.

With very best regards,



Georg Roessling, Ph.D.
Senior VP, PDA Europe
Roessling@pda.org

cc: Richard Johnson, PDA; Richard Levy, PDA

EUROPEAN COMMISSION
HEALTH AND CONSUMERS DIRECTORATE-GENERAL

Public Health and Risk Assessment
Medicinal products – quality, safety and efficacy

25 July 2013

The Rules Governing Medicinal Products in the European Union

Volume 4

EU Guidelines for

Good Manufacturing Practice for

Medicinal Products for Human and Veterinary Use

Part 1

Chapter 5: Production

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).

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
	The use of the term starting material in this chapter is unclear in that it generally refers to materials for the manufacture of active substances. For clarity, PDA suggests clarifying that within the context of this chapter, the meaning is active substance and / or excipients	
	In general PDA recommends omitting absolutes such as “contamination must be “avoided” in favour of “controlled.” The use of “avoided” does not allow for the use of risk management where the principle is that there may be a small, acceptable residual risk. We recommend replacing this globally with “controlled” throughout the chapter.	
	In general PDA believes that it is the role of GMPs to describe what to do rather than a prescriptive description of how to do it. The lists in section 5.20 are overly detailed and PDA recommends placing these in a separate guidance document if warranted.	

2. 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)*
5.19		Comment: In line with PDAs comments on the Guideline on setting health based exposure limits, PDA recommends clarifying that the toxicological evaluation referred to in this section could include any health based exposure limit. Proposed change (if any): Risk assessment should include among other parameters a toxicological evaluation of the products being manufactured using health based exposure limits (see Guideline...)	
5.19		Comment: Often single use items (e.g. gaskets) could be sufficient, if the cleaning process is effective. Proposed change (if any): "This may range from **single use items to** dedicating specific product contact..."	
5.20		Comment: PDA recommends using terminology consistent with ICH Q9 which refers to 'risk control measures' Proposed change (if any): Technical and organisational measures to ~~mitigate~~ **control the** risks of cross-contamination **should be considered when performing risk management**.	

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)*
5.21		Comment: Use ICH Q9 terminology. Proposed change (if any): Measures to prevent cross-contamination and their effectiveness should be **reviewed** ~~checked~~ periodically according to set procedures.	
5.26 last paragraph		Comment: The items listed are usually negotiated in a quality agreement rather than being in a specification. Proposed change (if any): Delete " ~~or specification"~~	
5.33 first paragraph		Comment: As written the paragraph appears to preclude the use of outsourced laboratories for identity testing. Proposed change (if any): Delete the word "~~themselves~~"	

Please add more rows if needed.