EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

30 January 2012

European Medicines Agency
7 Westferry Circus
Canary Wharf, London E14 4HB
United Kingdom

Re: Submission of comments on ' Concept Paper on the development of toxicological guidance for use in risk identification in the manufacture of different medicinal products in shared facilities' (EMA/CHMP/SWP/598303/2011)

Comments from:

Nancy Berg, President/CEO
ISPE (International Society for Pharmaceutical Engineering)
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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)*
	Industry scientists with experience in determining the safety of products for both patients and workers would like to work in partnership with the EMA to develop the guidance document to ensure the guidance provides a scientifically sound, risk-based approach. This may also help to accelerate the proposed timeline as both inspectors and industry are anxious to have guidance in place. ISPE is prepared to facilitate this collaboration.	
	ISPE agrees that the approach should be scientifically based and aim to limit the variability in deriving acceptable exposure limits to ensure consistency but cautions that this should not be so prescriptive that it requires the *exact* same value to be derived by all. How these values should be used allows some variability since the ideal use of these values should be to set an upper limit for statistical analysis of the process capabilities where it is expected that the process is controlled well below the upper limit.	
	Having sound guidance on the toxicological tools is important for industry, regulators and patients. The plethora of toxicological tools available all have similar methodologies based in good toxicological science. While the factors used to develop values may be somewhat different due to the focus of the limit (chemical residues vs. product to product carry over),	

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	the values developed using any of these methods may produce limits while not exactly the same number are effectively the same when considering the significance of the values. For example values of 8 and 12 mcg/day will drive the same types of controls to be used to manage the risk and as already stated companies should control below these limits for a robust process.	
	It is important to note that while multi-product facilities provide a financial benefit to industry, patients also benefit. Response to drug shortages can be facilitated much easier if products can be placed in existing facilities rather than wait for dedicated facilities to become available. Dedicated facilities could also increase the cost of medicines to patients and/or governments whereas the safe use of multi-product facilities ultimately helps to reduce the cost of medicines to the patient.	
	ISPE agrees that toxicological data is essential in a scientific approach to cleaning validation/verification and establishment of threshold values to be used as part of an overall Quality Risk Management in shared facilities.	
	ISPE released Risk-Based Manufacture of Pharmaceutical Products Baseline® Guide (Risk-MaPP) last year which included a methodology for determining the toxicological safe limits. While we understand EMA is concerned about the use of “professional judgment” described in the guide, it is important to note that many toxicologists within the bio-pharmaceutical industry vetted the document prior to publication. These same toxicologists would welcome an opportunity to collaborate with EMA on their guidance. Obviously once the EMA has	

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	established their guidance, ISPE will review the Risk-MaPP guide and make any necessary adjustments to the document.	

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)*
		Comment: Proposed change (if any):	

Please add more rows if needed.