8 October 2009

World Health Organization
Avenue Appia 20
1211 Geneva 27
Switzerland

SUBMISSION OF COMMENTS ON QAS/09.295 Rev.1:WHO GMP FOR STERILE PHARMACEUTICAL PRODUCTS

ISPE is pleased to provide comments on the above document, compiled by the Sterile Products Processing (SPP) Community of Practice within ISPE.

Our observations are in the areas of HEPA filtration, process simulation tests, biological indicators, and the use of goggles in some areas.

Our comments have been submitted, as requested, using the supplied WHO template.

We would much appreciate if the comments detailed in the document are addressed.

Yours sincerely,

Robert P. Best
President/CEO, ISPE

Comments on WHO Working Document QAS/09.295 Rev 1

Title of the document: WHO GOOD MANUFACTURING PRACTICES FOR STERILE PHARMACEUTICAL PRODUCTS.

Comments submitted by: ISPE
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Date: 6th October 2009

		General comment(s) if any :			Originator of the comments
# section	**# Pararaph If more than one**	**Comment / Rationale**	**Proposed change / suggested text**	**Classification L= low M= medium H= high**	**Originator of the comments (for WHO use)**
4.5		HEPA filters should be subjected to installed filter leakage test in accordance with ISO 14644-3 at least twice a year	Frequency of HEPA filter checks is not specified within the EU GMPs and typically is carried out on an annual basis only 6 monthly for LAF units not terminal HEPAS. EN/ISO 14644 specifies checks every 2 years	M	ISPE
4.22		Word not is in blue text	If deliberate leave as is if in error change text to black	L	ISPE
4.26		The process simulation test should imitate as closely as possible the routine aseptic manufacturing process and include all the critical subsequent manufacturing steps.	The process simulation test should imitate as closely as possible the routine aseptic manufacturing process and include all the critical subsequent manufacturing steps except were the activity is injurious to any potential microbiological contamination for example the use of nitrogen head space should only be simulated or the depth of	H	ISPE

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			vacuum pulled during freeze-drier media fills should not be a low as that utilised for product to avoid boiling the media.		
6.1		Sterilization records should be available for each sterilization run, and should be approved as part of the batch release procedure. Chemical or biological indicators may also be used but should not take the place of physical controls.	The use of Biological indicators should only be for validation purposes not as routine controls during manufacturing. This point should be emphasised.	M	ISPE
10.7	Starting with A/B	There is no mention of the use of goggles for grade A and B operators. These are expected by the EU and US GMP inspectors	Insert “Operators working in grade A and B areas should wear sanitised goggles” at end of paragraph	M	ISPE
		Please add rows as necessary (with "copy and paste" empty rows)			