World Health Organization
1211 Geneva 27
Switzerland

SUBMISSION OF COMMENTS ON QAS/09.297 Rev.1:WHO Good Practices for Pharmaceutical Microbiology Laboratories.

ISPE is pleased to provide comments on the above document, compiled by the Good Control Laboratory Practices (GCLP) Community of Practice within ISPE.

Our comments relate to the general nature of the document and also pertain specifically to the areas of personnel, premises, validation of test methods, equipment, reagents and culture media, reference materials and reference cultures, sampling, testing procedures, and two of the appendices (B and C)

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/09.297/Rev.1
Title of the document: WHO Good Practices for Pharmaceutical Microbiology Laboratories

Comments submitted by: ISPE
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Kindly complete the table without modifying the format of the document - thank you.

Template for comments

General comment(s) if any :	**Originator of the comments**
The document is of a very general nature without any specific guidelines for several aspects of microbiological testing including sterility testing, growth promotion tests, validation of equipment, OOS investigation etc. At a number of places ISO clauses are quoted; this may not be required since under references relevant ISO documents are listed.	ISPE

# section	**# Paragraph If more than one**	**Comment / Rationale**	**Proposed change / suggested text**	**Classification** **L**= low **M**= medium **H**= high	**Originator of the comments (for WHO use)**
Intro-duc-tion	1st para 2nd bullet	Under surfaces, include monitoring of garments and body parts	- detection, isolation, enumeration and identification of microorganisms (viruses, bacteria, fungi and protozoa) and their metabolites in different materials (e.g.: starting materials, water, air), products, surfaces including garments and body parts and the environment;	L	ISPE
Gloss -ary	Refer-ence	Do not include working cultures under the definition of reference cultures since it could lead to confusion	Reference cultures – Collective term for reference strain and reference stocks of cultures	L	ISPE

# section	# Paragraph If more than one	Comment / Rationale	Proposed change / suggested text	Classification **L**= low **M**= medium **H**= high	Originator of the comments (for WHO use)
	cultures	amongst the laboratories.	Working cultures – Term used for strains sub-cultured from reference culture and used for routine testing.		
Gloss -ary	Refer- ence stocks	ISO 11133-1:2000 has been referenced. This will create confusion in the sense as which reference is to be followed -- national reference laboratory or ISO. It is clarified under “reference strains” definition.	Bracketed words ISO 11133 – 1:2000 is to be deleted	M	ISPE
Gloss -ary	Refer- ence strains	ISO 11133-1:2000 has been referenced for defining strain to at-least to genus and species level. This information is available with national or international laboratories. The laboratories attached to a manufacturing organization need not have information if strain with them has been characterised. This responsibility lies with reference laboratory (we do not ask the source of USPRS from USP Commission).	To be rewritten as “Microorganisms used for production or assay purposes are catalogued and are either obtained from national or international collection centre or carry a traceability to those centres. Word ISO 11133 – 1:2000 is to be deleted	M	ISPE
1	1.1 Second sentence	In second sentence alternative qualifications are permitted. Alternate qualifications should have approval of competent authority.	The sentence is to be extended with words … as approved by competent authority	L	ISPE
1	1.4 5th and 6th lines	Delete the phrase “or if they do so under adequate supervision” since it could imply a person without adequate competence could also perform tests.	“Personnel may only perform tests on samples if they are recognized as competent to do so”.	H	ISPE
1	1.1 to 1.4	There is no mention about safety aspects while handling microorganisms	Include a suitable sub-paragraph under Section 1 on safety aspects of handling microorganisms.	H	ISPE
2	2.1	There is no mention about the stringent civil standards to be adopted for sterility testing laboratory.	Include a sub-section under Section 2 to briefly mention about the civil standards for sterility testing	M	ISPE

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			laboratory.		
2	2.1.4	In last sentence the words “and radioisotopic” appear out of place.	Words “and radioisotopic” may be deleted	H	ISPE
2	2.1.7	Delete this sub-section since it is not a good practice to use non-dedicated areas for microbiological testing.	Delete sub-section 2.1.7	H	ISPE
2	2.2.1	There is no mention about trending of results for environmental monitoring. Trending is an important aspect of environmental monitoring.	Include a statement in this section “Trending of environmental monitoring results shall be carried out”	M	ISPE
3	3.1 to 3.4	There is no specific mention about sterility test validation. Validation of sterility testing is an important aspect of sterility testing.	Include a sub-section specifically on sterility testing validation.	M	ISPE
3	3.1 to 3.4	There is no mention about recovery studies for environmental monitoring tests like surface swab testing in any of these sections.	Include a suitable statement in any of these sections or introduce a new section on recovery studies for environmental studies like surface and garment swab monitoring.	M	ISPE
3	3.4	This sub-section is not clear.	Either delete this sub-section or elaborate what is meant by this statement with examples.		ISPE
4	4.1	Appendix A is wrongly mentioned as examples of maintenance equipment and intervals. Appendix A is General use of reference cultures.	Correct the typographical error here		ISPE
4	4.2, 4.2.4	There is no mention in these sections about the various aspects of equipment qualification like DQ, IQ and OQ	Include a section on the various aspects of validation and qualification of equipment like DQ, IQ, OQ, PQ,	M	ISPE

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		while only PQ is mentioned. This is important for all equipment especially so for the sterilizers.	re-validation frequencies etc.		
4	4.2.4 (a)	This sub-section states that “Pressure cookers fitted only with a pressure gauge are not acceptable”. Does this mean if pressure cookers fitted with pressure and temperature gauges are acceptable?	Include clarification or state “Pressure cookers are not acceptable for sterilization purposes.”	M	ISPE
4	4th (last) para	This paragraph gives an option of using one autoclave for sterilization and decontamination with documented cleaning programme. This is not acceptable, decontamination autoclave should be different.	Delete this paragraph.	H	ISPE
4	4.2.7	This sub-section requires assessment of centrifugal force. This may be difficult instead it is suggested to assess the RPM of the centrifuge.	Modify the statement to “When centrifuges are used in tst procedures, an assessment of RPM shall be made. Where it is critical the centrifuge shall be calibrated”	M	ISPE
5	5.2.3	The required quality of water is vaguely stated. Water used for microbiological works shall meet pharmacopoeial standard of the country.	Modify the statement to “Distilled, deionised or reverse osmosis-produced water meeting relevant pharmacopoeial standards . . .”	M	ISPE
5	5.2.5	The sub-section is not adequately specific especially for sterility testing.	Consider the following addition to this sub-section “media for sterility testing shall be handled under laminar air flow modules (Class A) placed in Class B environment.”	M	ISPE
5	5.3.2	There is no mention about Growth Promotion Test to be carried out on media bought or prepared. This is required to be done on all batches of bout out and	Include suitable statement on carrying out GPT on every batch of media.	H	ISPE

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		prepared media.			
6	6.2.2	This sub-section refers to Appendix C as Preparation of working stocks. Actually the relevant appendix is Appendix A.	Correct this typographical error.	L	ISPE
6	6.2.3	This sub-section does not state how many passes of sub-culturing are permissible.	Include a statement for limiting sub-culturing of reference cultures, usually not more than 4 passes.	M	ISPE
7	7.2	Last sentence of this sub-section states “Testing of the samples should be performed as soon as possible after sampling.” This is ambiguous for testing of water samples.	Include a definitive statement for storage period for water samples, generally within 4 hours of sampling	M	ISPE
7	7.3	Sampling of sterile products is not adequately detailed.	Include statement on the need for sampling sterile products under Class A conditions.	H	ISPE
11	11.5.1	Statement on standards has a typographical error.	Modify the statement as – microbial limit testing / total bio-burden 1000 cfu per g for bacteria and 100 cfu per g for yeast and moulds.	L	ISPE
11	11.5.1	Standard for environmental monitoring is vague. It does not say exposure of plates for how long. There is also no mention about active air sampling.	Standard should state duration of exposure e.g.: 2 hours, 4 hours etc. Also include active air sampling requirements.	H	ISPE
App B	Calibra-tion frequen-cies	This table mentions calibration frequencies for reference thermometers and calibration weights as once in 5 years. This is too long a duration.	Increase the frequency of re-calibration to annually.	H	ISPE
App	Equip-	Under Laminar airflow cabinets it is stated (b) Check	Replace as (b) Check with settling plates.	L	ISPE

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C	ment valida-tion	with sterility plates.			
		Please add rows as necessary (with "copy and paste" empty rows)			ISPE