Vergleich EU GMP-Leitfaden Annex 1 Sterile und aseptische Herstellung

Ein Auszug aus dem Download Vergleich EU GMP-Leitfaden Annex 1 Sterile und aseptische Herstellung

5 Min. Lesezeit

von Fritz Röder

Vergleichstabelle EU-GMP-Leitfaden Annex 1 Sterile und Aseptische Herstellung Seite 5 von 61

Entwurf Annex 1 (Dez 2017)	Version Annex 1 (Nov 2008)	Beschreibung der Unterschiede & Kommentar	Kritikalität (1= niedrig, 3 = hoch)
e) Processes associated with the finishing and transport of sterile products should not compromise the finished sterile product in terms of container integrity or pose a risk of contamination and ensure that medicinal products are stored and maintained in accordance with registered storage conditions.		*Transport & Finish dürfen das Produkt nicht negativ beeinflussen (z.B. Container Closure Integrity, Lagerbedingungen)*	*2*
f) Persons responsible the quality release of sterile medicines should have appropriate access to manufacturing and quality information and possess adequate knowledge and experience in the manufacture of sterile dosage forms and their critical quality attributes in order to be able to ascertain that the medicines have been manufactured in accordance with the registered specification and are of the required safety, quality and efficacy.		*Verweis auf Know-How sowie die notwendige Ausbildung und Erfahrung der Verantwortlichen.*	*2*
3.2 Investigations should be performed into non-conformities, such as sterility test failures or environmental monitoring excursions or deviations from established procedures, with a specific focus regarding the potential impact to sterility, to not only the specific batch concerned but also any other potentially impacted batch. The reasons for including or excluding product from the scope of the investigation should be clearly recorded and justified within the investigation.		*- Abweichungen sollen auch die Sterilität der Produkte behandeln.* *- Auch weitere Chargen sollen in die Betrachtung miteinbezogen werden. Werden Chargen von der Betrachtung ausgeschlossen, soll die Rationale hierfür dokumentiert werden.*	*2*
4. Personnel	**Personnel**		
4.1 The manufacturer should ensure that there are sufficient appropriate personnel, suitably qualified and experienced in the manufacture and testing of sterile medicines and any of the specific manufacturing technologies used in the site's manufacturing operations, to ensure compliance with Good Manufacturing Practice applicable to the manufacture of sterile medicinal products.		*Neuer Hinweis auf "ausreichendes und qualifiziertes" Personal. Diese Forderung deckt sich aber ohnehin mit dem GMP-Leitfaden, Teil 1, Abschnitt 2.1 und ist daher bereits gängig.*	*1*
4.2 Only the minimum number of personnel required should be present in cleanrooms. The maximum number of operators in critical areas should be determined based on QRM principles, documented in the contamination control strategy, and validated during activities such as initial qualification and aseptic process simulations, so as not to compromise sterility assurance. This is particularly important during aseptic processing. Inspections and controls should be conducted outside the clean areas as far as possible.	36. Only the minimum number of personnel required should be present in clean areas; this is particularly important during aseptic processing. Inspections and controls should be conducted outside the clean areas as far as possible. 71. Care should be taken that any validation does not compromise the processes.	*Die maximale Personenanzahl im Reinraum soll nun auch risikobasiert festgelegt und im Rahmen der Validierung (Media Fill) bestätigt werden.*	*2*

Entwurf Annex 1 (Dez 2017)	Version Annex 1 (Nov 2008)	Beschreibung der Unterschiede & Kommentar	Kritikalität (1= niedrig, 3 = hoch)
4.3 All personnel (including those performing cleaning and maintenance) employed in such areas should receive regular training, qualification (including sampling of the operators bioburden, using methods such as contact plates, at key locations e.g. hands arms and chest) and assessment in disciplines relevant to the correct manufacture of sterile products. This training should include reference to hygiene, cleanroom practices, contamination control, aseptic techniques, and potential safety implications to the patient of a loss of product sterility and in the basic elements of	37. All personnel (including those concerned with cleaning and maintenance) employed in such areas should receive regular training in disciplines relevant to the correct manufacture of sterile products. This training should include reference to hygiene and to the basic elements of microbiology. When outside staff who have not received such training (e.g. building or maintenance contractors) need to be brought in, particular care should be taken over their instruction and supervision.	*Neu aufgenommen wurde die Qualifizierung der Mitarbeiter, inklusive Bioburdentest mit Kontaktplatten; außerdem wurde der Trainingsumfang um zahlreiche Themen erweitert.*	*2*
4.4 The personnel working in a grade A/B cleanroom should be trained for aseptic gowning and aseptic practices. Compliance with aseptic gowning procedures should be assessed and confirmed and this should be periodically reassessed at least annually and should involve both visual and microbiological assessment (using additional locations such as arms and chest). Only trained personnel who have passed the gowning assessment and have participated in a successful aseptic process simulation (APS) test, during which they performed their normal duties, should be authorized to enter any grade A/B area, in which aseptic operations will be conducted, or are being conducted, whilst unsupervised. The microbial monitoring of personnel in the grade A/B area should be performed to assess their aseptic behaviour. This monitoring should take place immediately after completion of a critical intervention and upon each exit from the cleanroom. It should be noted that there should also be an ongoing continuous monitoring program for personnel including some consideration of periodic monitoring under the supervision of the quality unit.		*Das mikrobiologische Monitoring von Mitarbeitern wird in diesem Abschnitt beschrieben und ist neu, war aber bis dato auch schon in der Praxis üblich.* *Mitarbeiter, die während der Abfüllung in Raumklasse A/B präsent sein sollen, sollen auf ihre Eignung im Rahmen des Media Fill/APS geprüft werden.*	*3*
4.5 There should be systems in place for disqualification of personnel from entry into cleanrooms, based on aspects including ongoing assessment and/or the identification of an adverse trend from the personnel monitoring program. Once disqualified, retraining and requalification is required before permitting the operator to have any further involvement in aseptic practices. This should include consideration of participation in a successful Aseptic Process Simulation (APS).		*Neu: ein Prozedere zur Disqualifizierung von Mitarbeitern zum Betreten der Raumklasse A/B wird erwartet.*	*3*
4.6 Manufacturers should establish written procedures outlining the process by which outside staff who have not received such training (e.g. building or maintenance contractors) need to be brought into grade A/B areas. Access by these persons should only be given in exceptional circumstances, evaluated and recorded in accordance with the PQS.		*Neu: ein Prozedere ist zu entwickeln, wie Betriebsfremde (z.B. für Wartungen) in Reinraumklasse B eingeschleust werden*	*2*

Entwurf Annex 1 (Dez 2017)	Version Annex 1 (Nov 2008)	Beschreibung der Unterschiede & Kommentar	Kritikalität (1= niedrig, 3 = hoch)
4.7 High standards of personal hygiene and cleanliness are essential. Personnel involved inthe manufacture of sterile preparations should be instructed to report any specific health conditions or ailments which may cause the shedding of abnormal numbers or types of contaminants and therefore preclude clean room access; periodic health checks for such conditions should be performed. Actions to be taken with regard to personnel who could be introducing an undue microbiological hazard should be described in procedures decided by a designated competent person.	39. High standards of personal hygiene and cleanliness are essential. Personnel involved in the manufacture of sterile preparations should be instructed to report any condition which may cause the shedding of abnormal numbers or types of contaminants; periodic health checks for such conditions are desirable. Actions to be taken about personnel who could be introducing undue microbiological hazard should be decided by a designated competent person.	*Neu: Die erwähnten Maßnahmen sind neuerdings auch in einer SOP zu beschreiben.*	*1*
4.8 Staff who have been engaged in the processing of human or animal tissue materials or of cultures of micro-organisms, other than those used in the current manufacturing process, or any activities that may have a negative impact to quality, e.g. microbial contamination, should not enter sterile product areas unless rigorous, clearly defined and effective entry procedures have been followed.	38. Staff who have been engaged in the processing of animal tissue materials or of cultures of micro-organisms other than those used in the current manufacturing process should not enter sterile-product areas unless rigorous and clearly defined entry procedures have been followed.	*Neu: auch bei der Verarbeitung von Gewebematerialien sollte man die Produktionsbereiche für die Sterilherstellung nicht betreten.*	*2*
4.9 Wristwatches, make-up and jewellery and other personal items such as mobile phones should not be allowed in clean areas.	40. Wristwatches, make-up and jewellery should not be worn in clean areas.	*Neu: Verbot persönlicher Gegenstände (z.B. Handy) im Reinraum.*	*2*
4.10 Changing and hand washing should follow a written procedure designed to minimize contamination of clean area clothing or carry-through of contaminants to the clean areas. Garments should be visually checked for cleanliness and integrity prior to entry to the clean room. For sterilized garments, particular attention should be taken to ensure that garments and eye coverings have been sterilized and that their packaging is integral before use. Reusable garments should be replaced based at a set frequency determined by qualification or if damage is identified.	41. Changing and washing should follow a written procedure designed to minimize contamination of clean area clothing or carry-through of contaminants to the clean areas.	*Neuerdings wird auf die visuelle Prüfung der Kleidung hingewiesen, was aber bereits übliche Praxis sein sollte. Mehrwegkleidung soll regelmäßig auf Eignung/Austausch geprüft werden.*	*2*
4.11 The clothing and its quality should be appropriate for the process and the grade of the working area. It should be worn in such a way as to protect the product from contamination.	42. The clothing and its quality should be appropriate for the process and the grade of the working area. It should be worn in such a way as to protect the product from contamination.	*Kein inhaltliches Delta*	*1*
4.12 The description of clothing required for each grade is given below:	43. The description of clothing required for each grade is given below:	*Kein inhaltliches Delta*	*1*
a) Grade D: Hair, beards and moustaches should be covered. A general protective suit and appropriately disinfected shoes or overshoes should be worn. Appropriate measures should be taken to avoid any contamination coming from outside the clean area.	• Grade D: Hair and, where relevant, beard should be covered. A general protective suit and appropriate shoes or overshoes should be worn. Appropriate measures should be taken to avoid any contamination coming from outside the clean area.	*Neu: Schuhe sind zu desinfizieren*	*1*
b) Grade C: Hair, beards and moustaches should be covered. A single or two-piece trouser suit gathered at the wrists and with high neck and appropriately disinfected or sterilized shoes or overshoes should be worn. They should shed virtually no fibres or particulate matter.	• Grade C: Hair and where relevant beard and moustache should be covered. A single or two-piece trouser suit, gathered at the wrists and with high neck and appropriate shoes or overshoes should be worn. They should shed virtually no fibres or particulate matter.	*Neu: Schuhe sind zu desinfizieren*	*1*

Quellen:

Dieser Text ist ein Auszug aus dem neuen Download Vergleich EU GMP-Leitfaden Annex 1 Sterile und aseptische Herstellung

Der Entwurf des Annex 1 des EU-GMP-Leitfaden beschäftigt viele Verantwortliche in der Pharmaindustrie.

Stellen Sie sich auch die Fragen:

- Was ändert sich?
- Bin ich darauf vorbereitet?
- Was muss ich nun tun?

Dieser Download hilft Ihnen bei der Beantwortung dieser Fragen. Der Autor Fritz Röder hat den aktuell gültigen Anhang 1 mit dem Entwurf verglichen, verschafft damit einen Überblick und

zeigt auf, wo Handlungsbedarf besteht. Ein Kritikalitätsindex von 1-3 bewertet die verschiedenen Änderungen.

Auch wenn der Entwurf noch keine Gültigkeit hat, er zeigt auf in welche Richtung die Behörden denken. Sie sollten darauf vorbereitet sein, denn bald schon kann eine finale Version erscheinen. Weitere Informationen zum **Download** **Vergleich EU GMP-Leitfaden Annex 1 Sterile und aseptische Herstellung** erhalten Sie **hier.**

Autor:

Fritz Röder
Dipl. Ing. (FH) Umwelttechnik/Umweltmesstechnik
Merck KGaA, Darmstadt
E-Mail: roederfritz@googlemail.com

