PDA
Parenteral Drug Association

Live Webinar:

Annex 1: come interpretare la pubblicazione del draft per la seconda consultazione

Giovedì 30 Aprile 2020 | ore 10.00

Relatori:
***Lucia Ceresa**, PDA Italy Chapter Vice President*
***Gilberto Dalmaso**, GDM Pharma Consulting*

PDA Italy Chapter
Connecting People, Science and Regulation®

Who we are...PDA in the world

- **PDA (Parenteral Drug Association)** is a pharmaceutical no-profit organization founded in 1946
- Leading **global provider of science**, technology, and regulatory information and committed to developing scientifically sound, practical technical information and expertise to advance pharmaceutical/biopharmaceutical manufacturing science and regulation with the final purpose of better serving patients
- PDA's governance is based on **regional chapters**: 14 chapters in USA and Canada, 4 chapters in EU (France, Ireland, UK and Italy), Israel, 1 chapter in LATAM and 6 chapters in APAC

Our mission:

« Connecting People, Science and Regulation»

Why join PDA?

- **Being part of an international pharma community:** exchange of knowledge, experience and challenges;
- **Regular updates** from PDA Global on industry trends, regulatory requirements and technological innovations:
  - PDA Glossary of Pharmaceutical and Biotechnology Terminology
  - *PDA Letter*
- **Connection to regulatory authorities**;
- **Free availability** of technical documents and reports:
  - Access to the full contents of all active Technical Reports on the Technical Report Portal
  - Industry-critical research at the *PDA Journal of Pharmaceutical Science & Technology*.
- **Advantageous discounts** in joining PDA US, EU and IT events.

For any additional information & for further details on how to join us, visit our pages:

- **www.pda-it.org**
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Technical webinars series on Annex 1: April-May 2020

Dr. Lucia Ceresa, *Charles River Microbial Solutions*

Dr. Lucia Ceresa is the Senior Technology and Market Development Manager at Charles River Microbial Solutions and she currently serving as Vice President of the PDA Italy Chapter, a member since 2005, and an active participant of the Steering Committee since 2009.

Dr. Ceresa has more than 25 years of industry experience, including pharmaceutical aseptic production and all aspects of validation and quality control, with focus on GMP's and Alternative Microbiological Methods.

She has extensive international experience within pharmaceutical operations, microbiology, rapid methods, aseptic processing and methodologies, validation and QC. After 10 years as a Permanent Qualified Teacher in Chemistry and Microbiology, she started her career initially within the life sciences industry at Millipore Corporation, followed by Gelman Sciences Corporation, Pall Corporation, and Particle Measuring Systems. Academic degree in Microbiology from the University of Milan in 1981.

Gilberto Dalmaso, *GDM Pharma Consulting*

Gilberto Dalmaso has over 25 years' experience in pharmaceutical microbiology and sterility assurance. During his distinguished career at GSK he led a series of technology-driven process improvements using scientific methods, while achieving GMP compliance and regulatory approvals.

Over his last five years with GSK, Gilberto led a series of initiatives implementing Process Analytical Technologies (PAT) and Rapid Microbial Methods (RMM) that improve quality and process understanding while yielding significant cost savings.

Today Gilberto is the Global Consultant and Subject Matters Expert for GDM Pharma Consulting. In this role he collaborates and consults with pharmaceutical companies to develop and implement science-based strategies and processes that utilize Quality by Design (QbD) principles to monitor, control, and improve the chemical, physical, and microbiological state of various production processes. He's also a qualified training for the most important regulatory agencies.

Disclaimer

I contenuti di questa presentazione sono frutto dell'opinione personale degli autori.

The statements within this presentation are the personal opinions of the authors.

Agenda

GMP Revision on Annex 1 Manufacturer of Sterile Products

- Dal documento del 2008 alla pubblicazione del 1° draft
- I commenti, l'iter di correzione e la pubblicazione del documento per la seconda consultazione
- Quali sono i punti ancora aperti alla discussione?
- I punti chiave da cominciare a considerare
- Agenda dei prossimi webinar

Annex 1 rev. 2017: review process and topics

- The revision draft of Annex 1 "Manufacture of Sterile Medicinal Products“ was published for public comments by the European Commission on 20 December 2017
- The revision intended to correct historical ambiguities and historical inaccuracies but mainly to promote and allow the inclusion of current new **technological and innovative process.**

  The key changes in short:
  - Introduction of new sections
  - Introduction of QRM Principles
  - Introduction of new technologies
  - Restructured to give more logical flow
  - Added details to a number of the previous sections

All those principles have not been changed in the second draft!

Annex 1 rev. : comments review process

- More than **140** companies and/or organizations commented the Draft Annex 1.
- More than **6200** lines of comments addressed the whole Annex 1.
- The **WG** (**PIC/s, EC, WHO**) [(1)] reviewed and suggested approach to comments and accepted or suggested alternatives.
- The "Rapporteur" identified each comment as H/M/L priority and substantive, non-substantive or typo.

(1)

- **PIC/S** is the abbreviation and logo used to describe both the **P**harmaceutical **I**nspection **C**onvention (**PIC**) and the **P**harmaceutical **I**nspection Co-operation **S**cheme (PIC Scheme) operating together in parallel.
- **EC** – European Commission
- **WHO**-**W**ord **H**ealth **O**rganization.

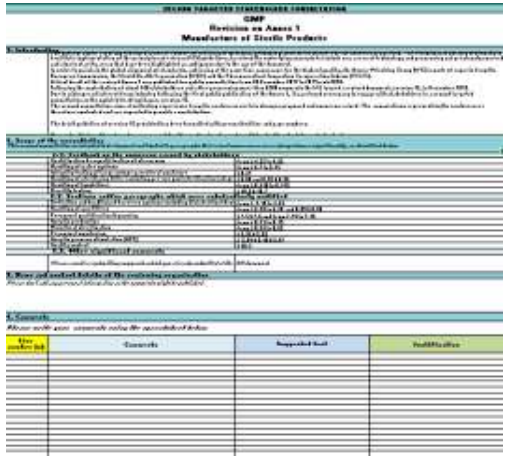
EMA Targeted Stakeholder list

The following organizations representing relevant stakeholders accepted to take part in the second consultation, to compile and send the comments to the European Commission):

- A3P (Association for Products Propres and Parentals)
- AESGP (Association of the European Self-Medication Industry)
- Animal Health Europe
- APIC (Active Pharmaceutical Ingredient Committee)
- EAEPC (European Association of Euro-Pharmaceutical Companies)
- **ECA (European Compliance Academy**)
- **EFPIA (European Federation of Pharmaceutical Industries and Associations)**
- EGGVP (European Group for Generic Veterinary Products)
- EIPG (European Industrial Pharmacists Group)
- GIRP (European Healthcare Distribution Association)
- ISPE (International Society for Pharmaceutical Engineering)
- Medicines for Europe
- **PDA (Parenteral Drug Association)**
- PHSS (Pharmaceutical & Healthcare Sciences Society)
- EQPA (European Qualified Person Association)
- Vaccines Europe

Annex-1-targeted-stakeholder-consultation 2020 TEMPLATE

1. Introduction



The current Annex 1 is being reviewed to better **ensure the sterility** of the medicinal products placed in the market. The revision was necessary to facilitate implementation of the principles of relevant **ICH Guidelines**, to extend the underlying concepts to include new areas of technology and processing not previously covered and also to clarify areas that have been highlighted as ambiguous due to the age of the document,

In order to maintain the global alignment of standard, achieving at the same time assurance of the highest quality, the Annex 1 working group is made of expert from:

- the **E**uropean **C**ommission,
- the **W**orld **H**ealth **O**rganization (**WHO**) and
- the Pharmaceutical Inspection Co-operation Scheme (**PIC'/s**).

Annex-1-targeted-stakeholder-consultation 2020 TEMPLATE

2. SCOPE

The **scope** of this second consultation is intended to be **focus** and **limited** to the paragraphs that raised concerns or were change more significantly, as intended below.

2.1. Feedback on the concerns raised by stakeholders		
	Qualification & requalification of cleanroom	from § 4.25 to 4.35
	Handling of water systems	from § 6.7 to 6.15
	Integrity testing of large volume parenteral container	§ 8.21
	Handling of sterilizing filter including pre-use post sterilization integrity testing (Pu	§ 8.88 and 8.95 & 8.96
	Handling of lyophiliser	from § 8.110 to 8.113
	Sterility testing	§ 10.6 & 10.7
2.2. Sections and/or paragraphs which were substantively modified		
	Definition and handling of barriers systems including disinfection/decontamination	from § 4.18 to 4.24
	Handling of gas filters	from § 6.18 to 6.20 and 8.89 & 8.90
	Personnel qualification & gowning	§ 7.5 & 7.6 and from 7.14 to 7.16
	Aseptic production	from § 8.11 to 8.19
	Moist heat sterilisation	from § 8.54 to 8.65
	Personnel monitoring	§ 9.32 & 9.33
	Aseptic process stimulation (APS)	§ 9.34 & 9.40 & 9.47
	Quality control	§ 10.1

What about the other paragraphs?

2.3 Please avoid re-submitting comments which you already submitted at the first consultation"

Annex-1-targeted-stakeholder-consultation 2020 TEMPLATE

Last Sections: 3 & 4

3. Name and contact details of the reviewing organization

4. Comments

- Line number (s)
- Comments
- Suggested text
- Justification

1
2
3
4

Annex 1, 2nd draft 2020: QRM

Scope

This Annex provides general guidance that should be used for the manufacture of all sterile products using the principles of **Q**uality **R**isk **M**anagement (**QRM**), to ensure that microbial, particulate and pyrogen contamination is prevented in the final product.

QRM applies to this document in its **entirety** and will not be referred to in specific paragraphs. Where specific limits or frequencies are written, these should be considered as a minimum requirement.

They are stated due to regulatory historical experience of issues that have previously been identified and have impacted the safety of patients.

Risk Assessment and Risk Management

In the document Risk in mentioned 119 times!

- **ICH Q9** "Quality Risk Management" adopted by EMA in their guidelines
- Risk Assessment required in chapter 4 "**Cleanroom and clean air equipment qualification**"
  - **Critical processing locations** should be based on a **documented risk assessment** and knowledge of the process and operations to be performed in the area
- Risk Assessment required in chapter 6 "**Utilities**"
  - The nature and extent of controls applied to utility systems should be determined **via a risk assessment documented** as part of the **CCS**
- Risk Assessment required in chapter 8 "**Sterilization by filtration**"
  - PUPSIT is required. An **alternative approach** may be taken as long as **a risk assessment has been performed** and compliance is achieved by using other mitigation.

Questions?

Thank you!

I prossimi webinars della serie Annex 1

Data: 6 maggio 2020 **Ora: 10:00-11:00**

***Gilberto Dalmaso* e *Andrea Simonetti* presenteranno:**

«Panoramica e requisiti di qualifica nei diversi processi produttivi»

- descrizione e analisi degli aspetti critici dei diversi processi e le specifiche fasi di qualifica
- complementarietà delle utilities: acqua, vapore, gas e vuoto
- APS-Aseptic Process Simulation; VI-Visual Inspection e CCI-Container Closure Integrity

Data 13 maggio 2020 **Ora: 10:00-11:00**

***Gilberto Dalmaso* e *Lucia Ceresa* presenteranno**

«Monitoraggio ambientale: un intero nuovo capitolo!»

- L'approccio del controllo della contaminazione nelle aree classificate
- Metodiche analitiche e criticità del monitoraggio incluso il personale
- Requisiti per il monitoraggio delle cleanroom e l'importanza dell'analisi del trend

Data 13 maggio 2020 **Ora: 10:00-11:00**

Gilberto Dalmaso e Lucia Ceresa presenteranno

«Come è cambiata la figura professionale nelle produzioni farmaceutiche»

- Quali sono i criteri di assunzione, responsabilità, capacità.
- I criteri educazionali e il razionale nella definizione dei training.
- I criteri di qualifica e di controllo degli operatori

https://www.pda-it.org/eventi/2020_annex-1_3-webinar-maggio/