Lonza Response to EC Consultation Document:

Targeted stakeholder consultation on the draft Guidelines on Good Manufacturing Practice for Advanced Therapy Medicinal Products

23 September 2016

Introduction

Lonza welcomes the opportunity to review and provide feedback on the European Commission draft proposals on the development of Good Manufacturing Practice for Advanced Therapy Medicinal Products ("ATMPs") pursuant to Article 5 of Regulation 1394/2007.

Lonza is one of the world's leading suppliers of active pharmaceutical ingredients (APIs) and biopharmaceuticals, as well as research and testing products and services. Lonza customers cover a wide spectrum of clients, from the world's largest pharmaceutical and biotechnology companies to medical research and testing organizations to small startups pioneering breakthrough medical treatments. Lonza is also a leading contract manufacturer of cell and gene therapy products, with facilities in Singapore, and Houston and Walkersville in the US, supplying a broad range of customers with investigational ATMPs for use in clinical studies which are run by our customers in the EU and globally. Lonza is therefore engaged in both the development and manufacture of ATMPs. Lonza is committed to supporting customers in the development through to commercial supply in a rapidly developing field and recognises the need to ensure that adequate GMP requirements are in place to ensure patient safety and product consistency with regard to all ATMPs.

Comments on the draft GMP guideline are provided in the following sections

Lonza feedback to European Commission

Section	Line No	Lonza Feedback
1/Introduction	102-106	Responsibility of the Quality Unit needs to be fully defined. Recommend that Annual Product Review is required for Licensed products
2.1/Risk Based approach (RBA) Intro	167-170	Include reference to ICH Q9 or Risk Management tools in general
3.4/Key personnel	429-434	The quality unit should be better defined, to include the role of Quality Assurance and responsibility for actions such as deviations, change control., Qualification/validation. Also include job descriptions as requirements
4.1 Premises general principles	440	General principles listed in the sub paragraph should include pest control
4.2.1/ Production areas/Design	461-465 and 472-474	The lack of segregation for early stage clinical products is a potential risk if not managed adequately
4.2.2/ Production areas aseptic environment	492-537	It is recommended that the section covering aseptic environment is consistent with current requirements for medicinal products (Eudralex Vol 4 Annex 1) and elsewhere in this document. For example: Room qualification only measuring 0.5µm particles. No qualification of 5µm particles required. This appears to be inconsistent with section further down
4.2.3/Environmental monitoring	539-616	It is recommended that the section covering aseptic environment is consistent with current requirements for medicinal products (Eudralex Vol 4 Annex 1) and elsewhere in this document
4.3/Storage areas	634-635	Arrangements for storage of rejected, returned and recalled materials and equipment should be consistent with Eudralex Vol 4 Part 1 Ch. 5 and 8
4.4/QC Areas	641-643	The approach for in-process testing should be consistent with that set out in Eudralex Vol4
6.4/Other documentation	842-855	Current proposal is not aligned with Eudralex Vol 4 requirements and should specify for example, training records, records of supplier audits, change control and pest control
7.2/Raw materials	934-936	Requirements for compliance with PhEur 5.2.12 should be clarified with respect to licensed ATMPs
7.2/Raw materials	934-936	There should be a requirement for a Quality Agreement to be in place for raw material suppliers
7.3/Starting materials	1033-1036	Further guidance on the use of non-GMP starting materials as an exception and the necessary risk assessment would be beneficial., together with clarity on how Competent Authorities would propose a control strategy.
8/Seed lot and cell bank system	1085 - 1090	Greater clarity is required concerning the use of non-GMP cell banks.
9.2/Handling incoming materials and	1168 -1172	This section allows for the possibility of not undertaking ID tests on incoming materials and allows for alternative use of manufacturer's documentation without specific testing. These principles are

products		inconsistent with requirements in EU GMP Chapters 5& 6, Guideline 2015/C 95/02 and Annex 8.
9.9/Rejected, recovered and returned materials	1412-1428	Appears to be inconsistent with earlier section which allows e systems for rejected products. Allows use of returned material without QP approval
10.1 c Qualifications of premises and equip general principles	1494-1499	More clarity on level of detail, control of documentation, need for an agreed protocol and expectations of reports.
10.2/Cleaning validation	1520-1521	Greater clarity on the meaning of 'closely related' ATMPs is required, especially for multi-product facilities and applicability to autologous products. This section only refers to equipment but is earlier referenced for facility cleaning.
10.3/Process validation	1601-1607	Greater clarity is required with respect to process validation. It is unclear how approaches for concurrent validation might work, so further detail would be required. Further clarity is required concerning the use of one validation process for similar product types
11.4/Handling unplanned deviations	1800-1802	Alignment with Annex 16 is proposed. Annex 16 indicates that unplanned deviations should cover specifications for active substances, excipients, packaging and final product. Use of risk assessment tools would be appropriate.
11.5/Admin of OOS products	1809-1817	There should be clarity with whom lies the responsibility of administering an out-of-specification product, . the sponsor or the clinician. Advice on re-processing should be consistent with other sections within the guidance.
12.1/QC general principles	1834-1846	Requirements for managing quality defects should be clarified.
12.4/Stability program	1978-1983	Greater clarity is required through cross reference to Eudralex Vol Chap 6
13.2/Obligations of contract giver	2002-2004	Propose that this should be aligned with Eudralex Vol 4 Ch 7 for licensed ATMPs
14.1/ Quality Defects	2040-2042	Propose that this is aligned with Eudralex Vol 4 Chapter 8 requiring notification of recalls to Competent Authority
14.2/Product recalls	2047-2053	Align with Eudralex Vol 4 Chapter 8 requiring notification of recalls to Competent Authority
17.1/Automated production – general principles	2116	Lonza support the overall approach to the use of automated equipment.
17.2/Automated equipment	2134-2138	Further clarification is required on the statement ' *but CE marking does not suffice as a means of demonstrating suitability*