European Industrial Pharmacists Group
Groupement des Pharmaciens de l'Industrie en Europe

EIPG Comments on EC Consultation Document
"Good Manufacturing Practice for Advanced Therapy Medicinal Products"

http://ec.europa.eu/health/human-use/advanced-therapies/developments/index_en.htm

General Comments

The European Industrial Pharmacists Group (EIPG) is a European association representing the national, professional organisations of pharmacists employed in the pharmaceutical or allied industries of the Member States of the EU, the EEA and European countries having a mutual recognition agreement with the EU on compliance control of regulated medicines. EIPG represents about 12,000 industrial pharmacists.

We have examined this latest version of the document and have focused on a number of details as we understand the objective of this consultation is a revision and refinement of the document. Our observations and suggestions are based on the practical experience of our members, mainly experts in quality and GMP.

We are satisfied that this document represents a solid foundation of guidance for those manufacturing ATMPs. We should like to re-emphasise, as shown in lines 167-170, that these rules should be applied not only to staff in industry but also to academic and hospital sites where ATMPs or their intermediates are manufactured. The issue is about the preparedness of these sites for GMPs and the awareness of Health Authorities (Drug Agency) in extending their inspection activity to these sites.

Detailed comments, observations and suggestions are reported with reference to the line(s) number(s)

167-170: it is observed that inspections by Local Health Authorities will be required not only to industry but also to hospitals and academic sites when they participate in any step of the process

188-189: examples would be helpful to clarify this requirement

240-241: a guidance about suppliers qualification could be useful, to clarify the "acceptable level"

255-257: examples should be helpful to clarify this requirement

280: a definition of "*substantial manipulation*" would be useful

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394-395: in grade A/B, gloves should be regularly disinfected during operations and masks and gloves should be changed at least for every working session

417: as protocols about vaccination vary from country to country, it would be better to define the minimum vaccination requirements

427-428: QC responsibility should be extended to auxiliary materials, such as sterile clothing, disinfectants

441(a): disinfection efficacy should be assessed

444(c): pressure differentials should be appropriate as required by the different area grades (A, B, C and D)

447(d): particle monitoring would be included

451-452: examples of "*appropriate control measures should be applied*" would be useful

496: it would be better to replace *sterilization* with "*terminal sterilization*"

499: *sterility* should be changed in "*aseptic conditions*"

506 Note 5: a closed system also protects the product from the personnel

527: reference to EU GMP- Annex 1 should be made

529 Note 6: the definition of "*at rest*" should be the following: the "at-rest" state is the condition where the installation is installed and operating, complete with production equipment but with no operating personnel present

530 table: the criteria of the new (2016) ISO 14644-1 should be considered

534-535: disinfectants rotation should be better described: the rotation is needed not only to avoid strain resistance, but also to achieve a broader range of bio decontamination activity

536: the air lock should be validated

546-548: in addition to alarm limits, a set of alert limits should be defined

551: for grade A areas, the continuous monitoring is not referenced (only if and when possible)

560: the term "*recommended*" could be misleading

591: the methods should be validated

673: the minimum requirements for computerized systems about security, user profiles, back-ups and audit trail should be mentioned. The electronic signature is never mentioned and considered

693: documentation should be stored in a way to protect it from destruction (e.g.: fire)

701: photographic and/or video recording

707-708: the ALCOA concept could be mentioned

815: the packaging integrity of the received materials should be documented

845: manufacturing process and aseptic process (media-fill)

889: the time of 30 years seems excessive

957-959: minimum provisions about supplier/vendor selection, qualification and monitoring are missing

962-964: it would be better to report "*BSE/TSE*"

977 and 1028-1029: it would be better to add a foot note about the use of "*barcodes*"

1000-1006: minimum requirements about quality agreement should be reported

1197: the current standard is normally from 80 to 85°C

1199: alert limits are not mentioned

1200-1202: for this material the supplier qualification is of paramount importance

1313: it could be useful to insert provisions about the depyrogenation of primary packaging

1322-1324: provisions for the maximum time for filtration should also be given

1331: no provisions are given for the use of gases (nitrogen, CO2 etc.) in the simulation (growth inhibition)

1348: the identification should be done to species level

1354: it is suggested to challenge the areas and process with the maximum number of persons (including maintenance personnel)

1438 & 1349: re-qualification at appropriate intervals, according to a Risk Based Approach

1724-1725: this is in agreement with supplier's certification

1800: it would be better to use the term "deviation" for unexpected events and "changes (temporary or permanent" for planned initiatives (the term: unplanned deviation is not the current industry standard)

1834: when QC activities (all or some) are outsourced, the contact lab should be qualified and suitable formal agreements established

1846: also mention hospitals and investigational sites

1863: it would be beneficial to have the definition of "Reference samples" and "Retain samples" together with the relevant requirements (taken form Annex 19)

1932-1934: including primary packaging

1939: paper and electronic raw-data should be considered and kept

2002-2004: one should do every reasonable effort to execute specialized tests under GMP (e.g.: PCR)

2046: a recall simulation should be executed periodically

2179-2178: more details or clarification about "the operating room" in the hospital and responsibilities towards Health Authorities should be reported

26th September, 2016