SUMMARY OF RESPONSES TO THE PUBLIC CONSULTATION ON COMMISSION GUIDELINES ON GOOD MANUFACTURING PRACTICE FOR INVESTIGATIONAL MEDICINAL PRODUCTS FOR HUMAN USE, PURSUANT TO THE SECOND SUBPARAGRAPH OF ARTICLE 63(1) OF REGULATION (EU) NO 536/2014

1. GENERAL REMARKS

Regulation (EU) No 536/2014 of the European Parliament and of the Council on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC[1] requires in the second subparagraph of Article 63(1) that the Commission adopts and publishes detailed guidelines of good manufacturing practice (GMP) for investigational products for human use.

Such detailed guidelines are necessary to complement the high-level principles and guidelines on GMP for investigational medicinal products for human use to be set out in a Delegated Act, pursuant to the first subparagraph of Article 63(1) of Regulation (EU) No 536/2014.

As guidelines on GMP for investigational medicinal products for human use already exist and are well functioning, hence there is no need to duplicate applicable sections. In consequence, the consultation document referred, when relevant, to specific parts, chapters or annexes of EudraLex Volume 4 or carries over relevant principles of EudraLex Volume 4, Annex 13.

The topics of the consultation document concerning detailed guidelines on good manufacturing practice for investigational medicinal products for human use was to be read in conjunction with the consultation on the Commission Delegated Act on Principles and guidelines of good manufacturing practice for investigation medicinal products for human use and inspection procedures, pursuant to the first subparagraph of Article 63(1) of Regulation (EU) No 536/2014, as the detailed Commission guideline will complement that Delegated Act.

With a view to prepare the guideline, the Commission services launched a public consultation in August 2015. Stakeholders were invited to provide their views on the guidelines of good manufacturing practice by 24 November 2015.

This document presents a factual summary of the responses to the public consultation. It does not present the views of the European Commission.

2. CONTRIBUTORS TO THE PUBLIC CONSULTATION

24 contributions were received. Five contributors claimed confidentiality or anonymity over their submissions. Those contributions will therefore not be publish or published only anonymously.

[1] OJ L 158, 27.5.2014, p.1.

The contributors can be classified into the following categories:

Sector	Contributors included
Public authorities	10
Industry stakeholders	8
Professional organisations	5
NGO	1

3. OUTCOME OF THE PUBLIC CONSULTATION

The contributors commented and remarked on the following topics and aspects:

General aspects:

- Clarification requested as to the status of the guidelines;
- Clarification requested as to GMP/GCP interface and role of sponsor;
- Terminology between the document and Regulation 536/2014 not yet aligned;
- Missing consideration of transition periods specified in Regulation 536/2014;
- Missing guidance on auxiliary medicinal products (AMPs) and non-investigational medicinal products (nIMPs);
- Revise the definition of reconstitution and specify proximity to administration.

Pharmaceutical quality system:

- Elaborate on the following aspects: Quality risk management, "importer", documentation, applicability of CAPA.

Personnel:

- Specifics details missing, such as organization, key personnel, training, personnel hygiene, consultants;
- Role in manufacturing of other than investigational medicinal products, e.g. AMPs, not addressed,
- Acceptance of transitional Qualified Person missing.

Premises and equipment:

- The current text is only limited to cross-contamination;
- Potential issues of cleaning solvent not fully addressed;
- Clarify applicability of qualification and validation.

Order:

- Revise definition and specify retention period of orders.

Product specification file:

- Definition of content, need for continual updates and format unclear;
- Arrangements for retention and reference samples missing;
- Physical storage and accessibility not clear.

Batch records:

- Clarification on retention times needed, perceived difficulties with longer periods, e.g. ≥25 years;
- Define clear responsibilities for storing by manufacturer or sponsor.

Production/Manufacturing operations:

- Specify difference between expiry date and retest date;
- Necessity of full validation questioned; validation should be proportionate to stage of product development;
- Verification of cleaning process is questioned;
- Demonstration of safety not only for biotechnology products but also biologics.

Labelling:

- Clarification on re-labelling of expiry date in terms of need for a QP certification bearing in mind that actual re-labelling activity may take place according to Article 61(5) of Regulation 536/2014;
- Clarification if re-labelling at the investigator site according to Article 61 (5)(c) of Regulation (EU) No 536/2014 is an outsourced activity.

Quality control:

- Retention and reference samples should be retained by the manufacturer for specified time periods;
- Further define the purpose of samples;
- To what extent should definitions of retention sample and reference sample be aligned with those of EudraLex, Volume 4, Annex 19?
- Specify storage period of samples;
- Applicability of samples for AMP missing;
- Clarify provisions for storage of samples outside EU;
- Batch size needs to be sufficient to guarantee full analytical control;
- Does definition of critical quality attributes include sterility?

Release of batches:

- Need for 2 step procedure by QP and sponsor, also for advanced therapy investigational medicinal products;
- Add expected content of the batch certificate as it is currently presented in the attachment 3 to EudraLex Volume 4, Annex 13;
- Import from third countries not sufficiently covered, mention QPs duties relating to imported comparator which does not have certificate of analysis;
- Clarify that the pedigree requirement as outlined in the revised EudraLex Volume 4, Annex 16, including the manufacturing sites of the starting materials and packaging materials, is applicable to commercial medicinal products only;
- Clarification on exemptions from manufacturing according to Article 61(5)(c)and supervision of such processes;
- Include all activities carried out pursuant to Article 61(5);
- Transfer of investigational medicinal products from one trial site to another;
- Reinsert information of distribution and shipping.

Recalls and returns:

- Insert sponsor responsibilities and make reference to importer;
- Define retention period for inventory records on returned IMPs.

Destruction:

- Define sponsor role in the destruction of IMPs;
- Clarify that destruction could also take place at investigator sites.