# SUMMARY OF THE RESPONSES TO THE PUBLIC CONSULTATION ON "THE DEFINITION OF INVESTIGATIONAL MEDICINAL PRODUCTS (IMPS) AND USE OF AUXILIARY MEDICINAL PRODUCTS (AMPS)" RECOMMENDATIONS OF THE EXPERT GROUP ON CLINICAL TRIALS FOR THE IMPLEMENTATION OF REGULATION (EU) NO 536/2014

## 1. GENERAL REMARKS

The Directive 2001/83/EC on the community code relating to medicinal products for human use excludes from its scope "*medicinal products intended for research and development trials*" (Article 3(3)).

Nonetheless, the Regulation (EU) No 536/2014 defines in Article 2(5) an investigational medicinal product (IMP) as "*a medicinal product which is being tested or used as a reference, including as a placebo, in a clinical trial*".

Therefore medicinal products with a marketing authorisation are IMPs too when they are used as the test product, reference product or placebo in a clinical trial. It becomes necessary to have a common understanding of the definitions and requirements of an investigational medicinal product (IMP) and an auxiliary medicinal product (AxMP) administered to subjects in clinical trials.

With this public consultation the Directorate General for Health and Food Safety, DG SANTE, intended to seek the views of stakeholders - and other interested parties - on the document *Definition of Investigational Medicinal Products (IMPs) and use of Auxiliary Medicinal Products (AMPs)* revised by the expert group on clinical trials in preparation for the implementation for the Clinical Trials Regulation (EU) No 536/2014.

**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

The number of contributions received was 26. Five contributors claimed confidentiality or anonymity over their submissions. Their contributions will therefore not be published or published only in anonymous form.

## 3. OUTCOME OF THE PUBLIC CONSULTATION

### 3.1 TITLE (DEFINITION OF INVESTIGATIONAL MEDICINAL PRODUCTS (IMPs) AND USE OF AUXILIARY MEDICINAL PRODUCTS (AMPs))

- Comments on the accuracy of the title were expressed in terms of the guideline going beyond simply providing a definition. The focus is also on AxMPs rather than IMPs.
- As a result of comments received, the abbreviation for Auxiliary Medicinal Product was changed from AMP to AxMP to avoid confusion with Authorised Medicinal Product.

## 3.2 SECTION 2 (MEDICINAL PRODUCTS INTENDED FOR RESEARCH AND CLINICAL TRIALS AND INVESTIGATIONAL MEDICINAL PRODUCTS (IMPs))

- A suggestion that the footnote simply be replaced with a reference to EU or countries that follow the Legislation (i.e., EEA).
- Concerns about the proposed definitions and examples of AxMPs and whether there is a third group of products, which are neither IMPs nor AxMPs. Questions were raised about the inclusion of placebos, as they will not have a marketing authorisation because of the need to demonstrate efficacy. The understanding is that products such as saline infusion solutions, which might be administered as part of treatment to a placebo arm of a trial, are being considered as IMPs.

## 3.3 SECTION 3 (AUXILIARY MEDICINAL PRODUCTS (AMPs)

*What is an IMP?*

- A number of respondents expressed concerns about the proposed definitions and examples of AxMPs. These concerns related especially to challenge agents and concomitant medications not being considered AMPs.
- Respondents had questions about how it would be possible to use an unauthorised medicinal product when an authorised product was available. Requests for specific examples of justifications were made. Also, there were comments about where the justification should be provided, i.e. in the covering letter or the clinical trial protocol.
- Questions about payment for IMPs, AXMPs, medical devices and background treatment/standard of care provided to clinical trial subjects were raised by a number of respondents.
- Remarks about importation of unauthorised medicinal products were received.
- Confusion was expressed by several respondents about the paragraph on unauthorised medicinal products being prepared in accordance with a magistral formula.

*Requirements for AxMPs?*

- Concerns with regard to the clarity of terminus "equivalent standards to GMP" raised.
- Comments on more clarity to the GMP requirements for non-authorized AMP are mentioned.
- Remarks to the degree of modification, which makes an authorised AMP into a non-authorized AMP.
- More examples were desired.

*Documentation requirements in the application dossier?*

- Comments on necessity of documentations for non-authorised AxMPs raised.
- A hint that AMPs may supplied by the sponsor or by the investigator site in accordance with concerned Member State regulations.
- A question if it is possible to enter AMP details in CTA files.
- Concerns with regard of the necessity of country specific labelling and package leaflet for AMPs.
- Minor re-wording useful for clarification in respect to the dossier for authorised AMPs.
- Typo: Full stop missing.
- Replace 'Medicinal Product' by 'AMP'

*Safety reporting*

- Asked for more clarity and details on reporting requirements of adverse events with regard to
  - Legislation: EU regulation 536/2014 and Dir 2001/83/EC
  - Responsibility of investigator and sponsor
  - Route of reporting
  - Differences between authorised and non-authorised AxMPs
  - Serious and non-serious adverse events.

*Annex*

- Examples are discussed.
- Additional examples e.g. for rescue/escape or challenge agents are proposed.
- Distinction from concomitant medication is asked for as definition and example.