From: eu-cooperation <eu-cooperation@pei.de>
Sent: 24 November 2015 15:41
To: SANTE-D6-GL-GMP-IMP
Cc: [redacted]; SANTE-D6-DA-GMP-IMP
Subject: Paul-Ehrlich-Institut comments_Public consultations on GMP for IMPs for human use and inspection procedures

Dear Sir or Madam,

on behalf of the Paul-Ehrlich-Institut, Germany, please find below our comments on consultation document: "Detailed Commission guideline on good manufacturing practice for investigational products for human use, pursuant to the second paragraph of Article 63(1) of regulation (EU) No. 536/2014"

General Remarks (in line with the comment from MHRA):

The two-step release for investigational medicinal products should be kept. We propose to add a section on distribution to reflect the requirements laid out in section shipping of the current Annex 13 with the following wording:

DISTRIBUTION

1. Investigational medicinal products should remain under the control of the sponsor until after completion of a two-step procedure: certification by the Qualified Person; and release by the sponsor for use in a clinical trial following fulfilment of the requirements of Article 4 of Regulation 536/2014. Both steps should be recorded and retained in the relevant trial files held by or on behalf of the sponsor. The sponsor should ensure that the details set out in the clinical trial authorisation and considered by the Qualified Person are consistent with what is finally accepted by the Competent Authorities. Suitable arrangements to meet this requirement should be established. In practical terms, this can best be achieved through a change control process for the Product Specification File and defined in a Technical Agreement between the Qualified Person and the sponsor.
2. The manufacturer/importer is responsible for ensuring that the distribution of the products minimises any risk to their quality and takes account of the applicable principles of Good Distribution Practice in accordance with the pharmaceutical quality system requirements listed in EU GMP Guide Part I: Chapter 1.
3. Transportation and distribution of investigational products should be conducted according to instructions given by or on behalf of the sponsor in the distribution order. Records to support the chain of custody and, where appropriate, temperature control of the product must be maintained. Responsibility for the control of the investigational medicinal product remains with the sponsor (or representative) until it has been accepted by the investigator site.
4. De-coding arrangements should be available to the appropriate responsible investigator site personnel before investigational medicinal products are received at the investigator site.
5. A detailed inventory of the shipments made by the manufacturer/importer should be maintained. It should particularly mention the addressees' identification.
6. Transfers of investigational medicinal products from one trial site to another should remain the exception. Such transfers should be covered by standard operating procedures. The product history while outside of the control of the manufacturer, through for example, trial monitoring reports and

records of storage conditions at the original trial site should be reviewed as part of the assessment of the product's suitability for transfer and the advice of the Qualified person should be sought. The product should be returned to the manufacturer, or another authorised manufacturer, for re-labelling, if necessary, and certification by a Qualified Person. Records should be retained and full traceability ensured.

Additional comments:

1. The two-step release should also apply to ATIMPs which are excluded from the "Detailed commission guidelines on GMP for IMPs for human use, pursuant to the second subparagraph of Article 63(1) of Regulation EU No 536/2014". Therefore, the section distribution of ATIMPs should be included in the requirements for manufacturing of ATMPs.
2. Line 100: Add "emulsifying" to read: - dissolving, emulsifying or dispersing ...
3. Line 110: add "unless otherwise justified" to read: ...as close as possible to the administration, unless otherwise justified and has to be defined in the clinical trial application.....
4. Line 349: Typ-0: Annex IV is referred to instead of Annex VI: labelling is set out in Annex VI to said Regulation.

Kind regards.

EU-Kooperation biomedizinische Arzneimittel / EU Co-operation Biological Medicinal Products
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