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Legislation

European Union

Commission Delegated Regulation (EU) 2017/1569 of 23 May 2017 supplementing Regulation (EU) No 536/2014 of the European Parliament and of the Council by specifying principles of and guidelines for good manufacturing practice for investigational medicinal products for human use and arrangements for inspections

Published in OJ L 238 of 16/09//2017 (http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32017R1569&from=en), Commission Delegated Regulation (EU) 2017/1569 specifies the principles and guidelines of good manufacturing practice for investigational medicinal products for human use the manufacture or import of which requires an authorisation as referred to in Article 61(1) of Regulation (EU) No 536/2014 and lays down arrangements for inspections of manufacturers in relation to compliance with good manufacturing practice in accordance with Article 63(4) of that Regulation.

As highlighted in the recitals of the new regulation, the manufacturing operations for investigational medicinal products should be subject to a highly effective pharmaceutical quality system because their manufacture presents additional challenges comparing to the manufacturing of authorised medicinal products, among other reasons because there are no fixed routines, there is a variety of clinical trial designs and consequently packaging designs.

Apart from that, the principles and guidelines of good manufacturing practice for investigational medicinal products for human use should be aligned as much as possible with those applicable to medicinal products for human use.

Commission Directive (EU) 2017/1572 of 15 September 2017 supplementing Directive 2001/83/EC of the European Parliament and of the Council as regards the principles and guidelines of good manufacturing practice for medicinal products for human use

Commission Directive 2003/94/EC of 8 October 2003 laid down the principles and guidelines of good manufacturing practice in respect of medicinal products for human use and investigational medicinal products for human use. Subsequently, however, Article 63(1) of Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC, stated that the Commission shall be empowered to adopt delegated acts in order to specify the principles and guidelines of good manufacturing practice and the detailed arrangements for inspection for ensuring the quality of investigational medicinal products. (See previous entry in this digest).

It therefore became necessary to adapt the provisions of Commission Directive 2003/94/EC by deleting references to investigational medicinal products for human use and this is precisely what Commission Directive (EU) 2017/1572 has done [OJ L 238 of 16 September 2017 (http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32017L1572&from=en)].

Commission Delegated Regulation (EU) 2017/1798 of 2 June 2017 supplementing Regulation (EU) No 609/2013 of the European Parliament and of the Council as regards the specific compositional and information requirements for total diet replacement for weight control

Published in OJ L 259 of 7/10/2017 (http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32017R1798&qid=1511183425227&from=en), Commission Delegated Regulation (EU) 2017/1798 provides that total diet replacement for weight control products shall comply with the compositional requirements set out in Annex I, taking into account the specifications in Annex II.

Of particular interest is Article 6, which deals with nutrition and health claims, stipulating that "nutrition and health claims shall not be made on total diet replacement for weight control products", although the nutrition claim 'added fibre' may be used for total diet replacement for weight control products provided that the dietary fibre content of the product is not less than 10 g.

Lastly, according to Article 7, when total diet replacement for weight control products are placed on the market, the food business operator shall notify the competent authority of each Member State where the product concerned is being marketed of the information appearing on the label, by sending to it a model of the label used for the product, and of any other information the competent authority may reasonably request to establish compliance with this Regulation, unless a Member State exempts the food business operator from that obligation under a national system that guarantees an efficient official monitoring of the product concerned.

Brexit's effects on marketing authorisations for medicinal products obtained via the centralized procedure

On 2 May 2017, the European Commission and the European Medicines Agency (EMA) published a 'Notice to marketing authorisation holders of centrally authorised medicinal products for human and veterinary use' (http://www.ema.europa.eu/docs/en_GB/document_library/Other/2017/05/WC500226603.pdf).

The aforementioned notice reminds marketing authorisation holders of centrally authorised medicinal products for human and veterinary use that EU law requires that such holders are established in the EU (or EEA) and that some activities must be performed in the EU (or EEA),

related for example to pharmacovigilance, batch release, etc. The Commission and the EMA also expect such holders to prepare and proactively screen authorisations they hold for the need for any changes and recall that the necessary transfer or variation requests will need to be submitted in due time considering the procedural timelines foreseen in the regulatory framework. In addition, the Commission and the EMA announce the preparation of a series of Q&As.

In fulfilment of this undertaking, the document 'Questions and Answers related to the United Kingdom's withdrawal from the European Union with regard to the medicinal products for human and veterinary use within the framework of the Centralised Procedure' (http://www.ema.europa.eu/docs/en_GB/document_library/Other/2017/05/WC500228739.pdf) has been prepared and published.

Entry into application of the EU Clinical Trial Regulation postponed

The European Medicines Agency (EMA) has issued a press release announcing the postponement of the application of Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC.

In accordance with this regulation, and in order to streamline and facilitate the flow of information between sponsors and Member States as well as between Member States, the Agency shall, in collaboration with Member States and the Commission, set up and maintain an EU database, accessed through an EU portal acting as a single entry point for the submission of data and information relating to clinical trials.

According to Article 99, in conjunction with Article 82, this regulation shall apply as from six months after the publication of the Commission's notice that the EU clinical trials portal and database have achieved full functionality.

Although October 2018 was initially scheduled as such date of application, the EMA has announced that, due to technical difficulties in the start-up of the aforementioned portal, the regulation will now come into application in 2019. See 'EMA Management Board: highlights of June 2017 meeting Focus on Brexit preparations and the development of the EU clinical trial portal and database' (http://www.ema.europa.eu/docs/en_GB/document_library/Press_release/2017/06/WC500229512.pdf).

Applications for a CHMP (Committee for Medicinal Products for Human Use) Scientific Opinion in the context of co operation with the World Health Organization (WHO) for the evaluation of medicinal products intended exclusively for markets outside the European Union (EU) for human use submitted to the

European Medicines Agency

By virtue of Article 58 of Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, the Agency's CHMP may give opinions, in co-operation with the WHO, on medicinal products for human use that are intended exclusively for markets outside the EU.

In August 2017, the Agency published a new version of its document 'EMA procedural advice for medicinal products intended exclusively for markets outside the European Union under Article 58 of Regulation No 726/2004 in the context of co-operation with the World Health Organisation (WHO)' (EMA/534107/2008 Rev.1). Available at http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2010/02/WC500074039.pdf.

Notification to the Joint Sectoral Committee by the European Union under Article 7 of the Sectoral Annex on Pharmaceutical Good Manufacturing Practices of the Agreement on Mutual Recognition between the European Community and the United States of America

1. According to Article 7 of the Sectoral Annex on Pharmaceutical Good Manufacturing Practices (GMPs) of the Agreement on Mutual Recognition between the European Community and the United States of America (GMPs Annex), as amended on 1 March 2017, each Party shall determine whether to recognize an authority according to the criteria specified in Appendix 4. Each Party shall promptly notify the Joint Sectoral Committee of any determination to recognize an authority of the other Party. The Joint Sectoral Committee shall maintain a list of recognized authorities and shall keep the list up-to-date. The list shall be made publicly available by each Party.

The European Union has notified the Joint Sectoral Committee that "for the product scope indicated in Article 4 and Appendix 3 to the GMPs Annex the Food and Drug Administration of the United States of America has the capability, capacity and procedures in place to carry out GMP inspections at a level equivalent to the EU and enforce compliance with GMP and therefore, shall be added to the list of recognised authorities under the GMPs Annex".

2. It should be recalled that, according to Article 4 of the GMPs Annex, the provisions of said Annex apply to marketed finished pharmaceuticals for human or animal use, intermediates (for the EU as defined in EU legislation) and in-process materials (for the United States as defined under U.S. law), certain marketed biological products for human use, and active pharmaceutical ingredients, only to the extent they are regulated by the authorities of both Parties as listed in Appendix 2 and subject to Article 20. And Appendix 3 contains the list of products covered by this Annex.

3. The notification was signed in Brussels on 11 August 2017 and published in OJ L 237/6 of 15.9.2017 (https://publications.europa.eu/en/publication-detail/-/publication/a7e4815b-99da-11e7-b92d-01aa75ed71a1/language-en).

Amendment to Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH)

1. Annex XVII to Regulation (EC) No 1907/2006 prohibits the placing on the market or use for supply to the general public of substances that are classified as carcinogenic, mutagenic or reproductive toxicant (CMR), category 1A or 1B, and of mixtures containing such substances in specified concentrations.

2. Commission Regulation (EU) 2017/1510 of 30 August 2017 amending the Appendices to Annex XVII to Regulation No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) as regards CMR substances has been adopted and published in OJ L 224 of 31.8.2017 (http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32017R1510&from=EN).

Judgments and decisions

European Union

National measures prohibiting the cultivation of genetically modified food and feed

1. The Judgment of the Court (Third Chamber) of 13 September 2017 in Case C-111/16, in response to a request for a preliminary ruling from the *Tribunale di Udine* (District Court, Udine, Italy) in criminal proceedings against Giorgio Fidenato, Leandro Taboga and Luciano Taboga, has interpreted Article 34 of Regulation (EC) No 1829/2003 of the European Parliament and of the Council of 22 September 2003 on genetically modified food and feed. And it has done so in relation to the national measures adopted by the Italian Government to prohibit the cultivation of the genetically modified maize variety MON 810 (Decree prohibiting the cultivation of varieties of genetically modified maize MON 810 on the basis of Article 54 of Regulation (EC) No 178/2002) of 12 July 2013).

2. Article 34 of Regulation No 1829/2003, entitled ‘Emergency measures’, states that where it is

evident that products authorised by or in accordance with this Regulation are likely to constitute a serious risk to human health, animal health or the environment, measures shall be taken under the procedures provided for in Articles 53 and 54 of Regulation No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety.

It should be recalled that, according to Regulation No 178/2002 (Article 53), where it is evident that food or feed originating in the Community or imported from a third country is likely to constitute a serious risk to human health, animal health or the environment, and that such risk cannot be contained satisfactorily by means of measures taken by the Member State(s) concerned, the Commission, on its own initiative or at the request of a Member State, shall immediately adopt one or more of the following measures, depending on the gravity of the situation: (a) in the case of food or feed of Community origin: (i) suspension of the placing on the market or use of the food in question; (ii) suspension of the placing on the market or use of the feed in question; (iii) laying down special conditions for the food or feed in question; (iv) any other appropriate interim measure; (b) in the case of food or feed imported from a third country: (i) suspension of imports of the food or feed in question from all or part of the third country concerned and, where applicable, from the third country of transit; (ii) laying down special conditions for the food or feed in question from all or part of the third country concerned; (iii) any other appropriate interim measure. And, in emergencies, the Commission may provisionally adopt the measures referred to in paragraph 1 after consulting the Member State(s) concerned and informing the other Member States.

Aside from this, Article 54 of the aforementioned Regulation provides that where a Member State officially informs the Commission of the need to take emergency measures, and where the Commission has not acted in accordance with Article 53, the Member State may adopt interim protective measures. In this event, it shall immediately inform the other Member States and the Commission.

3. According to the Court of Justice:

   (a) The European Commission is not required to adopt emergency measures within the meaning of Article 53 of Regulation No 178/2002 when a Member State officially informs the Commission, in accordance with Article 54(1) of that regulation, of the need to take such measures, as long as it is not evident that products authorised by Regulation No 1829/2003 or in accordance with that regulation are likely to constitute a serious risk to human health, animal health or the environment.

   (b) Article 34 of Regulation No 1829/2003, read in conjunction with Article 54 of Regulation No 178/2002, must be interpreted as meaning that a Member State may, after officially informing the European Commission of the need to resort to emergency measures, and

where the Commission has not acted in accordance with Article 53 of Regulation No 178/2002, first, adopt such measures at the national level and, second, maintain or renew such measures, so long as the Commission has not adopted, in accordance with Article 54(2) of that regulation, a decision requiring their extension, amendment or abrogation.

(c) Article 34 of Regulation No 1829/2003, read in conjunction with the precautionary principle as set out in Article 7 of Regulation No 178/2002, must be interpreted as meaning that it does not give Member States the option of adopting, in accordance with Article 54 of Regulation No 178/2002, interim emergency measures solely on the basis of that principle, without the conditions set out in Article 34 of Regulation No 1829/2003 being satisfied.

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