EUROPEAN COMMISSION
Directorate-General for Health and Food Safety

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NOTICE TO STAKEHOLDERS

WITHDRAWAL OF THE UNITED KINGDOM AND EU RULES IN THE FIELD OF CLINICAL TRIALS

The United Kingdom submitted on 29 March 2017 the notification of its intention to withdraw from the Union pursuant to Article 50 of the Treaty on European Union. This means that unless a ratified withdrawal agreement[1] establishes another date, all Union primary and secondary law will cease to apply to the United Kingdom from 30 March 2019, 00:00h (CET) ('the withdrawal date'). The United Kingdom will then become a 'third country'.[2]

Preparing for the withdrawal is not just a matter for EU and national authorities but also for private parties.

In view of the considerable uncertainties, in particular concerning the content of a possible withdrawal agreement, sponsors (both academic researchers and pharmaceutical companies) conducting or planning to conduct clinical trials, as well as investigators and other persons involved in the preparation and conduct of clinical trials in the EU are reminded of legal repercussions, which need to considered when the United Kingdom becomes a third country.

Subject to any transitional arrangement that may be contained in a possible withdrawal agreement, as of the withdrawal date, the EU rules on clinical trials, and in particular Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use[3] no longer apply to the United Kingdom. This has, in particular, the following consequences:[4]

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1 Negotiations are ongoing with the United Kingdom with a view to reaching a withdrawal agreement.

2 A third country is a country not member of the EU.

3 OJ L 121, 1.5.2001, p. 34.

4 Directive 2001/20/EC is going to be repealed by Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use (OJ L 158, 27.5.2014, p. 1). However, in view of the timelines set in its Article 99, this Regulation is not going to apply before the withdrawal date.

1. SUPPLY OF INVESTIGATIONAL MEDICINAL PRODUCTS

According to Article 13(1) of Directive 2001/20/EC, the import of investigational medicinal products into the EU is subject to the holding of an authorisation. This authorisation is also required if only part of the manufacturing (e.g. packaging or repacking, for example as part of blinding activities) is performed in the third country. Article 13(2) of Directive 2001/20/EC requires the holder of this authorisation to have permanently and continuously at his disposal the services of at least one qualified person located in the EU. The qualified person is responsible for ensuring that each production batch of an investigational medicinal product intended to be used in a clinical trial has been manufactured and checked in accordance with the standards of good manufacturing practices at least equivalent to those laid down in the EU and that each production batch has been checked in accordance the clinical trial authorisation (Article 13(3)(b) of Directive 2001/20/EC). Regarding comparator investigational medicinal products which are authorised in a third country, the qualified person is responsible for ensuring, subject to exceptions, that each production batch has undergone all relevant analyses, tests or checks necessary to confirm its quality (Article 13(3)(c) of Directive 2001/20/EC). Retesting (analytical control) in the EU is not mandatory if already carried out in the third country (Article 11(2) second subparagraph of Commission Directive 2003/94/EC[5]).

As of the withdrawal date, these rules will apply to investigational medicinal products imported from the United Kingdom to the EU.

2. ESTABLISHMENT REQUIREMENTS FOR THE SPONSOR OR THE LEGAL REPRESENTATIVE

According to Article 19 of Directive 2001/20/EC, the sponsor of a clinical trial or a legal representative must be established in the EU. As of the withdrawal date, a sponsor established in the United Kingdom and conducting a clinical trial in the EU-27 has to ensure that a sponsor or a legal representative is established in the EU-27. The change of the sponsor or of the sponsor's legal representative is typically a substantial amendment,[6] which requires notification to the competent authority/information of the Ethics Committee in accordance with the procedure set out in Article 10(a) of Directive 2001/20/EC.

3. SUBMISSION OF CLINICAL TRIAL INFORMATION

Provisions of EU law relating to clinical trials[7] provide for the submission of certain clinical trial information to the EU clinical trials database EudraCT.

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5 Commission Directive 2003/94/EC of 8 October 2003 laying down the principles and guidelines of good manufacturing practice in respect of medicinal products for human use and investigational medicinal products for human use, OJ L 262, 14.10.2003, p. 22.

6 See point 123(a) of the Communication from the Commission — Detailed guidance on the request to the competent authorities for authorisation of a clinical trial on a medicinal product for human use, the notification of substantial amendments and the declaration of the end of the trial (CT-1) (OJ, 30.3.2010, p. 1).

7 Cf. Articles 41 and 46 of Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use (OJ L 378, 27.12.2006, p. 1),

Regarding protocol-related information, as of the withdrawal date, UK-specific trial information will no longer have to be submitted to EudraCT, except when the trial is part of an agreed Paediatric Investigation Plan and the United Kingdom is the only country in which the protocol has been submitted.

Regarding result-related information, results of clinical trials conducted in the United Kingdom and completed before the withdrawal date must be submitted to EudraCT if the reporting of these results is due before the withdrawal date. Results of clinical trials conducted only in the United Kingdom and results of multi-country trials where the United Kingdom was the only EU/EEA Member state where the clinical trial was conducted have to be submitted to EudraCT, also after the withdrawal date, if this is required for non-EU/EEA studies (i.e. if the trial is part of an agreed Paediatric Investigation Plan or falls in the scope of Article 46 of Regulation (EC) No 1901/2006).

The websites of the Commission on clinical trials (https://ec.europa.eu/health/human-use/clinical-trials_en) provide general information. These pages will be updated with further information, where necessary.

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Article 57 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 (OJ L 136, 30.4.2004, p. 1), and the implementation guidelines published in EudraLex, Volume 10 (https://ec.europa.eu/health/documents/eudralex/vol-10_en).