Requirements on the management of clinical trials ongoing in Italy that Sponsors will have to meet after 29 March 2019, in case of no-deal Brexit

AIFA informs Sponsors of clinical trials ongoing in Italy that, due to the uncertainty about the conclusion of the negotiations concerning the withdrawal of the United Kingdom from the European Union (EU), it is highly recommended that they meet in advance some requirements by 29 March 2019. Given the present regulatory framework and waiting for any additional agreement between United Kingdom and the European Union, in fact, since 30 March 2019 the United Kingdom will have to be considered a Third Country.

In this regard, AIFA would like to recall the notice on the withdrawal of the United Kingdom and EU rules in the field of Clinical Trials the European Commission already published (https://ec.europa.eu/info/sites/info/files/notice_to_stakeholders_brexit_clinical_trials_final.pdf)

and the notice on control and batch testing of medicinal products and Brexit

(https://ec.europa.eu/health/sites/health/files/files/documents/brexit_batchtesting_medicinalproducts_en.pdf).

Please note that related requests for substantial amendments must be submitted by 29 March, according to the following instructions.

Requirements related to the Legal Representative. According to the European Directive 2001/20/EC, the Sponsor or its Legal Representative must be established in a EU Member State; therefore, in case of a UK-based Legal Representative of a Sponsor not established in the European Union (EU-27), a new Legal Representative will have to be appointed in one of the EU Member States. Such change will have to be communicated by submitting a notified substantial amendment to AIFA and concerned Ethics Committees through the OsSC, by 29 March 2019, or including it in other substantial amendment requests already being submitted by the same date. In this regard, please see point B of the FAQs published on the AIFA Portal (http://www.aifa.gov.it/content/sperimentazione-clinica). In case it is impossible to fulfill such requests through the OsSC by 29 March, the Sponsor is allowed to notify such change to AIFA and concerned Ethics Committees through the OsSC's Forum by 29 March 2019, updating the situation in the OsSC as soon as possible.

Failing to comply with this regulatory requirement, in fact, could result in the halt of the clinical trial, due to the related legal implications.

Change of the Qualified Person and of the batch release certification site. According to the European Directive 2001/20/EC, the Qualified Person and the site responsible for the batch release must be located in a EU Member State: if the site is located in the United Kingdom, it will have to be transferred in one of the other EU Member States. Such change will have to be communicated to AIFA and the Coordinating Ethics Committee by submitting through the OsSC a substantial amendment to be evaluated, also together with other substantial amendment requests to be evaluated, by 29 March 2019. The request will also have to relate to the transfer or change of the Qualified Person, depending on the case.

In case fulfilling such requests through the OsSC by the above-mentioned date is impossible, the Sponsor is allowed to submit such change to AIFA and the Coordinating Ethics Committee in paper format by 29 March 2019, updating the situation in the OsSC as soon as possible.

Investigational medicinal product supplying. Investigational batches authorized/released in the United Kingdom before 29 March 2019 can be used until their expiration, without repeating in a EU site the analytical tests on the finished product, in the case the analytical test and the batches' shipment have taken place before that date.

As of 30 March, the import into the EU of medicinal products batches for investigational use coming from UK-based sites will need a manufacturing/import authorization and a declaration of a Qualified Person residing in a EU Member State. This also applies to batches authorized for investigational use before 29 March 2019 in UK-based sites, but shipped after this date, or to batches for which a first part had already been shipped from the United Kingdom before 29 March.

The afore-mentioned requirements apply to no profit Sponsors trials as well.

Sponsors who don't have the possibility or encounter technical difficulties in fulfilling the requests set out in this press release, are kindly invited to inform AIFA by 29 March 2019 sending an e-mail to sperimentazione.clinica@aifa.gov.it; the object of the e-mail must mandatorily be "Brexit requirements".

The operating instructions on the management of clinical trials may be updated according to the outcome of the ongoing European negotiations.