Client Alert

October 2014

The European Medicines Agency Adopts Policy on Proactive Publication of Clinical Trial Data

A few days ago, the European Medicines Agency (EMA) finally adopted its policy on the proactive publication of clinical trial data (the "Policy"). The objectives are to allow, in the interest of public health, public scrutiny of the EU decisions relating to medicinal products and application of new knowledge in future research. In practice, the Policy will reduce the EMA's workload in responding to requests for access to documents that concern the published clinical trial data.

So far transparency occurred through requests for access to documents, including clinical trial documents, that were submitted to, and handled by, the EMA in accordance with Regulation 1049/2001[1] and the existing EMA policy[2] on access to documents. The Policy does not limit the application or the rights given by Regulation 1049/2001. It also applies without prejudice to new Regulation 536/2014 on clinical trials (Clinical Trials Regulation) that institutes public access to the EU database of clinical trials. The Policy therefore is only one — limited — piece of the transparency puzzle.

The Policy will come into effect on 1 January 2015 for marketing authorisation applications and on 1 July 2015 for applications for extension of indication or for line extension. The EMA still has to determine the effective date for all other post-authorisation procedures. The clinical data becoming, as a general rule, accessible after the grant of the marketing authorisation (MA) or the withdrawal of the MA application, in practice it will not start becoming accessible until 2016. Clinical trial data submitted before 1 January or 1 July 2015 are subject to the rules on access to documents and the transparency provisions of the Clinical Trials Regulation, unless the documents are resubmitted in a new regulatory application.

Companies may somewhat reduce the impact of the Policy by carefully writing clinical reports and preparing their regulatory dossiers.

Scope

- **Centralised procedure**. — The Policy covers only clinical trial data provided in relation to medicinal products authorised through the centralised procedure. Access to clinical data for medicinal products authorised through the decentralised, mutual recognition or national procedure remains the responsibility of each Member State (*i.e*. national rules on access to documents) and subject to the transparency provisions of the Clinical Trials Regulation. The scope of the Policy therefore is different from that of the Clinical Trials Regulation which is limited to clinical trials conducted in the EU but covers all medicinal products, regardless of the MA procedure.

[1] Regulation (EC) No 1049/2001 of the European Parliament and of the Council of 30 May 2001 regarding public access to European Parliament, Council and Commission documents.

[2] European Medicines Agency policy on access to documents (related to medicinal products for human and veterinary use) (POLICY/0043) (EMA/110196/2006).

- **Marketing authorisations and post-authorisation procedures**. — Access will be given to the clinical data submitted, by the company or third parties, in relation to MA applications, post-authorisation procedures and scientific assessment of applications for medicinal products intended exclusively for markets outside the EU (Art. 58 of Regulation 726/2004).

- **Clinical trial data. —** The EMA will proactively publish clinical trial data, *i.e.* clinical reports and individual patient data (individual data separately recorded for each participant in a clinical study). At first, the publication will concern:

    - clinical study reports (CSRs) (module 5) and the appendixes 16.1.1 (protocol and protocol amendments), 16.1.2 (sample case report form) and 16.1.9 (documentation of statistical methods);

    - clinical overviews (module 2.5); and

    - clinical summaries (module 2.7).

    At a later stage, the EMA plans on making individual patient data (*i.e.* raw data) available, in compliance with privacy and data protection laws. Nevertheless, one may wonder how this will fit with the Clinical Trials Regulation that expressly prohibits access to personal data. Although the Policy does not specify it, we assume that it does not cover articles that have been published in scientific journals and copies of which have been submitted by the company. At that time, the Policy will be amended after consultation with the stakeholders. The EMA will balance the protection of patient privacy and the need to retain scientific value of the clinical data.

    The information will be made available in a searchable format and will be permanently available.

    Access to other documents will remain subject to the rules on access to documents and the transparency provisions of the Clinical Trials Regulation.

Redaction of Commercially Confidential Information (CCI)

The Policy defined CCI as "*Any information contained in the clinical reports submitted to the EMA by the applicant the information that is not in the public domain or publicly available and where disclosure may undermine the legitimate economic interest of this applicant*."

The EMA considers that clinical reports do not, in general, contain CCI but acknowledges that they can and sometimes do. The Policy therefore allows the company to redact CCI by means of redaction principles. Annex 3 of the Policy contains a limited list of information that may be considered CCI and the justification thereof. Other data may be redacted as well, provided that the justification given by the company is agreed upon by the EMA. Justifications may be based on the nature of the product, the competitive situation of the therapeutic market, the approval status in other countries, the novelty of the clinical development and new development by the company.

In practice, the company will submit its redacted documents after the CHMP opinion. The EMA will check the redaction proposed by the company and the justifications thereof. The company will be able to discuss its redaction with the EMA, but the EMA has the final word in the event of disagreement (Annex 4 - Process for publication of clinical reports). So, companies now have several months for redacting the documents rather than the current five days (under the EMA policy on access to documents).

The same concept will be used by the EMA for the application of the rules on access to documents.

Restricted Access - Registration and Terms Of Use

To access the data, the "user" must register with the EMA's web-portal (user ID/password) and agree to terms of use set out by the EMA. These "barriers" are meant to balance transparency and the need to protect CCI and thereby to ensure that the data will be used only for legitimate purposes rather than for unfair commercial use by a competitor.

The Policy distinguishes between:

- Users who want to access the clinical data for research purposes, such as academia, researchers or health technology assessment bodies. They are allowed to download, save, cut and paste and print the documents, provided that they disclose their identity. The Terms of Use for those users are contained in Annex 1 to the Policy.

- Users who want to access the clinical data for general information purposes. They may see the clinical data only on-screen, and must commit not to download, save, edit, photograph, print, distribute or transfer the data. The Terms of Use are contained in Annex 2 to the Policy.

Otherwise, the Terms of Use are the same for all users. In particular, no user may use the clinical data for commercial purposes or unfair commercial use or for re-identification of the trial subjects or other individuals. Users may also not access the information using a method other than the interface provided by the EMA, or remove, bypass, circumvent, neutralise or modify any technological protection measures which apply to the information.

This "agreement" between the user and the EMA is subject to UK law. More importantly, it is extended for the benefit of the company that holds the intellectual property rights on the data. If a user does not fulfil his commitments, the EMA will revoke his access to the data. This sanction, however, is not sufficient in light of the damages that can be caused to the company. While the company may legally enforce the agreement against an infringing user, this enforcement seems somewhat unrealistic, especially as the EMA does not disclose the names of the users to the company unless a Court requires it.

Tension with the Clinical Trials Regulation

The Clinical Trials Regulation requires that clinical study reports be submitted within 30 days of the date of the MA (or the date of withdrawal of the MA application) and mandates public access to the EU database of clinical trials. Public access to the documents in the database may be refused on a few grounds, such as CCI or personal data, but no restriction or condition is set out for accessing the documents. Concerns have already been voiced that the Policy infringes the transparency provisions of the Clinical Trials Regulation.

The EMA considers that the Policy will serve as a complementary tool ahead of the implementation of the new Clinical Trials Regulation, as it may take until 2019 or 2020 before the first clinical trial results under the Clinical Trials Regulation become publically available and the first data in accordance with the Policy is likely to be accessible in 2016. This however means that the concept of CCI developed by the EMA under the Policy will drive the application of the transparency provisions of the Clinical Trials Regulation.

Contacts

Geneviève Michaux
gmichaux@hunton.com

Prof. Lucas Bergkamp
lbergkamp@hunton.com

Gary C. Messplay
gmessplay@hunton.com