

EU Clinical Trials Regulation: EMA steers away from transparency by misinterpreting exception provisions

The European Medicines Agency's (EMA) proposal regarding the specifications of the European Union (EU) clinical trials database can jeopardise the transparency advances obtained through the European Clinical Trials Regulation. We call on the EMA to stay true to the Regulation and ensure that its implementation improves public access to scientific evidence about the effects of medicines on human health.

On 2 April, 2014, the adoption of the new EU Clinical Trials Regulation showed a strong political commitment to transparency by both the European Parliament and Council (1). In fact, public access to clinical trial data allows independent analysis, enhancing knowledge about the real benefits and harms of medicines (a). Yet, as soon as the Regulation was approved, the European Federation of Pharmaceutical Industries and Associations (EFPIA) called on “*the Commission and EMA [to] interpret the Clinical Trial Regulation in a manner that respects (...) incentives for companies to make long-term investments in biomedical research*” [i.e., to protect what they consider commercially confidential information] (2). Judging by the proposal on the specifications of the EU database on clinical trials, which the EMA circulated for public consultation (from 21 January to 18 February, 2015), it appears that the EMA has responded to industry demands (3).

EMA proposal misinterprets the Clinical Trials Regulation and waters down transparency provisions

The EMA's draft proposal aims to interpret the transparency exceptions established in the European Clinical Trials Regulation (Regulation (EU) No 536/2014) (2). However, it misinterprets the Regulation and, as a result, regards non-disclosure as the norm rather than the exception. This creates leeway for non-compliance of sponsors to their legal obligations.

Juan Erviti, Secretary of the *International Society of Drug Bulletins (ISDB)* highlights:

“The EMA's draft is at odds with the principle enshrined in the Clinical Trials Regulation, which is to increase public access to valuable information on clinical trials. This is unacceptable.”

The EMA goes as far as proposing a **very broad definition of “commercially confidential information”**. Its implementation would allow clinical trial sponsors to circumvent the publication of whole documents (including trial protocols, subject information sheets, investigator brochures, the investigational medicinal product dossier, etc.) simply on the grounds that their economic interests *might* be potentially undermined (b,c).

Anel.la Santos Quintano, Policy Advisor with *Health Action International (HAI)*, says:

“According to EU regulations, non-disclosure on the grounds of commercial confidentiality is an exception, not the norm. It is worrying to realise that the EMA's proposal fails to take this into account, even in the case of safety data. Transparency of clinical trial data should always be the default position.”

a- Such analyses allow researchers to compare the effectiveness of treatments and provide healthcare professionals and patients with information to support informed choices.

b- According to EMA's draft, commercially confidential information encompasses “any information contained in the data or documents submitted to the database that is not in the public domain or publicly available and where disclosure may undermine the legitimate economic interest of the sponsor” (ref. 3). Moreover, despite the claim that “*the implementation of the transparency rules of the Clinical Trial Regulation is without prejudice to the application of Regulation (EC) No 1049/2001 and citizens' right to request documents under that Regulation*”, this definition could influence the way the EMA answers to information requests.

c- In our opinion, any exception to disclosure should be justified by the companies who should have to explain how the release of the information they claim to be commercially confidential would truly harm their interests; it should only involve the removal of specific elements within a document and should never be applied to entire sections or certain types of documents (ref. 4).

The EMA also proposes to **defer the trial information (e.g., trial protocols, investigational medicinal product dossier (IMPD) safety and efficacy sections) up to 10 years after the end of a trial** by establishing a complex classification system that ranks clinical trial documents into different categories (as per the “*stage of development*” of a medicinal substance or the “*intent*” of a given trial). Most strikingly, neither the EU Clinical Trials Regulation nor the Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects provide such a “classification” (d). On the contrary, the EU Clinical Trials Regulation clearly highlights the importance of providing public information, even requiring Member States to establish penalties in cases of non-compliance.

According to Pierre Chirac, coordinator of the *Medicines in Europe Forum* (MiEF):

“Clinical trial sponsors will feel entitled to postpone or even avoid the publication of clinical data on the grounds of commercial confidentiality or “trade secrets” protection. Moreover, by proposing to defer the publication of information, such as protocols, up to 10 years after the end of a trial, the EMA demonstrates that it regards clinical trials as industry data, not as scientific data of public interest”(e).

In addition, the document states that “*the EU database will not contain any individual patient listings from clinical trials*” even though such listings are part of clinical study reports (f). De-identified participants’ listings cannot be regarded as patient personal data. They are scientific data that researchers need in order to re-analyse clinical trials’ results. Clinical trial participants often accept putting themselves at risk, hoping that their contribution will benefit society through the advancement of science.

Freedom of information is a fundamental right of European citizens, underlined by the EU Clinical Trials Regulation, to which the EMA must also comply

According to the *Charter of Fundamental Rights* of the EU and to Regulation (EC) N°1049/2001, freedom of information is a fundamental right of European citizens (4). Adopted on 2 April, 2014, the new EU Clinical Trials Regulation is indicative of a strong political commitment to transparency; a commitment to which the EMA must also comply.

Having actively followed the legislative process, which led to the approval of the Clinical Trials Regulation, our organisations re-iterate their commitment to full transparency and urge the EMA to:

- **Publish clinical trial protocol at the time of the decision of the trial** and withdraw the proposal to defer or hamper such disclosure by making only “minimal information” or “summaries” available;
- **Withdraw the proposal for a broad definition of “commercially confidential information”**, as its implementation would result in the censorship of whole documents of public interest and make transparency the exception rather than the rule;
- **Withdraw the proposal to defer the publication of information about a clinical trial** (regardless of whether it is a phase I, II, III or IV trial);
- Facilitate the publication and access to de-identified individual listings of efficacy and safety data (**raw data**) to allow secondary research and analysis, and ensure that all clinical trial data information made available is in a **legible, easily usable, downloadable and searchable format**.

For more information, please read the full joint response available at:

http://english.prescrire.org/Docu/DOCSEUROPE/20150218_EMAaddendumTransparency.pdf

d- According to the EMA, “*the period of 10 years has been chosen to give a reasonable period after the trial has been completed, before publication, 10 years corresponding, by analogy, though not actually linked to, the data protection period provided for in the EU.*” The EMA seems thereby to confuse two concepts. Regulatory data protection means that generic and biosimilar producers cannot use data of the “innovator” industry during 10 years for request for a marketing authorisation even if it is publicly available. It does however not prevent for data transparency, which is needed to avoid publication bias, allow for the reanalysis of clinical trial results and cost-effectiveness assessments.

e- Moreover, industry-funded research often benefits from public funds (access to investigators and research teams at public research sites; public funding for basic research through EU grants and member state funding, etc. It is therefore more than reasonable to expect that all data from biomedical research is made publicly available.

f- We are unfortunately far from November 2012 EMA’s announcement that it would “*proactively publish clinical-trial data and enable access to full data sets by interested parties*”—the aim being to allow for reanalysis of trials’ results (ref. 5).

References:

- 1- "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" *Official Journal of the European Union*, 27 May 2014: L 158/1 – L 158/76.
- 2- "EFPIA calls for collaboration in the implementation of clinical trials regulation following vote in the European Parliament" press release, 3 April 2014: 2 pages.
- 3- European Medicines Agency "'Draft proposal for an addendum, on transparency, to the "Functional Specifications for the EU Portal and EU Database to be audited' (EMA/42176/2014)" Released 21 January 2015.
http://http://www.ema.europa.eu/docs/en_GB/document_library/Other/2015/01/WC500180618.pdf
- 4- Lemmens T "Access to pharmaceutical data, not data secrecy, is an Essential Component of Human Rights" 8 April 2014.
<http://www.law.utoronto.ca/blog/faculty/access-pharmaceutical-data-should-be-framed-human-right-not-data-secrecy> : 3 pages.
- 5- http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/events/2012/07/event_detail_000656.jsp&mid=WC0b01ac058004d5c3

About us

AIM. The Association Internationale de la Mutualité (AIM) is an international umbrella organisation of not-for-profit healthcare mutuals and health insurance funds in Europe and in the world which operate on the basis of solidarity. Currently, AIM's membership consists of 59 member organisation (including many national umbrella organisations) in 28 countries. In Europe they provide coverage of healthcare and other risks to more than 160 million people. AIM strives via its network to make an active contribution to the preservation and improvement of access to health care for everyone. More info: www.aim-mutual.org. Contact: menno.aarnout@aim-mutual.org

HAI. Health Action International (HAI) is a non-profit network of consumers, public interest NGOs, health care providers, academics, media and individuals working to increase access to essential medicines and improve their rational use through research excellence and evidence-based advocacy. More info: www.haieurope.org. Contact: ancel.la@haieurope.org

ISDB. The International Society of Drug Bulletins, founded in 1986, is a worldwide Network of bulletins and journals on drugs and therapeutics that are financially and intellectually independent of pharmaceutical industry. Currently ISDB has around 80 members in 41 countries around the world. More info: www.isdbweb.org. Contact: press@isdbweb.org.

MiEF. The Medicines in Europe Forum (MiEF) was launched in March 2002 including more than 70 member organizations in 12 European Member States. It represents the four key players on the health field, i.e. patient groups, family and consumer bodies, social security systems, and health professionals. It is a testament to the importance of European medicines policy. Medicines are not merely consumer goods, and the European Union represents an opportunity for European citizens to seek further guarantees of efficacy and safety. More info: english.prescrire.org/en/79/549/49237/3676/ReportDetails.aspx. Contact: pierrechirac@aol.com