Debate heats up over access to clinical trial data

The debate over the public disclosure of clinical trial data is becoming more intense as three major events converge to create a perfect storm. Whether this will lead to anarchy in the world of drug development (as some stakeholders suggest) or greater efficiency and a level playing field for innovators (as others suggest) remains to be seen.

First is the European Medicines Agency's (EMA) draft policy on publication and access to clinical trial data (Policy 70), which is due to be discussed at the EMA Management Board's 11-12 December 2013 meeting. Originally it was to be adopted at this meeting and implemented from 1 January 2014, but this now may be delayed due to the quantity of comments received.[1]

Second is litigation brought against the EMA by two pharmaceutical companies, AbbVie and InterMune.[2,3] The companies are challenging the agency's decisions to grant third parties access to clinical study reports (CSRs) and other information they submitted as part of marketing authorisation applications.

Finally, the European Parliament, the Council of the EU and the European Commission are holding informal "trilogue" negotiations on a proposed new Clinical Trials Regulation to replace the existing *Clinical Trials Directive (2001/20/EC)*. The aim is to reach agreement before the Parliament's plenary vote in March 2014, where it is hoped that the legislation will be passed at first reading. (See the October 2013 issue of *MedNous* for a related article.)

EMA Policy 70

The EMA's draft policy is at the centre of the debate. It outlines the agency's plans to make publicly available the data and results from clinical trials on which marketing authorisations are based. In the draft, the EMA defines three categories of clinical trial data which would determine the level of proactive publication.

Data and documents that contain commercially confidential information (CCI), such as details of the investigational medicinal product itself or bioanalytical data characterising the product, would not be made available under the policy, but could still be requested under the EMA's existing access-to-documents policy (Policy 43).

Those without "protection of personal data (PPD) concerns", for example where the personal data has been de-identified, would be deemed "open access" and would be proactively made available on the EMA's website.

Information with PPD concerns – essentially raw trial data – would be considered "controlled access", meaning the data would have to be adequately de-identified and would only be available upon request under certain conditions. All documents, data and information in a CSR that do not fall under the previous category would be in this category.

The EMA is now sifting through over 1,000 responses to its three-month consultation on the draft which ended in September this year. Though the agency could not comment on how the final policy is shaping up, a spokesperson told *MedNous* that "there are quite divergent views… encompassing those that feel we are not going far enough to those who would like to see parts of the proposal tempered". This is not surprising, given the broad stakeholder base, which includes the pharmaceutical industry, academia, health technology assessment (HTA) bodies, regulators and healthcare and patient advocacy groups, among others.

The European pharmaceutical industry has been the most outspoken in its opposition to the plans, saying they will: weaken safeguards intended to ensure patient privacy; undermine the trust in the regulatory approval system and introduce risks of misinterpretation and misuse of clinical data into the process; and impair incentives for companies to invest in biomedical research by disclosing companies' CCI.[4]

In comments to *MedNous*, Richard Bergström, director general of the European Federation of Pharmaceutical Industries and Associations (Efpia), noted that "advances in big data technology and analytics make the re-identification of patients a real concern". This is one of the reasons why his organisation has teamed up with its US counterpart, PhRMA, to promote a global industry approach to data sharing which is set out in a document entitled *Principles for Responsible Clinical Trial Data Sharing* due to be implemented from January 2014.[5]

One of the main criticisms of the *Principles* document by stakeholders in opposing camps is that the industry commits to making publicly available synopses of CSRs following a product's marketing approval, rather than offering up the full reports. Companies will evaluate requests for full CSRs, but only from "qualified scientific and medical researchers" pursuing legitimate research.

When *MedNous* asked why Efpia believes full CSRs should not readily be shared with the public as a matter of policy, Mr Bergström replied that "making full CSRs, as they are written today, available to the public poses a risk in the potentially sensitive information that may be disclosed, including sensitive patient data or commercially confidential information. The former point poses the danger that personal information about patients will be used or abused; the latter threatens scientific innovation, which is necessary to produce new and improved medicines for patients."

European Biopharmaceutical Enterprises (EBE), the Efpia group representing biotechnology companies of all sizes, shares Efpia's concerns. Moreover, EBE is worried that its members, a majority of which are small and medium-sized enterprises (SMEs) having "small product portfolios, limited human resources capabilities, and fragile and delicate financial business models", may be disproportionately affected by the EMA's proposals.[6]

The EMA, on the other hand, believes that access to patient-level trial data could make drug development more efficient by allowing all developers to learn from past successes and failures. An article authored by a group of EMA officials including its senior medical officer Hans-Georg Eichler and its executive director, Guido Rasi, explains why access to full and appropriately de-identified data sets from clinical trials will benefit the research-based biopharmaceutical industry.[7]

It argues that access to this information will lead to

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improvements in the design and analysis of subsequent trials. In addition, the authors say that lessons from past trials about the heterogeneity of treatment effects will not only streamline drug development but may also enhance a drug's value in the marketplace. Moreover, wider access to patient-level data will allow sponsors to present more robust comparative-effectiveness information about their products soon after licensing and at a very limited cost as compared with that of head-to-head trials, the article says.

Mr Bergström acknowledges some of these arguments but counters that "transparency isn't just about just clinical trials – it's a question of adapting an entire industry and its relationship to the system it operates in, healthcare as a whole."

For researchers, however, there is no substitute for a full CSR. Silvio Garattini, founder and director of Italy's Mario Negri Institute for Pharmacological Research, has dismissed the industry's concerns, particularly with regard to patient privacy. "There is no reason patient de-identification would be a problem. Measures can be taken to keep the data anonymised," he told *MedNous*. He pointed out that having independent groups confirm data validity could actually benefit industry by being much more persuasive for health bodies.

HTA organisations are also pushing for greater access to trial data. Germany's Institute for Quality and Efficiency in Health Care (IQWiG), for example, states that it needs full trial information and results so that it can provide "appropriate and meaningful assessments of drugs".[8] Indeed, it believes the EMA should go further and not restrict the policy to only data submitted after 1 January 2014 as proposed. To this end, it calls for open access to trial data submitted before 2014 as well as trial data not connected to a marketing authorisation application. The European Network for Health Technology Assessment (EUnetHTA) has expressed similar views.[9]

Advocacy group Health Action International (HAI) Europe has weighed in on the debate, too. In an interview with *MedNous*, HAI Europe's policy advisor Ancel-la Santos Quintano said that her organisation supports the EMA's proposals. However, it would like to see raw data disclosed proactively. She explained that "patient-level data contains key information about a drug's safety and efficacy profile" and as such, it should not be considered CCI.

"Scientific knowledge evolves through the checks and balances of the peer review process – independent examination of clinical trial data and the publication of independent findings can only enhance this process," she added. Like Professor Garattini, Ms Santos believes that re-identification of patient data is not a valid concern as this information can be adequately safeguarded.

Some patient groups have come forward with concerns about privacy, but the European Patients' Forum has said that in principle it is in favour of sharing trial data with the caveat that the implications must be considered carefully.[10]

Will litigation derail the EMA's plans?

A final ruling by the Court of Justice of the EU in the AbbVie and InterMune cases is not expected before the end of 2014. In the meantime, however, the EMA is seeking to overturn interim relief that prevents it from releasing the companies' information before the court's final decision. A hearing in this regard was held in mid-October 2013 and the outcome is expected shortly, according to the European Consumer Organisation (BEUC), which has intervened to support the EMA.

A BEUC spokesperson told *MedNous* that the final ruling "will inevitably have an impact on the EMA policy which we assume will have to be adapted accordingly".

As for the future Clinical Trials Regulation, BEUC assumes "that the political signal the institutions will give with the adoption of the regulation will influence the rulings. That is why we urge the Member States to endorse the position taken so far by the European Parliament on the issue of transparency, i.e. to confirm in the regulation that in principle clinical trials data should not be considered commercially confidential once a marketing authorisation has been granted."

If the first trilogue on 6 November 2013 was an indication of the regulation's future direction, inclusion of this language does not look promising. The Council apparently did not embrace the position of the Parliament's Committee on the Environment, Public Health and Food Safety, which had proposed to acknowledge in the introductory sections (recitals) that clinical trial data should not be considered CCI. The Council instead agrees with the Commission's proposal to publish only summaries rather than full CSRs.

Reacting to this development, Ms Santos said: "The Council's position at trilogue negotiations falls short on data transparency. Publishing summaries of trial results is not enough. Clinical study reports are the most detailed source of information on each trial and must be made publicly available. HAI regrets that Member States have barely discussed this important question." The next trilogue was due to take place in mid-November, as *MedNous* went to press.

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This article was written by Karen Finn, contributing editor to *MedNous*.

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