

# Regulatory Writing

## Full publication of clinical trial data: Opening Pandora's box?

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### Abstract

The European Medicine Agency's draft policy on the publication of clinical trial data for consultation (POLICY/0070, EMA/240810/2013) is causing quite a stir. The draft policy provides for the publication of large parts of the clinical

study reports included in a common technical document submission, along with the accompanying summary documents and overview. The varied stakeholders (pharmaceutical companies, patients) will have different opinions on the draft. The European Federation of Pharmaceutical Industries and Associations, a major representative of the pharmaceutical industry, have been particularly critical. While greater transparency is to be welcomed, inappropriate analyses of the data causing unwarranted public alarm and identification of anonymised information remain major concerns.

**Keywords:** EMA, Clinical trial data, Publication

On the 24th June of this year, the European Medicines Agency (EMA) issued its draft policy on the publication of clinical trial data for consultation, after lengthy interaction with different stakeholders (see [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/Other/2013/06/WC500144730.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Other/2013/06/WC500144730.pdf)). The draft forms part of a drive towards greater transparency, a new buzzword in many different institutions that serve the public.

### What is being proposed

In the draft policy the EMA would commit to proactively publish (as of March 2014) modules of the common technical document in a submission (along with the individual clinical study reports themselves included in module 5) on their website, regardless of whether or not approval has been granted. Certain parts, for example, the module on biopharmaceuticals are regarded as containing commercially confidential information and will not be made available. Other parts, mainly the patient

level data in the individual, will be designated as 'controlled access' (where the gatekeeper would be the EMA, following as yet poorly defined procedures and criteria for release of this information).

The policy is a complement to the existing 'Policy on access to documents (related to medicinal products for human and veterinary use)' (POLICY/0043)(EMA/110196/2006), which came into effect in 2010 (note the 4-year delay between the publishing of the policy and its coming into effect - the EMA hasn't always moved quickly on its promises of greater transparency).

### Main industry worries

The devil, as always, is in the detail. The European Federation of Pharmaceutical Industries and Associations (EFPIA), which agglutinates national pharmaceutical industry associations and leading pharmaceutical companies, has set out its opposition to many of the details of the draft policy (see [http://www.efpia.eu/uploads/EFPIA\\_comments\\_on\\_EMA\\_draft\\_policy\\_access\\_to\\_CT\\_data\\_FINAL.pdf](http://www.efpia.eu/uploads/EFPIA_comments_on_EMA_draft_policy_access_to_CT_data_FINAL.pdf)). According to this industry association, the three main worries are that the proposed policy might not fully safeguard patient confidentiality, that the policy may undermine trust in the regulatory approval system and so act as a disincentive for investment, and that commercial secrets may see the light of day, with the ensuing disincentive to fund innovative research.

#### *Will patient confidentiality be preserved?*

As mentioned above, patient level data will be subject to 'controlled access'. Any entity or person wishing to have access to such data should agree to a legally binding data-sharing agreement designed to ensure that the intended use is in the interests of public health (the requestor will have to explain in detail what the information will be used for, for example a meta-analysis) and in line with the spirit of informed consent. In addition, the requestor will have to agree not to try to identify patients through linking to other databases or programs (for example, hospital discharge records

might enable identification of patients in SAE listings).

The draft policy also states that the data will be appropriately 'de-identified' (presumably by the EMA) in a similar fashion to the recommendations for publishing raw clinical data in journals.<sup>1</sup> The EFPIA questions whether such de-identification would be sufficient in light of rapid advances in re-identification technology and would prefer to have more control over how and what is released (that is that the requestor is referred to the company with the EMA as interlocutor). With the vetting system proposed by the EMA, it is hard to determine the likelihood of that the anonymity of patient data, collected after the patient has signed an informed consent guaranteeing their privacy, is broken and the data re-used for purposes other than the lofty ideals of improving public health. The EFPIA also suggests that it should not be possible for data to be downloaded. However, many of the (legitimate) uses for such data would be in meta-analyses or re-analyses, which would be extremely tedious if this was the case.

A final point on confidentiality is that, according to the draft policy, data on investigators and other trial staff (names, addresses, appointments, qualifications, and clinical duties) should be fully available. I would hope that by address, the draft policy is referring to business address and not home addresses (which may appear on CVs included in clinical study report [CSR], appendices). Certainly the EFPIA considers that there is dubious legal basis for this, and cite a number of EU regulations to support their point of view. I suppose a worry here is that some investigators and patients, if they know that personal information may be compromised, will be less inclined to participate in a study.

#### *Trust in the regulatory approval system and disincentives for investment*

The question of whether implementation of the draft policy will undermine trust in the regulatory approval system will probably have a very different answer depending on whether or not you are part of the pharmaceutical industry. In the eyes of the general public, the credibility of the system has taken plenty of hits recently and books such as *Bad Pharma*, by Ben Goldacre, have generated plenty of discussion. With the new proposal, sceptics will be able to see data on which an approval or rejection is based, and come to their own conclusions as to whether the decisions are consistent across applications and appropriate. Such a utopian vision could generate greater trust in the system (provided

of course that appropriate decisions are being made). A potential danger though is that data may be used to generate flawed analyses that generate undue public alarm. Going further, would it be such a far-fetched scenario to imagine companies funding investigators to trash competitors' programmes? It is hard to predict how this will play out.

Pharmaceutical companies, moreover, are very used to confidential dealings with the health authorities and the thought that much of their submission dossier may be readily perused by one and all must be disquieting. The ready availability of such information could be a disincentive for investment. Although not explicitly stated by the EFPIA, a worry must be that this release of information will benefit generics companies over innovators. It is interesting to note that since implementation of the existing policy on release of clinical trial data (POLICY/0043)(EMA/110196/2006), more than 1.6 million pages of clinical trial data have been released,<sup>2</sup> with most of the requests for disclosure of information coming not from healthcare professionals or members of the public, but from pharmaceutical companies. Presumably these requests were made to gain competitor information and not with the public good in mind. There is a big difference though between having to interact with the EMA to procure information under the current policy and having much of it freely available on the Internet as per the current proposal. With the information more readily accessible individual investigators and small start-ups may also use the information available as stimulus to launch truly innovative projects that will attract investment. Thus, the overall effect on innovation is hard to predict.

#### **Benefits for medical writers**

Much of the debate about this greater transparency has focussed on the overall interests of pharmaceutical companies themselves. As medical writers, on the level of doing our jobs, we may actually stand to benefit from having ready access to what could develop into a huge repository of regulatory writing. At present, we only have access to regulatory documents from the companies we work for but we have no idea how other companies may be approaching similar challenges. And although a quick look on the Internet can usually retrieve the applicable guidance, there are very few actual examples of text from real documents. So if you are not convinced that your company is taking the best approach in their CSRs, then you will be able to go to the published trials and see what other companies have done. Wondering to what extent others

cross-reference the protocol in the materials and methods of a CSR? It will now be possible to find out. Examples of clinical summaries and overviews will also in principle be freely available. In the long term, the opportunity to see what others have done could well lead to greater harmonization of approaches, as the ones that work best are copied and gain predominance.

### **Conclusions: Are we opening Pandora's box?**

The policy on publication and access to clinical trial data is still in draft form and it is impossible to know the extent to which the final form will differ from the present one. As it stands, the policy may improve

access to data for legitimate purposes, but there are also risks of inappropriate usage. The revised policy may well alleviate some of these concerns. Nevertheless, once the policy is in effect, the EMA would be advised to be on stand-by for rapid action in case the law of unintended consequences applies.

### **References**

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