**Clinical Trials Directive: The Parliament's political dilemma**

This is an analysis of some of the most important amendments submitted by MEPs to the Commission’s draft regulation (COM(2012) 369 final) to revise the clinical trials directive. The proposal will be debated in the Environment Committee in the European Parliament on 24th April. By the February deadline, 731 proposals for amendment had been submitted.

The most contentious political questions are probably about disclosure – whether, how and when the results of clinical trials should be disclosed.

The Commission’s proposal would require publication of a “summary of trial results” within a year of the end of the trial.

The rapporteur, Glenis Wilmott (S&D), proposes something more – the publication of a “Clinical Study Report”. Clinical Study Reports are well defined in international regulatory guidelines and by the European Medicines Agency. Short of the publication of raw data, they are the most scientifically useful account of a clinical trial that we have. They are prepared for many, but currently not all, clinical trials. Investigators, researchers, writers, authors and sponsors are well acquainted with them.

A few MEPs, notably Margrete Auken, and Michèle Rivasi (Greens/EFA) would go further, requiring full disclosure of raw data, stripped of any personal/private information, within one year of the end of the trial.

Other MEPs, mainly EPP and ALDE, support the disclosure of trial summaries, but with the addition of criteria for what a summary should contain. However, they also seek to limit what must be disclosed, by reference to commercial confidentiality and intellectual property protection.

Two shadow rapporteurs, Philippe Juvin (EPP) and Cristian Silviu Buşoi (ALDE), together with Francoise Grossetête (EPP), support the publication of a trial summary but propose a new annex, setting out what should be contained in such a summary. Their proposal has some similarities with what is proposed in coming years in the US under the Food and Drug Administration Amendments Act of 2007.

They also propose amendments that would limit access to information on the database on which the trial summaries would be placed. The Commission proposal would allow various exceptions to disclosure, including personal data and commercial confidentiality. Juvin, Bosoi, Grossetête and others propose a special emphasis on protecting commercial confidentiality for trials intended to support an application for a marketing authorization for a new use. Juvin would add an exception for scientific information that has not been published in a journal. Juvin, Grossetête and others also propose an exception for information “undermining intellectual property rights”.

Taken together, these amendments would substantially reduce access to information on clinical trials. Take, for example, the added stress on commercial confidentiality. In a series of recommendations for the European Medicines Agency the Ombudsman has set out very clear guidelines or principles, derived from case-law, for determining genuine commercial confidentiality. An amendment giving added weight to commercial confidentiality is likely only to muddy the waters here, and detract from the ombudsman’s recommendations.

The exception for information “undermining intellectual property” is also unclear and uncertain. Medical journals often insist on “first publication” for articles submitted but they are also on record as saying that this policy will not be affected by prior disclosure that is required by law. More generally, it would be relatively easy to combine disclosure with the protection of legitimate intellectual property rights.

Opinion among MEPs also varies in relation the timing of disclosure of results. In the most extreme case, Christofer Fjellner (EPP) proposes that all clinical trial data should be confidential until a marketing authorization is granted. One effect of this is that there may never be any publication of results of trials not used in support of a marketing authorization. It would also bring no increase in transparency since the EMA is already committed to publishing trial results after an authorization is granted.

Philippe Juvin proposes a two year deadline for publication of trial summaries. As previously mentioned he would also allow a delay in disclosure of information until it is published in a scientific journal. This could allow companies to postpone disclosure indefinitely, merely by claiming that they intend to publish an article in a journal.

**Implications of Parliament choices**

To summarise, the choices before the European Parliament in terms of what should be disclosed range from publication of all trial data, publication of a Clinical Study Report, or publication of a trial summary with or without guidelines for what a summary should contain.

Even with the addition of rules for what it should contain, a trial summary has very little value as science or evidence. Trial summaries will vary in form and are very vulnerable to bias, conscious or unconscious. Unconscious bias can be difficult to avoid when there are perhaps billions of euros riding on the outcome of a complex clinical trial. Conscious bias or concealment of results can occur also: without demonising everyone in the industry, there have been far too many well-attested examples of bias or concealment in relation to trial results over the last twenty years, which regulators would be blind to ignore.

Full transparency could be achieved by publication of raw data but realistically there does not seem to sufficient support in the Parliament (or Council or Commission) to achieve this. One interesting amendment by Christel Schaldemose (S&D) would require the Commission to carry out within two years “an evaluation of the management of raw data, and the feasibility of introducing an open access for independent scientists to raw data from all clinical trials”.

In the meantime the requirement to publish a Clinical Study Report would provide a scientifically useful outcome for all clinical trials and a solid evidence for medical science and practice.

Sadly, the amendments limiting disclosure in terms of commercial confidentiality and intellectual property, together with the amendments delaying disclosur, would rob the regulation of much of its effect – with the consequence that transparency would be left largely to the discretion of the industry. They would leave the industry in effective control over what to disclose and what not to disclose.

We don’t need regulation to require companies to disclose what they want to disclose. The results that they do not want to disclose are the ones that are likely to be the most useful scientifically, and indeed ethically.

In support of its Open Data Campaign (<http://www.bmj.com/open-data>) the British Medical Journal estimates that nearly half of all clinical trials are never reported. Trials with positive results are nearly twice as likely to be reported as those with negative or null results, yet negative trial outcomes may be just as valuable in terms of evidence, science and medical care.

Non-publication of negative results can have two particularly bad consequences. Doctors may continue to prescribe a medicine, even though there is (unpublished) evidence that it does not work or that it may be dangerous. The same or a similar clinical trial may be carried out by other researchers that would not have been carried out if the results of the first trial were known – the effect being that new patients would be subject to unnecessary risk in an unnecessary second trial.

**Industry lobbying for commercial confidentiality**

What of the industry position on the draft regulation? The devil is in the details. The industry and individual companies frequently proclaim their support for transparency but seek to qualify both the content and the binding nature of any transparency rules in practice – as most of the amendments mentioned above would do. (A few companies have promised to release trial results in some form to qualified researchers but would still retain ultimate discretion as to what to disclose and when.)

As mentioned, the Ombudsman issued a set of recommendations on commercial confidentiality for EMA, and the agency is making a positive effort to implement those recommendations. Now an American company Abbvie, with the support of the industry on both sides of the Atlantic, has issued legal proceedings in the ECJ against the EMA (Case T-44/13) and by implication against the recommendations of the Ombudsman. They appear to rely on the fact that most requests to the agency for access to clinical trial results come from competitors, which is no surprise, but their action is an assault on transparency, good evidence and good science. Given the wide industry support behind this case, we can assume that the same thinking permeates industry efforts to influence the evolution of the proposed regulation nonclinical trials.

Some of the arguments against transparency have cited personal data as a problem but this is a red herring. The Commission’s proposal is clear that “protecting personal data in accordance with Regulation (EC) No 45/2001” is a justification for non-disclosure, and so it should be – the Parliament is not going to change that. There may be some (few) cases of clinical trials (small trials, rare diseases) where disclosure of personal data is unavoidable but these cases are protected under the proposed regulation.

Finally there is one argument against transparency that is put forward by some companies and their lawyers, more often from the US than the EU. This argument is one of ownership – the claim that they own the results of clinical trials, and therefore cannot and should not be forced to disclose them against their will.

I could understand that if we were dealing with, say, mobile phones here but we are not. We are dealing with people, their health and their lives. Patients in clinical trials agree to certain risks with the implied promise that they are contributing to the public good. At its worst, to claim ownership is to claim the right to keep secret information that could save lives.

Clinical trials put people at risk, which is one of the reasons why they need prior authorisation. It is perfectly permissible and desirable for the authorities to set conditions to try to ensure the maximum public benefit from such trials. If anyone owns the results of clinical trials it is the volunteers who participated, and who put themselves at greater or lesser risk.

Pharmaceutical companies and their lawyers will continue to proclaim their commitment to transparency while also seeking to retain the maximum control over that what they disclose. They will argue against enhanced transparency in the debate over the proposed regulation on clinical trials, and in their case before the European Court.

Their position is wrong. Worse, it is morally repugnant. END

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