The EU Clinical Trials Regulation

Legislators see light at the end of the tunnel

The adoption of new legislation to stimulate the flagging clinical research environment in Europe is close to becoming a reality. By streamlining and harmonising the clinical trial approval process across the EU via a new Clinical Trials Regulation (CTR), the administrative burden and delays that have led to higher costs for trial sponsors should be significantly reduced, making the EU a more attractive place to carry out trials for both commercial and non-commercial sponsors.

Indeed, a spokesperson for the European Association for Bioindustries (EuropaBio) pointed out to *MedNous* that one of the objectives of the CTR is to facilitate the conduct of clinical research by small- and medium-sized enterprises (SMEs) and academics.

Since *MedNous* reported on the proposed CTR in October 2013, proverbial mountains have been moved by negotiators in the European Parliament, the Council of the EU and the European Commission (collectively known as the EU "institutions"), who late last year hammered out a compromise version of the text that will replace the current *Clinical Trials Directive (2001/20/EC)*.

Some of the fundamental aspects of the new EU clinical trials system are much the same as the European Commission had envisioned when it first proposed the legislation in 2012. For example, trial sponsors will submit a single application to a central European portal, replacing the existing system which requires submission of an application to each member state where the trial will be conducted.

In addition, there will be a publicly accessible database to hold the information on all clinical trials carried out in the EU, which will have to be registered before they start. This includes 'lay summaries', as well as the clinical study report which will have to be submitted to the database 30 days after the marketing authorisation has been granted (or the application has been withdrawn). The European Medicines Agency will set up and run the database, in collaboration with the European Commission and the member states.

A two-part assessment system has also remained intact, and although some of the specifics have changed, it is still designed to ensure that there is a single assessment outcome and trial authorisation per member state concerned.

Part I will involve the review of scientific and benefit-risk data by a reporting member state (RMS), which will lead the assessment in conjunction with the other member states where the trial is to take place (member states concerned). The sponsor will propose one of the member states concerned as the RMS, but it is possible that a different member state will end up with the role if the one named by the sponsor is unwilling to take on the job. The industry is pleased that sponsor involvement in this process was included in the final version, as it had been taken out at one stage, Gabriella Almberg, director of government affairs at the European Federation of Pharmaceutical Industries and Associations (Efpia), told *MedNous*.

Part II will involve an assessment of the trial's national aspects by each member state concerned. This includes, for example, subject recruitment and damage compensation.

The legislation still takes a risk-based approach in that certain rules such as traceability requirements will be less stringent for "low-intervention" trials. However, these lower-risk trials will be subject to the same application procedures as other trials.

In general, the timelines for authorisation of trials will be 60 days, and if no decision is taken within this period, there is a "tacit approval". However, various extensions may be permitted under certain circumstances, such as when additional information is requested from the sponsor (up to 31 days) and/or when trials involve advanced therapy medicinal products (ATMPs) or other novel medicines including biologicals (up to 50 days). There is some concern within industry over how this will work in practice, as it remains to be seen how often this extension will be applied, Ms Almberg said.

Although these timelines are not as ambitious as originally proposed by the Commission, Ms Almberg explained that one must look at the benefits of the regulation as a whole – particularly the single application process and explicit language stating that reviews by member states' independent ethics committees, which fall under national jurisdiction, must still be aligned with the timelines set out in the CTR. Sponsors and researchers have long complained of delays caused by ethics committees under the current regime, and trying to find a way around this via the CTR has been no small feat.

Adoption expected soon

The Parliament's Environment, Public Health and Food Safety Committee unanimously approved the compromise text on 22 January 2014; it is now awaiting a final vote by the full Parliament (critically, ahead of its elections), which is due to take place at its plenary on 2-3 April 2014.

Assuming all goes smoothly in the Parliament in April, early adoption by the Council is expected shortly thereafter, the chair of the Council's Working Party on Pharmaceuticals and Medical Devices under the Greek Presidency of the EU, Dimitris Florinis, told *MedNous*.

It is thus "very likely" that the Presidents of the European Parliament and the Council will be able to sign the legislation before Greece hands over the EU Presidency to Italy on 1 July 2014, he said. "From the perspective of the Greek Presidency, the handling of this proposal is a purely technical issue," Mr Florinis added.

If all goes according to plan, the CTR should enter into force sometime in 2016.

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