The EU Clinical Trials Directive

Debate over new legislation reaches final stage

The next few months will be critical for anyone involved in clinical research. After more than a year of intense lobbying from the pharmaceutical industry, academia, hospitals and patient advocacy organisations, lawmakers are nearing a point where hard decisions, or compromises, will have to be made on the future of the legal framework governing European clinical trials. It is hoped that the yet-to-be-adopted legislation will boost investment in EU research by cutting delays and costs.

The European Parliament's Committee on the Environment, Public Health and Food Safety (ENVI) in June 2013 released a report with proposed amendments that build on a draft regulation unveiled by the European Commission last year.[1] The Commission had proposed to overhaul the current regime for approving and conducting clinical trials via a proposed Clinical Trials Regulation, as reported in the July/August 2012 issue of *MedNous*.

This new piece of legislation will replace and repeal the *EU Clinical Trials Directive (2001/20/EC),* one of the most controversial laws in the extensive cache of EU pharmaceutical legislation aimed at protecting the public while ensuring patients have timely access to medicines.

The Commission proposed some radical changes to address unnecessary administrative burdens and a lack of harmonisation in applying the law across all EU member states. The draft regulation introduces a single portal where sponsors can file one standardised application for all the member states in which it intends to carry out a trial. It takes a risk-proportionate approach, so that low-risk trials will be subject to less burdensome requirements.

ENVI amendments

According to Gabriella Almberg, director of government affairs at the European Federation of Pharmaceutical Industries and Associations (Efpia), ENVI has "clarified a lot". However, the industry is still concerned about a handful of key issues.

One of these is transparency. Ms Almberg told *MedNous* that Efpia does not support ENVI's insertion of language that would require sponsors to submit a clinical study report (CSR) within 30 days of marketing authorisation. As an alternative, industry has pledged to make available synopses of CSRs within a reasonable period of time after approval and to evaluate requests for full CSRs, including patient-level and study-level data, and share them under certain conditions.

Efpia also takes issue with ENVI's approach to choosing the reporting member state (RMS) that will take the lead on assessing application aspects relating to scientific and benefit-risk data. Instead of the sponsor choosing the RMS, ENVI has proposed that the Commission come up with 'objective criteria' for making this decision. "It makes sense for the sponsor to choose the RMS based on its past scientific experience with specific member states," explained Ms Almberg.

The two other priorities for Efpia relate to approval timelines and the definition of 'vulnerable' patients.

The academic, hospital and charity sectors have a slightly different perspective. Various organisations from these sectors, including Cancer Research UK, published a joint position paper in August 2013 that outlines their ongoing concerns. Cancer Research UK's policy manager, Daniel Bridge, told *MedNous* that one of the main issues is ENVI's proposal to define low-risk trials as having only a "very small and temporary or no impact on the subject's health". Mr Bridge explained that particularly in oncology, nearly all treatments are likely to have significant impacts and associated side effects on patients, so these types of drugs would be unfairly excluded from the benefits of risk proportionality.

Overall, however, stakeholders appear to feel that the regulation will be a major step forward. Mr Bridge said that people seem "quietly confident" that the Parliament and Council of Ministers will hammer out the details during negotiations in November and December, and that the formal adoption will likely be a 'rubber stamp' approval early next year before the Parliament's May 2014 elections.

Efpia, however, is concerned about lawmakers' ability to reach agreement by then. In particular, Ms Almberg mentioned the proposed timelines for approving a clinical trial application, which some member states feel are not achievable. She thus expects that the complicated technical issues faced by some member states "risks slowing down agreement with the Council".

The Parliament's first reading is scheduled for 10 March 2014; there had been hopes that the regulation would come into effect by 2016, but that will largely depend on whether the law is adopted before the elections.

In the meantime, sponsors that are looking for a more streamlined application review process can turn to the Voluntary Harmonisation Procedure (VHP) set up by the Heads of Medicines Agencies (HMA) Clinical Trials Facilitation Group. It offers a co-ordinated assessment of multinational clinical trials before the initial phase of the national process, on a voluntary basis.

However, notwithstanding its lack of a legal basis, the VHP has limitations. One major shortcoming is that not all member states choose to participate in it. The new clinical trials regulation would build on some of the positive aspects of the VHP while addressing its weaknesses.

References:

1. European Parliament, "Procedure file: Clinical trials on medicinal products for human use", www.europarl.europa.eu.

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