Europe proposes laxer regulation of clinical trials

The culprit is an 11-year-old creature known as the European Commission's Clinical Trials Directive that apparently creates a mountain of bureaucratic red tape and overly stringent oversight, leading to an average 152-day delay in the start of trials.

The consequence, many companies and researchers say, has been a substantial decline in the number of applications to conduct clinical trials in the European Union — to 3800 in 2011 from 5028 in 2007 — as companies bailed for countries in which the rules are more industry friendly.

Faced with the fallout, the European Commission is proposing to substantially overhaul the clinical trials environment on the continent so that it features a more streamlined, centralized and harmonized application procedure; a more "risk-based" approach to regulation that reduces industry's reporting and insurance requirements; and reduced costs for both pharmaceutical firms, who sponsor 60% of trials on the continent, and academics and other organizations, who pick up the tab for the remaining 40%.

The *Proposal for a Regulation of the European Parliament and of the Council on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC* (http://ec.europa.eu/health/files/clinicaltrials/2012_07/proposal/2012_07_proposal_en.pdf) is expected to take effect in 2016 and stem the drift of trials to less-regulated environments with larger patient pools.

It is "built for success — restoring Europe's reputation as an attractive place for clinical trials, and ensuring the protection of health, safety, rights and well-being of patients and the reliability of data generated," Frédéric Vincent, spokesperson for health and consumer policy at the European Commission, writes in an email.

The overhaul allows for a "single portal" for submitting applications, to be managed by the commission, rather than a "patchwork of 27 national frameworks." The assessment procedure for a multination, multisite trial would be coordinated by a "reporting Member State," proposed by the trial sponsor. Ethical issues such as informed consent or the adequacy of trial sites, as well as liability issues,

© 2012 Thinkstock

The number of applications to conduct clinical trials in the European Union declined to 3800 in 2011 from 5028 in 2007.

would be decided at the national or local level, as long as the assessment procedure is independent and complies with international standards.

Some clinicians believe the end result will be more ready access to new products and suitable treatments.

"There is high need for more involvement and facilitated streamlined recruitment of patients into clinical trials. This should be a matter of routine, whenever there is uncertainty about choice of treatment (which is frequent in primary care)," Dr. Paul Van Royen, dean of the Faculty of Medicine and Health Sciences at the University of Antwerp in Belgium, writes in an email.

But others worry that Europe is lowering its ethical bar. "With the differentiation between a centralized assessment and a decentralized assessment under the wing of each Member State, there's no longer a clear synthesis between the ethical border and the scientific border," Dr. António Vaz Carneiro, professor of medicine and head of the Center for Evidence Based Medicine in the Faculty of Medicine at the University of Lisbon in Portugal, writes in an email. "This differentiation can be problematic in itself, since it could create difficult problems to overcome. After all, the ethical assessment has to bear in mind the scientific aspects. Bad clinical research is always anti-ethical."

Others, such as Dr. Eva Hummers-Pradier, professor of general practice/family medicine at the University Medicine Göttingen in Germany and chairperson of the European General Practice Research Network, say that while the proposal lays the groundwork for a less onerous approach to oversight, "time limits must be appropriate to allow for thorough reviewing by experts. In the current text, there are lots of different deadlines, which is not really feasible. And many are very short. This could potentially result in a lack of rigorous review and put patients (and science) into danger."

The proposal alters some reporting requirements, for example, by allowing for direct reporting of unexpected adverse reactions by the trial sponsor to a central European database. In the past, trial sponsors notified authorities in each member state, who then were responsible for reporting to the database. The revisions also allow for electronic submission of annual safety reports to the European Medicines Agency.

It also allows certain types of adverse events to be exempt from reporting requirements if specified by the clinical trial protocol. The overhaul permits European Commission inspection of clinical trial sites and waives the need for trial sponsors to provide trial-specific compensation to people who suffer adverse events during trials "where there is no additional risk or where that additional risk is neglible." But it would require member states to establish some manner of "national indemnification mechanism" if trials pose a high risk to patients.

Some European organizations stress the need for fine-tuning. "Further guidance is needed to clarify the extent of patients' involvement, the terminology used by the Commission in the proposal, and the workings of some of the provisions contained therein, e.g. regarding co-sponsorship, risk adaptation and safety reporting," Monika Kosinska, secretary general of the European Public Health Alliance, writes in an email. "The relationship with evolving pieces of EU [European Union] legislation such as data protection and relevant databases must also be clear to ensure that research results can be disclosed for the benefit of patients." — Tiago Villanueva Gutierrez Arruda Marques MD, Lisbon, Portugal

CMAJ 2012. DOI:10.1503/cmaj.109-4302