CLINICAL TRIALS

Europe Debates Ethics Reviews, Data Release

European countries are embroiled in a debate over how to redo rules for clinical trials, an effort to replace a controversial 12-year-old directive that critics say bound human research studies in red tape. But preserving stringent patient protections without tipping into excessive bureaucracy—and getting 27 countries to agree—is no easy task.

Among the sticking points are changes in the requirements for ethics reviews and a proposal that the results of all clinical trials in the European Union be made publicly accessible. The new rules face a vote in Parliament in April.

The regulation would replace unpopular rules that the European Union adopted in 2001. These rules, clinical trialists say, added layers of unnecessary bureaucracy that slowed clinical research and made it more expensive, especially for academic researchers (*Science*, 30 May 2003, p. 1353).

The European Commission's new plan, several years in the making, garnered praise when it was publicly unveiled in July 2012. Particularly welcome is a streamlined process for approval of trials that take place in more than one E.U. country. The new rules will also have the force of law in member states. Previous rules gave countries some flexibility, leading to more than a dozen interpretations of key passages and complicating cross-border trials, says Joerg Hasford, chair of the Association of German Research Ethics Committees.

But some have reservations. The commission's proposal left out any reference to ethics committees, saying only that applications should be evaluated "by a reasonable number of persons who collectively have the necessary qualifications and experience." That prompted criticism that the new regulation would allow studies to go forward without independent ethical review and that researchers might "shop around" for loose oversight.

The reaction was particularly strong in Germany, where ethics committees play a powerful role in reviewing trial applications. The German Medical Association said the proposal undermines "protection of study subjects, scientific quality, and public trust in clinical research." In February, four of the five parties in the German Bundestag also released a statement of concern. The worries weren't limited to Germany; the European Group on Ethics in Science and New Technologies, which advises the European Commission, said it was "deeply concerned" by the failure to explicitly require ethics committee review. Some U.S. experts echo that worry: "I definitely don't think they should move to something where there's a reduced role for ethics boards," says Kay Dickersin, director of the Center for Clinical Trials at the Johns Hopkins Bloomberg School of Public Health in Baltimore, Maryland.

Safe and effective? The European Union is drawing up new rules for clinical trials.

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In amendments proposed in early February, the European Parliament's lead legislators on the issue, Glenis Willmott from the United Kingdom and Michèle Rivasi from France, sought to assuage the critics. They proposed explicitly requiring the approval of an ethics committee that includes both health professionals and patient representatives, similar to the current 2001 rule. The challenge will be to preserve ethics reviews that satisfy individual countries, such as Germany, while minimizing red tape thanks to cross-border differences. The commission should set up a platform that encourages ethics committees to cooperate across national boundaries, Willmott says. Those amendments received wide support at parliamentary committee hearings on 19 and 20 February and look likely to be accepted.

Also sparking controversy is how much data from completed trials should be released. (Detailed results are already shared with drug approval agencies, but not always with the general public.) Now, many trials—especially those with negative results—are never published. The commission's proposal calls for the sponsor to share a summary from each completed study, but Willmott and Rivasi want to go further. They suggest that upon a trial's completion, the sponsor publish the full "clinical study report," which includes efficacy and safety data. Sponsors who fail to comply could be fined—up to €7000 per day in Rivasi's proposal.

That effort could push the bounds of trial registration, which has already changed substantially on both sides of the Atlantic. In 2004, an alliance of 12 leading medical journals announced that they would not publish any clinical trial that had not been registered from the start in a public database, such as the one established by the World Health Organization or on clinicaltrials.gov, part of the National Institutes of Health (NIH). Then in 2007, the U.S. Congress mandated that NIH create a "results database," which includes summary data from some trials. "That was a big, huge game-changer," says Deborah Zarin, the director of clinicaltrials.gov. "We now have about 8000 sets of results." They are less complete than what Willmott and Rivasi propose, however. And listings of results so far are a drop in the bucket compared with the more than 140,000 trials that appear on clinicaltrials.gov.

Whether the E.U. proposal will survive the parliamentary vote scheduled for 25 April and negotiations with the European Council, which represents member states, is far from clear, says Peter Gøtzsche, director of the Nordic Cochrane Centre in Copenhagen. "It is running into a lot of opposition" from the pharmaceutical industry and other lobbyists, he says. Negotiations are expected to last through autumn. The commission has said it hopes the regulation could take effect by 2016.

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