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Data Sharing — Is the Juice Worth the Squeeze?

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The past few years have seen considerable interest in the sharing of patient-level data from clinical trials. There is a clear and logical "ethical and scientific imperative"[1] for doing so, to permit activities ranging from verification of the original analysis to testing of new hypotheses. This interest has resulted in many publications and meetings, attention from the Institute of Medicine,[2] proposed changes in journals' policies,[3] and enormous effort from pharmaceutical sponsors and other groups to provide access to patient-level data.[4] It is critical that we learn from these early experiences as we move forward.

Beginning in May 2013, GlaxoSmithKline made available to investigators the patient-level data and study documents from more than 200 trials that had started since January 1, 2007; the later addition of others resulted in access to data from more than 1500 trials sponsored by GlaxoSmithKline, including all their global intervention trials since the formation of GlaxoSmithKline in 2000. Beginning in January 2014, requests for data could be made through a public website, clinicalstudydatarequest.com (CSDR), and were subject to approval by an independent review panel.[4] Other trial sponsors joined CSDR.

In March 2015, the Wellcome Trust took over running the independent review panel for CSDR. In an attempt to increase participation even further, a small number of sponsors were given the right to veto data requests for commercial reasons, although such vetoes were strongly discouraged. Wellcome recruited a new panel, which started reviewing proposals in December 2015. As the members of the original independent review panel, we can report on the first 2 years of applications for access to data and on the results of a brief survey about project status that was sent to the lead investigators of all approved protocols, as well as a survey of sponsors about publications of which they were aware. At the time, data from 3049 trials were available through the website, from Astellas, Bayer, Boehringer Ingelheim, Daiichi Sankyo, Eisai, GlaxoSmithKline, Lilly, Novartis, Roche, Sanofi, Takeda, UCB, and ViiV Healthcare.

Overall, 177 research proposals were submitted between May 7, 2013, and November 14, 2015. The panel had 30 working days within which to complete their reviews; all reviews were completed before December 31, 2015. Access was granted for 144 of these proposals; 33 were withdrawn after the panel requested additional details, and in all but 6 of those cases a new proposal was submitted because data from additional studies were needed. In 58 cases, the panel required the requesters to improve their lay summary. These 177 proposals included requests for data from 237 studies not yet in the system; access was granted to data from 179 of these. The commercial veto option was never exercised.

Most proposals (148) were for a new study and publication, with confirmation of original studies' results (3) being quite uncommon. Statistical methods ranged widely and included predictive models (63), meta-analysis (28), survival analysis (15), and tests of new analysis methods (14). The most

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common content areas were cancer (34), cardiovascular disease (21), asthma and chronic obstructive pulmonary disease (13), and HIV (8).

Unfortunately, we received only 24 responses to our investigator survey. More than half the respondents (13) indicated that they were still analyzing the data obtained from CSDR; 3 indicated that they had completed their analysis, and 8 said their application for data access was still under review, awaiting their resubmission, or pending finalization of the legal agreement between the research or applicant institution and the sponsor. Reported products from the research included manuscripts (3), abstracts (8), oral presentations (5), and posters (3). The inquiry to sponsors identified only one manuscript that had been published and four others that had been submitted for publication.

We hope these results will be instructive for others as the field of clinical trial data sharing continues to mature. Despite a very large expenditure by the pharmaceutical industry to make available patient-level data from over 3000 clinical trials, the output so far has been modest. It's noteworthy that 174 of the 177 proposals submitted did not involve reanalysis of original results or disproving of the findings of the original analyses; the bulk of the proposals were for new research. Thus, sponsors' fears regarding making these data available have not been realized.

A large majority of the researchers who submitted proposals were granted access. However, fewer than 200 proposals were submitted over the first 2 years, and though it may still be early, only one published paper has so far emerged from the proposed projects. The wider public and the press have shown little interest in the data-sharing site since the initiative was launched. A published report on four submissions suggests that one contributor to the small yield might be the inefficiency of the approval process, but at least part of the problem in those four cases appeared to be that the requesters provided incomplete information in support of the proposals.[5]

Comments from respondents to our investigator survey also suggest that analyzing data behind a firewall is burdensome and inadequate for meta-analyses of patient-level data that come from different sources. In other words, true data sharing would be preferable to data access on a dedicated website.

Even if a lack of knowledge about the system — despite considerable initial efforts at publicity — meant that relatively few proposals had been submitted, it would not explain why so few papers have emerged from the 144 proposals that were approved. Unfortunately, given the limited response to our survey, we cannot provide a definitive reason for such a meager return.

Making trial data broadly available is ethically imperative and scientifically justified and has the potential to increase public understanding of and support for clinical research. But it seems critical to find ways to improve the use and output of data-sharing projects before the clinical research community invests the substantial effort and resources required to broaden the effort to include academic and other noncommercial investigators.

Disclosure forms provided by the authors are available at NEJM.org.

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