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Preparing for Responsible Sharing of Clinical Trial Data

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therefore careful selection of the appropriate assay is an important clinical and research consideration.

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Since publication of their article, the authors report no further potential conflict of interest.

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DRS. WHITE AND ZANNAD REPLY: Standl inquires about findings in the EXAMINE trial regarding incident heart failure, since these exploratory data were not part of the article on our primary results. Because concerns have been raised recently about other DPP-4 inhibitors and increased rates of hospitalization among patients with heart failure, we have initiated analyses of heart-failure outcomes in our trial. In patients with type 2 diabetes and a recent acute coronary syndrome, including patients with a history of heart failure and those with elevated baseline levels of N-terminal pro–brain natriuretic peptide, cardiovascular outcomes inclusive of hospitalization for heart failure were not increased with alogliptin as compared with placebo. In addition, alogliptin neither induced new-onset heart failure nor worsened heart-failure outcomes in patients with a history of heart failure before randomization. We will continue to analyze results related to this important question in our trial.

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TO THE EDITOR: Mello et al. (Oct. 24 issue)[1] identify ensuring the responsible use of data as a key aspect of any system for expanded access to participant-level data. In their careful framework for considering the legal, ethical, and policy implications of such sharing, however, they omit a powerful mechanism to meet this aim. Open computer code facilitates replication, which both advances knowledge[2] and holds powerful interests accountable.[3]

Regardless of which of the four proposed models are adopted, data-use agreements should require data requesters to publish their computer code alongside any analysis. The program should be complete, in that it takes as its input the provided trial data and finishes by providing every table, figure, and summary statistic reported in the final paper.

Just as proposals for an increase in the level of shared clinical trial data use openness as a mechanism to hold data generators accountable, openness can hold data requesters accountable. If scientists can make progress in ensuring the replicability of studies that include the use of genetically modified mice,[4] surely the far easier task of ensuring replicable reanalyses can be achieved.

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No potential conflict of interest relevant to this letter was reported.

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TO THE EDITOR: Mello and colleagues outline the potential benefits and risks of participant-level data sharing. They highlight technical and ethical concerns as sponsors and investigators move

these initiatives forward. However, insofar as innovations overcome important limitations such as intellectual property and privacy, two points remain relevant.

First, implementing responsible participant-level data sharing is a moral imperative to accelerate discovery with limited resources and to address the ominous quality of scientific output. Current siloed and fragmented science fails to answer important questions in an increasingly complex world.[1] Conversely, participant-level data sharing shifts the paradigm to collaboration, which enables the pooling of skills, insights, and resources from different teams.[2]

Second, concurrently with this wave of data availability, computational tools can now tackle big data opportunities. It is possible to manage large-scale data sets, reformat them to link and integrate, and construct analytic algorithms in an effective and timely fashion.[3] A perfect storm is exposing a large volume of data to new tools, paving the way to groundbreaking collaboration across networks to increase productivity and boost the quality of medical science.

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Dr. Abdallah reports being an employee of and holding equity in Sanofi. No other potential conflict of interest relevant to this letter was reported.

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Access to Patient-Level Trial Data

TO THE EDITOR: The Chief Medical Officers Roundtable (CMOR), of which we are members, welcomes the Perspective article by Eichler et al. (Oct. 24 issue),[1] who are representatives of the European Medicines Agency (EMA), on access to patient-level trial data. CMOR formulates positions on medical topics, and its members include chief medical officers of major biopharmaceutical companies. CMOR supports a transparent, harmonized process for access to patient-level clinical trial data.

Any approach to clinical trial data sharing must be in the interest of patients. Data sharing should be based on two tenets. First, principles should apply uniformly to all who generate clinical trial data — industry, academia, regulators, health systems, foundations, and others. There will be little benefit to patients if access does not occur across sectors. Second, the responsible release of data requires input from independent experts and agreements to respect confidentiality, promote scientific excellence, refrain from misleading conclusions (which can harm patients if they discontinue beneficial treatment),[2] and safeguard future innovation by retaining incentives for investigators.

Access should be determined after the submission of a proposal to a panel that includes independent experts. Evaluation should be based on scientific merit, relevance, researcher qualifications, potential conflicts of interest, and plans for dissemination of findings after peer review. To this end, the CMOR supports the consensus study launched by the Institute of Medicine. It is, to our knowledge, the only broadly inclusive initiative and has the international participation of academia, industry, the National Institutes of Health, the Food and Drug Administration, the EMA, journals, patient organizations, foundations, and others.[2]

Contrary to the assertion by Eichler et al. that industry opposes the sharing of patient-level data, many companies are creating processes like those mentioned above.[2] Industry already shares results through ClinicalTrials.gov, public websites, and scientific publications.[3]

Furthermore, the European Federation of Pharmaceutical Industries and Associations and the Pharmaceutical Research and Manufacturers of America have moved beyond the status quo in adopting the Principles for Responsible Clinical Trial Data Sharing, which will be implemented in January 2014 and include the following major points.[4] First, patient- and study-level clinical