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FEATURE

TRANSPARENCY IN THE DRUG INDUSTRY

From promises to policies: is big pharma delivering on transparency?

As increasing numbers of pharmaceutical companies establish policies for granting third party access to their clinical trial data, the onus shifts to those ready to begin sifting through the data

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On 30 January, Johnson & Johnson joined a growing cast of major drug companies pledging to grant third party access to their clinical study data.[1] Third party access to industry data has occurred on an ad hoc basis for decades. But unprecedented public concern over inaccessible data has led drug companies to streamline the process for granting access.[2 3] Since 2012, Boehringer Ingelheim, GlaxoSmithKline, Roche, Sanofi, ViiV Healthcare, and Pfizer have established similar systems to enable access to detailed trial data including clinical study reports and electronic individual participant data. And it would seem we can only expect more announcements in the future, considering the enthusiasm expressed by the Chief Medical Officers Roundtable for a "transparent, harmonized process for access to patient-level clinical trial data."[4] (Box 1)

Industry's harmonized approach

Although the details of each company's approach differ, there seem to be more commonalities than differences in the philosophy and approach of all companies.

Firstly, all companies are in favor of a "controlled access" model of data sharing under which data are not "open access"—that is, free and unrestricted—but rather limited to approved requestors. In the case of Johnson & Johnson, the Yale Open Data Access (YODA) Project team will referee requests for data. For Roche, GlaxoSmithKline, and others using the joint ClinicalStudyDataRequest.com system, the gatekeeper is a four person review panel. (GlaxoSmithKline, which established the panel, has indicated a desire to replace this panel with one possessing greater credibility and independence.) The criteria for granting access might vary slightly by gatekeeper, but the general principle is to ensure that only qualified researchers pursuing legitimate research—however judged—are granted access.

Secondly, no company intends to share electronic participant level data directly with third parties, but rather only grant access to these data. This seeming semantic difference in practice means that approved requestors will have to work with participant level data within a secure environment designed to prevent the downloading of the data onto one's personal computer. Currently, seven companies are working with SAS Institute Inc to host data on a web based portal.⇓

Thirdly, all companies intend to redact information before granting third party access to reduce the risk of possible re-identification of participants. Companies do, however, differ in their judgments regarding the potential commercial confidentiality of clinical trial data. For example, Sanofi will redact from clinical study reports what it deems "commercially sensitive information," [5] whereas GlaxoSmithKline has taken the view that commercially confidential information is no longer present in those clinical study reports it will make available (published studies of approved or terminated products).

Fourthly, all companies have pledged more than is ready to share. Although there are thousands of trials that should be available based on the recent pledges, the cost of preparing the data—locating old trials, anonymizing, and redacting their data—are high enough that preparation is largely only being done in response to specific approved requests. This seems pragmatic, but does raise the question of why trial data are not readily available. The fact that companies would need to search for older trial data raises questions about how companies themselves evaluate the safety and effectiveness of their own products.

Fifthly, all companies usually only make available data from trials that tested a drug in an indication that was approved by regulators; trials investigating off-label use are not being offered. The reason for this is not clear, but one possibility is that companies want to head off the potential that dissemination of such trial data and clinical study reports is construed as illegal off label promotion. Some companies are even more restrictive. Sanofi, for example, will only release certain trials related to products approved since 1 January 2014.[5]

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Box 1. The Chief Medical Officers Roundtable (CMOR) are from 21 companies

- AbbVie
- Amgen, Inc
- Astellas
- Astra Zeneca PLC
- Becton Dickinson
- Biogen
- Bristol-Myers Squibb
- Boehringer Ingelheim
- Eli Lilly and Company
- EMD Serono, Inc
- Genentech
- GlaxoSmithKline Ltd
- F Hoffman La-Roche
- Janssen
- Merck
- Novartis Pharma AG
- Novo Nordisk A/S
- Otsuka
- Pfizer Inc
- Sanofi

Finally, all companies are doing this free of charge (so far), consistent with the notion that those who market products have a duty to share the evidence of their products' performance.

Despite all the similarities, the companies have not fared equally well in the court of public opinion. Here, GlaxoSmithKline has garnered the bulk of praise, probably because it was the first to announce many of these initiatives and also because it signed the AllTrials petition, something no other company has done. Roche has not received similar praise, but has worked closely with GlaxoSmithKline over the past year to achieve a remarkably similar policy.[6] Roche, however, has not signed AllTrials. The AllTrials petition declares that "all trials past and present should be registered, and the full methods and the results reported." Separate to the petition, the AllTrials website features a working document that outlines in greater detail a vision of how the goals might be achieved. It describes "four levels of information in clinical trial reporting": trial registration, summary results reporting, "full details about the trial's methods and results," and participant level data. AllTrials is only concerned with the first three.

In a statement, Jeffrey Helterbrand, senior vice president and global head of biometrics at Roche explained: "We believe that our Roche data sharing policy meets or exceeds the three main points that AllTrials is asking of us to commit to, and right now want to focus on our own internal processes to meet the commitments we have in our Roche data sharing policy."

In January, Helterbrand gave a keynote speech at a conference on data sharing entitled "Why Increased Data Sharing Rewards Great Science."[7] In his talk, Helterbrand explained why Roche believed the long term benefits of expanded third party access to data outweighed some of the potential harms often invoked such as the potential for misleading analyses based on shared data.

Also presenting at the conference was the US Food and Drug Administration (FDA). In contrast to Roche and industry in general, the FDA appeared clear that whatever benefit might come from sharing data, the FDA wants to be a spectator, not participant in the conversation. FDA, despite holding more data than any other party on the planet, explained that data release was "not a central focus of core regulatory mission . . . We encourage independently organized efforts to create, curate and share clinical trial datasets from all sources."[8]

The way forward

To borrow physician and *Bad Pharma* author Ben Goldacre's phrase, the past is riddled with "fake fixes," and there remain reasons to be skeptical of the transparency policies industry is actively putting into practice. The reality is that most of these systems are still new and largely untested; the ClinicalStudyDataRequest.com website lists just six requests with signed data sharing agreements.

One concern is whether the granularity of data being provided is sufficient. The most raw of clinical trial data—the original case report forms—remain outside most discussions, which largely focus on electronic individual participant level datasets. However, if the raw data were not properly recorded, participant level datasets will contain errors. When such errors are not random, as FDA reviewer Thomas Marciniak detected was the case in the rosiglitazone study RECORD, they have the potential to bias conclusions.[9] Analyses using individual participant level datasets carry considerable caché, however, and most third party researchers might choose to analyze what is on offer, not follow Marciniak's lead and demand raw data. The team aiming to restore paroxetine study 329 has opted for the latter. GlaxoSmithKline's intimation that it will fulfill the request might help pave the way for others.[10]

Secondly, there might be some concern that the electronic data access system is more than simply a way to prevent the downloading of data, but a convenient way to monitor requestors and prevent truly independent research. But GlaxoSmithKline and Roche have both suggested to the *BMJ* that this is not the case. "The foundation is built on trust. If you write a research proposal and say this is what you are going to do, then you do it, and at this stage the only way we'd know otherwise is when the research paper is submitted for publication," explained Roche's Helterbrand. The data request website, however, leaves room for doubt. Despite an assuring statement that "The study sponsor does not view the research that is being conducted," the text goes on to explain that "a log of activities is stored."[11]

Nonetheless, Andrew Freeman, head of medical policy at GlaxoSmithKline, was clear that the log has nothing to do with surveillance of researchers. (Box 2)

The greatest concern may be that the current industry framework continues to treat clinical trial data as the property of trial sponsors and not part of an intellectual commons to be maintained and governed by a third party such as a regulator.

But as the access-to-data debate has moved from promises to policies, procedures, and systems designed to facilitate wider access to clinical trial data, the onus to document how well the system is working falls on those requesting data. Are the systems—both those that make data available as well as those that fund, staff, and train independent scientists to make use of such data—sufficient to allow for the replication of past studies, reduce waste, and increase value of future research?

Competing interests: I have read and understood the BMJ Group policy on declaration of interests and declare the following interests: I personally know many of the actors involved in the events described in this article; I spoke at the mentioned January conference on data sharing; and YODA and the Institute of Medicine paid all expenses for me to join a June 2012 YODA planning meeting in New Haven and an October 2012 workshop on data sharing in Washington, DC, respectively. On behalf of the *BMJ* and independently, PD is actively campaigning for greater access to data from clinical trials; *BMJ* is a co-founder of the AllTrials campaign.

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Box 2. GlaxoSmithKline addresses concerns about surveillance

Andrew Freeman, head of medical policy, Office of the Chief Medical Officer

"It is very important to us that users have confidence in the system and if, as you'd said in your original note, there could be a perception of 'surveillance', we should address this because it's not our intent. The system has been built so users can do their research in a private workspace. Nobody would access this to view the research being conducted, unless there was a specific request from the researcher for help. There is no tracking or monitoring and no details kept of the research in this workspace.

"Logs of what is imported to and exported from the system are stored so that if there is an issue with how the system is operating it can be investigated. So, for example, if a researcher imports a particular computer program code that they intend to use as part of their research and this in some way compromises the system, it can be identified so the problem can be addressed. Also, as you know there are controls in place to prevent patient level-data being removed from the system to help ensure that patient confidentiality of those involved in the research is protected. However, if these controls are triggered inappropriately there may be a need to manually confirm that patient level data is not leaving the system."

Figure

Data will not be downloadable, but instead access to data will occur through approved requestors' web browser. This figure displays the login page for the SAS Institute Inc portal