COMMENTARY

Global Regulatory Agencies and Data Transparency

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Abstract: Egilman et al. review the current data sharing practices of three global regulatory agencies — Health Canada, the European Medicines Agency and the Food and Drug Agency. While there has been progress towards increasing transparency over the past decade, progress has been slow.

To decide whether to permit the marketing of medical products, national regulatory agencies rely upon vast quantities of information from clinical trials. Growing recognition that this information has value, apart from the regulatory decisions themselves, has led to a global movement for greater data transparency.[1] Among the benefits of broader access to research data are deeper understanding of disease progression (from combining the placebo arms of clinical trials), insights from novel comparisons of different treatments, and new ideas for promising avenues of research.[2]

In this issue, Egilman and colleagues report on the status of data transparency efforts at three major national regulatory agencies — the European Medicines Agency (EMA), Health Canada (HC), and the US Food and Drug Administration (FDA).[3] Each of these agencies releases certain information from clinical trials in response to requests, applying its own standards for redaction of confidential information.

In recent years, the agencies have each developed programs to release data proactively. In 2014, the European Medicines Agency gained the authority to release clinical study reports and patient level data for studies submitted after January 1, 2015. In 2018, the US Food and Drug Administration launched a pilot program to release clinical study reports. In 2019, Health Canada launched a major effort to release clinical reports (but not individual patient data) for drugs, biologics, and devices.

The results so far? The EMA is the clear leader in proactive data release. To date, EMA, HC, and FDA have proactively released data on 119, 16, and 1 therapeutics, respectively. FDA's pilot program ended after just one report was made public. EMA and HC's disclosures were comparable in scope for the same drugs, with minimal redactions. The length of time between making the decision to release data and the actual data release is 522 for the EMA, compared to 135 days for HC.

Egilman et al. did not compare directly the three agencies in their responsiveness to data requests. Where the researchers were able to evaluate releases for the same drugs, the FDA appeared to disclose more information for comparable medications than EMA, although the time from request to release for both agencies exceeded 900 days.

The findings reflect both the progress of data transparency over the last decade and the challenge

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of making large amounts of trial information accessible quickly. In particular, the burden of review and redaction for historical documents seems to be quite large, substantially limiting the speed of release. The authors suggest a "harmonized approach for clinical report disclosure to help reduce inefficiencies." Such an approach could eventually lead to standards for companies to submit "releasable" documents soon after sending the originals, easing the burden of redaction. FDA has the opportunity to learn from the best practices of EMA and HC and to help lead the global conversation on how best to make useful information more widely available quickly.

As the movement for transparency advances, however, two additional issues will come to the fore. The first is the extent to which greater transparency feeds the disinformation crisis. Poor quality research on newly released clinical study information could lead to mistaken conclusions that spread across the world and confuse patients and clinicians alike. One approach to mitigating this danger is to utilize trusted intermediaries, such as the Yale University Open Data Access (YODA) initiative, which only permit individual patient level data access to qualified researchers.[4] Scientific journals will play a critical role in assuring the soundness of the methodology of submitted research. To justify the risks and costs of transparency, it will be important for the research community to track the use of newly available clinical trial data to improve the health of populations.

A related matter is the impact of data transparency on the credibility of regulatory agencies themselves. Certainly, transparency will lead to greater appreciation of the vast work of regulatory agencies in reviewing complex clinical studies. It is also predictable, however, that academic and independent scientists will re-analyze data submitted to agencies and challenge the resulting regulatory decisions. Regulators will have to adapt to a new set of demands for explaining their decisions.

A companion project, then, is a different type of openness: transparency in regulatory decision making. Regulatory agencies differ in their policies on release of key documents outlining their standards and decision making. These include guidance for industry; complete response letters that outline why medical products are not approved (a practice at the EMA, but not the FDA); statistical analyses from withdrawn applications; and explanations for clinical holds.[5] Agencies also have different styles of responding to criticism from academic researchers, industry groups, and consumer advocates.

At a time of doubt in many social institutions, the public's confidence in the safety and effectiveness of medical products is very much at stake. Greater data transparency has the potential to enhance not only scientific progress, but also public understanding and confidence in the safety and effectiveness of a wide range of medical products. Engaged and capable regulators are necessary to bring this potential to reality.

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Note

Dr. Sharfstein reports that he served as Principal Deputy Commissioner of the US Food and Drug Administration from March 2009 to January 2011. The authors have no other potential conflicts of interest to disclose.

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