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Symposium Articles

SYMPOSIUM

**Blueprint for  
Transparency at the  
U.S. Food and Drug  
Administration**

Guest edited by  
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*Letter from  
the Editor*

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**INTRODUCTION**

*Anna L. Davis, James Dabney Miller,  
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**Blueprint for Transparency at the  
U.S. Food and Drug Administration:  
Recommendations to Advance the  
Development of Safe and Effective  
Medical Products**

*Joshua M. Sharfstein, James Dabney  
Miller, Anna L. Davis, Joseph S. Ross,  
Margaret E. McCarthy, Brian Smith,  
Anam Chaudhry, G. Caleb Alexander,  
and Aaron S. Kesselheim*

**BACKGROUND**

The U.S. Food and Drug Administration (FDA) traditionally has kept confidential significant amounts of information relevant to the approval or non-approval of specific drugs, devices, and biologics and about the regulatory status of such medical products in FDA's pipeline.

**OBJECTIVE**

To develop practical recommendations for FDA to improve its transparency to the public that FDA could implement by rulemaking or other regulatory processes without further congressional authorization. These recommendations would build on the work of FDA's Transparency Task Force in 2010.

**METHODS**

In 2016-2017, we convened a team of academic faculty from Harvard Medical School, Brigham and Women's Hospital, Yale Medical School, Yale Law School, and Johns Hopkins Bloomberg School of Public Health to develop recommendations through an iterative process of reviewing FDA's practices, considering the legal and policy constraints on FDA in expanding transparency, and obtaining insights from independent observers of FDA.

**RESULTS**

The team developed 18 specific recommendations for improving FDA's transparency to the public. FDA could adopt all these recommendations without further congressional action.

**FUNDING**

The development of the *Blueprint for Transparency at the U.S. Food and Drug Administration* was funded by the Laura and John Arnold Foundation.

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**Transparency at the U.S. Food and  
Drug Administration**

*Robert M. Califf*

Given the profound public health and economic ramifications of decisions made by the U.S. Food and Drug Administration, the degree to which FDA activities should reflect an approach founded on complete transparency versus one focused on preserving confidentiality of information deserves public discussion. On one hand, reasonable requirements for transparency are critical to stimulating effective innovation, knowledge dissemination, and good business practice. On the other, ensuring the vitality of the medical products industry requires protecting legitimately proprietary information. With current standards reflecting a lengthy accumulation of legal, regulatory, and practical precedent, recent significant changes in the environment in which the FDA operates should prompt a critical examination of current practices. In this article, I comment on Sharfstein and colleagues' "Blueprint for Transparency," which calls for multiple specific actions to increase transparency at the agency across five key areas, including interactions between FDA and industry, public disclosure of internal FDA analyses, deliberations concerning generics and biosimilars, expanded access to raw study data, and approaches to countering misleading information in the public sphere. I evaluate these recommendations in light of my experience as a clinician, researcher, and former FDA Commissioner, and reflect on possible outcomes that could result from enacting these practices.

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**FDA Transparency in an Inescapably  
Political World**

*Daniel Carpenter*

Transparency requires more than disclosure of data. It requires a mechanism and policy for conveying information to the public. In order for the aims of the excellent report of the FDA Transparency Working Group to be realized, a publicity initiative will need to accompany the plan of action. The FDA will need to actively convey information about the evidence concerning benefit-risk profiles of drugs, sometimes pointing out misleading claims by manufacturers or sponsors. In other cases, the FDA will need to make available its procedures, including possible conflicts of interest, not only in drug approval, but also in guidance documents and in rulemaking. Transparency as a process of letting the public see into the agency should be accompanied by a proactive strategy of distributing information about the products regulated by the agency.

**Symposium articles** are solicited by the guest editor for the purposes of creating a comprehensive and definitive collection of articles on a topic relevant to the study of law, medicine and ethics. Each article is peer reviewed.

**Independent articles** are essays unrelated to the symposium topic, and can cover a wide variety of subjects within the larger medical and legal ethics fields. These articles are peer reviewed.

**Columns** are written or edited by leaders in their fields and appear in each issue of *JLME*.

**Next Issue:**

**The Transformation of Informed Consent**

A Symposium Guest Edited by Susan M. Wolf, Ellen Clayton, and Frances Lawrenz

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Clinical Trial Transparency: The FDA Should and Can Do More**

*Amy Kapczynski and Jeanie Kim*

The *Blueprint for Transparency at the FDA* recommends that the FDA proactively release more clinical trial data. We show that the FDA possesses the legal authority to act on this recommendation, and describe several reasons that the agency should do so. In particular, the primary existing route for researchers to obtain access to this data, the Freedom of Information Act (FOIA), has important limits, as our own recent experience shows.

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FDA and the Marketplace of Ideas for Medical Products**

*Nathan Cortez*

The market can produce skewed information about investigational products awaiting FDA approval. But the FDA rarely steps in to correct such misleading information, despite statutory authority to do so. This article evaluates a recommendation by the FDA Transparency Working Group that FDA more clearly signal when and how it will correct misleading information about investigational products, and why such a recommendation is particularly important after the 21st Century Cures Act.

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Disclose Data Publicly, without Restriction**

*Peter Doshi and Tom Jefferson*

Ethical, evidence-informed decision making is undermined by the grave concerns that have emerged over the trustworthiness of clinical trials published in biomedical journals. The inescapable conclusion from this growing body of research is that what we see, even in the most highly regarded peer-reviewed journals, cannot be trusted at face value. Concerns of inaccurate, biased, and insufficient reporting of trials are impossible to resolve without access to underlying trial data. Access to such data, including things like clinical study reports—huge, unabridged, detailed reports of clinical trials—would minimize the risk of distortions and selective publication. But the FDA, the world's greatest custodian of those data, just sits on them. We see no reason why FDA should not publicly release clinical study reports with minimal redactions. The European regulator is already doing this, but FDA's holdings are far greater. Data transparency is not simply an "opportunity" FDA might consider, but rather an ethical imperative. The *Blueprint* is good but does not go far enough. We do not need gates, barriers and committees between us and access to aggregate reports on drugs and other interventions which we are prescribing or using daily. Let's leave the nannies at home.

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Withholding Information on Unapproved Drug Marketing Applications: The Public Has a Right to Know**

*Sammy Almashat and Michael Carome*

The Food and Drug Administration (FDA), as a matter of long-standing policy, does not inform the public of instances whereby applications for new drugs or new indications for existing drugs have been rejected by the agency or withdrawn from consideration, nor does it disclose the agency's analyses of the data submitted with such applications. This lack of transparency is unjustified and prevents patients, researchers, and healthcare providers from gaining insight into why a drug's application was not approved. The FDA's policy is particularly troubling in cases where the agency has found a currently marketed drug to be ineffective or unsafe for a newly proposed indication. Disclosure of the FDA's findings in such cases would promote public health by encouraging healthcare providers to avoid prescribing drugs for unapproved (off-label) uses that the agency has deemed to be potentially dangerous or ineffective. The FDA's counterpart agencies in Europe and Canada have demonstrated the feasibility of disclosing information on rejected and withdrawn drug marketing applications. The FDA should follow suit and allow the American public to know when a drug is deemed unsafe or ineffective for a certain use.