Commentary: Evaluating Oversight of Human Drugs and Medical Devices

Susan Bartlett Foote

The article on "Evaluating Oversight of Human Drugs and Medical Devices: A Case Study of the FDA and the Implications for Nanotechnology" undertakes the substantial task of evaluating oversight of drugs and medical devices.[1] The authors have combined literature review from a variety of disciplines with an elaborate expert elicitation using 28 criteria. The article's goal is to use this work "to guide discussions regarding appropriate FDA oversight."

Section I contains a laundry list of statutory directives to the Food and Drug Administration (FDA) from Congress and subsequent regulatory efforts by the agency to provide assurance of safety and effectiveness of drugs and medical devices. The section contains a brief discussion of efforts to regulate "combination products" (defined as those products which do not fall neatly into the drug, device, or biologics categories set forth in law) and reference to a 2007 FDA report on regulation of nanotechnology. Section II describes the expert elicitation process used in the research and Section III applies the data to evaluation criteria. Finally, Section IV is the authors' attempt to describe the lessons of their work for nanobiotechnology oversight.

This article aspires to provide "useful information from multiple disciplines and perspectives." The expert elicitation and criteria development have employed social science statistical techniques. And there is reference to a variety of sources in the vast literature on the FDA. However, the analysis would be stronger with a more in-depth institutional or contextual dimension based in the administrative law field, as well as an understanding of the political science literature on federal agencies. It is through this institutional lens that this comment will evaluate the discussion and the conclusions of the piece.

The FDA does not exist in a vacuum. The agency is housed within the Department of Health and Human Services (DHHS). Its authority, like that of most regulatory agencies, comes from Congress. The various amendments described in some detail in the article are statutory and direct the agency's actions. The Commissioner of the FDA is appointed by the president and must be confirmed by the Senate. Congress has significant oversight functions; FDA Commissioners routinely appear before congressional committees

Susan Bartlett Foote, J.D., M.A., *holds a J.D. from Boalt Hall, University of California School of Law and an M.A. in history from Case Western Reserve University. She is a founder and serves on the Board of Directors of the Medical Technology Leadership Forum, a think tank on medical technology issues. She was a Robert Wood Johnson Health Policy Fellow and Senior Legislative Counsel in the U.S. Senate from 1990-1995.*

to answer questions about their decisions and priorities. FDA authority is constrained by legislative directives and administrative law principles. For example, Congress has provided the ground rules for notice and comment rulemaking, both in the Administrative Procedures Act of 1946, as well as in specific legislative initiatives.[2] The FDA cannot engage in any decision making that is inconsistent with statutory commands. FDA decisions can be challenged in the courts based on administrative law principles, such as exceeding statutory authority or failing to follow administrative procedures. And politics matter. As one former Commissioner recently commented, "The FDA Commissioner has the second hottest seat in Washington."[3] In other words, the FDA as an institution exists within a context that includes Congress, the Executive branch, and the courts.

Agency behavior reflects the institutional context in which it resides. Administrative law scholars have documented phenomena such as risk aversive behavior by agency officials and employees. Fearing backlash from Congress, the Executive branch, or the courts, regulators often avoid or delay controversial decisions or make decisions in a way that seeks to avoid the risk of criticism.[4]

In addition, there is a temporal dimension that the authors acknowledge is lacking in aspects of their research. The FDA represents over one hundred years of regulation of medical products, with a rich history reflecting scientific innovation and regulatory response. Congress and the Executive branch, including the president and the Secretary of DHHS, reflect political forces and policy preferences that vary depending on the times. Add to this the influence of individual commissioners, based on their relationships with Congress and the president, party affiliations, and personalities. These political and institutional issues must be understood in order to evaluate legislative and regulatory efforts in their time and over time.

An additional factor is the influence of regulated entities on Congress and on agency priorities. The FDA regulates a large percentage of all consumer products used in the United States. The drug industry and the medical device industry include thousands of companies that collectively hold a multi-billion dollar stake in FDA decisions. The influence of industry has waxed and waned depending on political forces. In the administrative law field, undue influence by regulated entities is known as "regulatory capture."[5] A countervailing force in FDA politics has been the influence of broad-based consumer groups as well as disease-specific groups such as AIDs or breast cancer organizations. All of these organizations can use their support in Congress or their relationships with an administration to achieve their own ends.

FDA decisions can be challenged in the courts based on administrative law principles, such as exceeding statutory authority or failing to follow administrative procedures. And politics matter. As one former Commissioner recently commented, "The FDA Commissioner has the second hottest seat in Washington."

An example of an institutional analysis that has relevance to FDA regulation of nanotechnology is the article called, "Can Regulation Be as Innovative as Science and Technology? The FDA's Regulation of Combination Products."[6] This article provides an overview of innovation in combination products, summarizes the evolution of the FDA, and evaluates its initial efforts to regulate combination products. Nanotechnology is included in the overview, as many promising novel combinations include nanorobots that can travel through the body to find illness and target the delivery of drugs and biologics. Using an institutional analysis, the article concludes that the history of the FDA "is one of iterative, incremental changes through carefully defined legislative distinctions and highly specific regulatory pathways. Politics and administrative law are likely to prevent the FDA from being a bold innovator."[7] These conclusions are based not on opinions, but on a thorough analysis of the interplay of the agency, Congress, the administration, and interest groups in the face of innovations in science and technology.

If the authors of "Evaluating Oversight" had used institutional analysis to explore the 2007 Nanotechnology Task Force report, we might have gotten deeper

insights into reasons for the report's recommendation not to advocate for a new regulatory framework now, but to evaluate the adequacy of the current paradigm for the combination products of the future. Such an analysis might have shed some light on questions such as the following: Why was a Task Force convened? Who determined the make-up of the Task Force? What political pressures was the Task Force facing, such as the need to manage stakeholders or members of Congress? Are the recommendations the result of the agency's desire to duck the issue? What was Congress's influence over the report, and is that likely to change with a new administration? I do not offer answers to these questions in this commentary, but am suggesting that a deeper understanding of politics and administrative law might lead inquiring minds in that direction. These efforts might facilitate analysis of FDA oversight approaches and the implications for nanotechnology oversight, the goal of the article under discussion.

The authors of "Evaluating Oversight" have invested much of their effort into eliciting the opinions of experts on a detailed list of criteria relevant to assessing the oversight function. They employ solid methodological tools grounded in social science techniques. However, the authors admit the serious limitations of their study. Indeed, the limitations are significant enough for the reader to question whether the expert elicitation really contributes to a better understanding of the FDA or the implications for nanotechnology oversight. The study limitations include the fact that only 15 experts participated in the survey, and only 31 experts were solicited. Even if the authors had gotten a 100% response rate, one can ask whether the numbers would have been sufficient to produce meaningful results.

Another limitation is the manner in which the experts were identified and categorized. The authors sought a wide variety of backgrounds and the respondents were divided into four categories, including government, industry, NGO/nonprofit, and academics. I would submit that "government" as a category is troubling, given that it could include a current employee of FDA, or of another government agency, a member of Congress, or his or her staff, among others. These individuals occupy very different positions in government and are likely to have different perspectives. However, at the end of the day, only one "government" expert was included in the group of 15. One cannot draw meaningful conclusions using these numbers and these categories. As a result, the lengthy discussion of the statistical analyses performed does not contribute to the core questions raised in the paper. Because the authors readily admit to the limitations of the study, perhaps they would have been well advised to omit the statistical analysis altogether.

A more reliable method to assess "expert" opinion is to analyze the multitude of reports or statements issued by groups of experts. The authors do refer to some of these. For example, they cite a 2006 Union of Concerned Scientists report on politics in science. There are many other evaluations of aspects of FDA performance by government agencies such as the Government Accountability Office (GAO) and in congressional committee reports. Think tanks such as the Institute of Medicine publish evaluations. In addition, trade, consumer, and professional associations submit their views in congressional testimony, comments submitted during rulemaking processes, and position papers. Rather than rely on a single "government" survey respondent, or a handful of "industry" experts, oversight analysis should use published perspectives that represent the views of a variety of interested parties.

The authors then proceed to discuss each of the 28 criteria, from the expert elicitation survey. That discussion then is related "to existing literature, case law, and regulations using a historical, case studies approach." The discussion includes many interesting facts, but the absence of institutional and political realities divorce the discussion from critical context.

For example, criterion D6 is "financial resources." The authors note that the experts agreed that resources were "insufficient." The authors then provide a paragraph saying the resources are insufficient, conclusions based on the literature presumably but with no citations included. There is no discussion about the congressional appropriations process — whether these insufficiencies existed over a hundred years or varied in different periods, and why the agency is judged to be chronically underfunded. There is limited discussion of the relatively recent requirement of private sector funds, known as "user fees" in the area of drug and device review specifically. It is well known that in some areas of agency activity, there are "haves" and "have nots," due in some part to the user fees.[8]

I would submit that it is difficult if not impossible to discuss 28 criteria in a single article. The result, as the one example above demonstrates, is cursory and somewhat superficial analysis. Limiting the criteria to a smaller list of key issues focused more directly on nanotechnology oversight needs might have provided greater in-depth analysis.

In their conclusion, the authors raise questions about whether a new regulatory scheme needs to be created for nanotechnology, whether regulatory definitions need to be changed, whether agency resources are adequate, whether there is adequate scientific capacity, and whether stakeholders are adequately rep-

resented. These are all good questions. The challenge for the reader is whether, after absorbing the extensive discussion presented, we are any better informed to address those questions as concerned citizens or as policy makers.

Acknowledgements

Preparation of this article was supported in part by National Science Foundation (NSF) Grant No. 0608791 (PI, S. M. Wolf; Co-PIs, E. Kokkoli, J. Kuzma, J. Paradise, and G. Ramachandran). Any opinions, findings, and conclusions or recommendations expressed in this article are those of the author and do not necessarily reflect the views of the NSF.

References

1. J. Paradise et al., "Evaluating Oversight of Human Drugs and Medical Devices: A Case Study of the FDA and Implications for Nanobiotechnology," *Journal of Law, Medicine & Ethics* 37, no. 4 (2009): 546-586.
2. Many of the expansions of the FDA regulatory authority are quite detailed and specific in terms of scope of authority, tools available for implementation, and procedures that must be followed in developing regulations to implement the statutes. The FDA has very limited discretion in implementing these directives. For an illustration of these constraints relevant to another agency in the Department of Health and Human Services (DHHS), the Centers for Medicare and Medicaid Services (CMS), see S. B. Foote, "Why Medicare Cannot Promulgate a National Coverage Rule: A Case of *Regula Mortis*," *Journal of Health Politics, Policy and Law* 27, no. 5 (2002): 707-744.
3. Remarks of former Commissioner Jane S. Henney, at the Medical Technology Leadership Forum, Indianapolis, IN, December 8, 2008, cited in "FDA in the 21st Century: Issues and their Impact on Medical Technology," at 3, *available at* <www.mtlf.org/docs/ForumReport-Inpls-Finals.pdf> (last visited October 30, 2009).
4. See D. P. Carpenter, "Groups, the Media and Agency Waiting Costs: Political Economy of FDA Drug Approval," *American Journal of Political Science* 46, no. 3 (2002): 490-505.
5. See D. S. Egilman, A. H. Presler, and C. S. Valentin, "Avoiding Regulatory Capture of the Food and Drug Administration," *Archives of Internal Medicine* 167, no. 7 (2007): 732-733.
6. S. B. Foote and R. J. Berlin, "Can Regulation Be as Innovative as Science and Technology? The FDA's Regulation of Combination Products," *Minnesota Journal of Law, Science & Technology* 6, no. 2 (2005): 619-644.
7. See *id*., at 644.
8. Prescription drug user fees were first enacted in 1992 and medical device user fees followed in 2002. Adjustments to the fees have occurred in reauthorization measures. See *Prescription Drug User Fee Act of 1992* (PDUFA), Pub. L. No. 102-571, 106 Stat. 4491 (1992); *Medical Device User Fee and Modernization Act of 2002* (MDUFMA), Pub. L. No 107-250; 116 Stat. 1588 (2002). Actual use of these fees has been controversial.