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## Governance by the Backdoor: Administrative Law(lessness?) at the FDA

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Lars Noah\*

# Governance by the Backdoor: Administrative Law(lessness?) at the FDA

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## I. INTRODUCTION

In previous work, I have accused the U.S. Food and Drug Administration (FDA) of acting in a lawless fashion.<sup>1</sup> In those articles, I focused on the agency's efforts to evade constitutional constraints and

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\* Professor of Law, University of Florida; author of *LAW, MEDICINE, AND MEDICAL TECHNOLOGY: CASES & MATERIALS* (3d ed. 2012). In citations to legislative materials, the editors have graciously allowed me to deviate from *Bluebook* Rule 12.4(c) by supplying additional information that more precisely identifies the location of particular subsections.

1. See Lars Noah, *The Little Agency That Could (Act with Indifference to Constitutional and Statutory Strictures)*, 93 *CORNELL L. REV.* 901, 924 (2008) (“[O]ver the course of a century of struggling to protect the public health with its limited statutory powers and often inadequate resources, the FDA evidently has institutionalized a practice of cavalierly ignoring legal constraints.”).

statutory limits on its jurisdiction.<sup>2</sup> Less often have I addressed the seemingly more prosaic procedural irregularities in the way that the FDA conducts itself, except insofar as these have allowed it to cross substantive boundaries largely unnoticed. Even if the agency never strayed from the confines of its delegated authority, however, efforts to circumvent procedural requirements can have serious consequences for the quality of its work and those subject to its commands. A preference for staying under the radar whenever possible means evading critical checks exercised by all three branches of government.

The FDA has used a variety of procedural short cuts when implementing its statutory powers. Part II of this paper focuses on the agency's shift from the promulgation of binding rules to the issuance of nonbinding guidance documents. Although Congress and the White House seem to have become increasingly comfortable with the agency's practice, the FDA may have gotten a little carried away with this mechanism for announcing its policies. Part III of this paper explains how the agency secures widespread adherence to its technically nonbinding policies, whether expressed through guidance documents or left largely unspoken. The FDA enjoys significant leverage over regulated entities, by virtue of its powers of enforcement and product licensing, and in both settings it can communicate threats and offers that (more often than not) secure "voluntary" compliance with whatever the agency demands. Even if the FDA limits itself to requesting concessions that it could have—after expending greater effort—imposed directly, such a backdoor approach sacrifices the procedural safeguards dictated by the legislative, executive and judicial branches.

## II. ANNOUNCING AGENCY INTENTIONS AND EXPECTATIONS

During the last quarter of a century, federal regulators have found it increasingly difficult to promulgate regulations,<sup>3</sup> and guidance doc-

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2. See *id.* at 903, 917–25; see also Lars Noah, *Regulating Cigarettes: (Non)sense and Sensibility*, 22 S. ILL. U. L.J. 677, 691 (1998) (arguing that the FDA "should not be free to ignore the outer boundaries of its delegated authority in pursuit of a well-meaning crusade against a public health problem"). See generally Lars Noah, *Interpreting Agency Enabling Acts: Misplaced Metaphors in Administrative Law*, 41 WM. & MARY L. REV. 1463, 1530 (2000) ("The rush to defend seemingly desirable regulatory initiatives should not blind us to the potentially serious institutional consequences of adopting a stance of excessive faith in administrative agencies."); *id.* at 1498 ("As creatures of statutes lacking any independent constitutional pedigree, agencies cannot invoke some kind of inherent authority to justify actions that find no warrant in their enabling legislation.").

3. See Thomas O. McGarity, *Some Thoughts on "Deossifying" the Rulemaking Process*, 41 DUKE L.J. 1385, 1386 (1992) (discussing "the increasingly stiff and formalized structures of the informal rulemaking process"); *id.* at 1462 (same). See

uments have become a more frequently used format for announcing agency intentions and expectations.<sup>4</sup> Under the Administrative Procedure Act (APA),<sup>5</sup> “interpretative rules” and “general statements of policy” need not undergo notice-and-comment rulemaking,<sup>6</sup> though courts have struggled to draw a line between “legislative” and “nonlegislative” rules.<sup>7</sup> Technically, guidance documents lack any binding effect,<sup>8</sup> but agencies often seem to expect regulated entities to abide by

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*generally* CORNELIUS M. KERWIN & SCOTT R. FURLONG, *RULEMAKING: HOW GOVERNMENT AGENCIES WRITE LAW AND MAKE POLICY* (4th ed. 2010). Commentators continue to debate this question. Compare Jason Webb Yackee & Susan Webb Yackee, *Testing the Ossification Thesis: An Empirical Examination of Federal Regulatory Volume and Speed, 1950–1990*, 80 GEO. WASH. L. REV. 1414 (2012), with Richard J. Pierce, Jr., *Rulemaking Ossification Is Real: A Response to Testing the Ossification Thesis*, 80 GEO. WASH. L. REV. 1493 (2012).

4. See HOUSE COMM. ON GOV'T REFORM, NON-BINDING LEGAL EFFECT OF AGENCY GUIDANCE DOCUMENTS, H.R. REP. NO. 106-1009, at 5 (2000) (finding that just three federal agencies had generated over 5,500 guidance documents during the late 1990s); see also *id.* at 1 (criticizing such “backdoor” regulation as “an abuse of power”).
5. Pub. L. No. 79-404, 60 Stat. 237 (1946) (codified as amended at 5 U.S.C. §§ 551–559, 701–706 (2012)).
6. See 5 U.S.C. § 553(b)(A) (2012); Robert A. Anthony, *A Taxonomy of Federal Agency Rules*, 52 ADMIN. L. REV. 1045 (2000); William Funk, *A Primer on Nonlegislative Rules*, 53 ADMIN. L. REV. 1321, 1322–35 (2001); see also McGarity, *supra* note 3, at 1393 (“Perhaps more troublesome to the goals of open government is the increasing tendency of agencies to engage in ‘nonrule rulemaking’ through relatively less formal devices such as policy statements, interpretative rules, manuals, and other informal devices.”); *id.* at 1441–43 (same). Technically, one should not contrast guidance-making with rulemaking; instead, the former represents a subset of the latter—guidance-making is a form of (exempt) rulemaking under the APA. See 5 U.S.C. § 551(4)&(5) (2012). Moreover, after passage of the Freedom of Information Act (FOIA), Pub. L. No. 89-487, 80 Stat. 250 (1966) (codified as amended at 5 U.S.C. § 552 (2012)), agencies have incentives to publish otherwise exempt rules, see 5 U.S.C. § 552(a)(1)(D), (2)(B) (2012); see also *infra* note 8 (discussing the publication of exempt rules and their effect).
7. For recent surveys of the extensive case law and academic commentary on this question, see David L. Franklin, *Legislative Rules, Nonlegislative Rules, and the Perils of the Short Cut*, 120 YALE L.J. 276 (2010); Stephen M. Johnson, *In Defense of the Short Cut*, 60 U. KAN. L. REV. 495, 509–35 (2012); Morgan Douglas Mitchell, Note, *Wolf or Sheep?: Is an Agency Pronouncement a Legislative Rule, Interpretive Rule, or Policy Statement?*, 62 ALA. L. REV. 839 (2011).
8. See Jacob E. Gersen, *Legislative Rules Revisited*, 74 U. CHI. L. REV. 1705, 1708–13 (2007); *id.* at 1705 (“The distinction between legislative rules and non-legislative rules is one of the most confusing in administrative law. . . . To describe the legislative rule debate is to conjure doctrinal phantoms, circular analytics, and fundamental disagreement even about correct vocabulary.”). When published, however, exempt rules may have an intermediate (precedential) effect. See Peter L. Strauss, *Publication Rules in the Rulemaking Spectrum: Assuring Proper Respect for an Essential Element*, 53 ADMIN. L. REV. 803, 806, 824, 828–33, 843, 849–50 (2001); see also *id.* at 811 (“[A]ctions validly adopted pursuant to congressionally authorized rulemaking procedures have the kind of authority we commonly ascribe to statutes; actions that meet the publication requirements of section 552(a) have such authority as we commonly ascribe to

announcements that have not emerged from rulemaking procedures.<sup>9</sup> In addition to avoiding the need to follow procedural requirements under the APA, agencies may shy away from issuing legislative rules in order to dodge judicial review.<sup>10</sup> More recently, one commentator suggested that avoidance of scrutiny by the White House's Office of Management and Budget (OMB) also may serve as a motivating factor.<sup>11</sup> As another commentator summarized:

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precedents; and in other cases, agencies are not permitted to treat their actions as having legal force on citizens.”); *id.* at 816 (“Nothing in the APA permits an agency to claim legislative force for a publication rule.”).

9. See Robert A. Anthony, *Interpretive Rules, Policy Statements, Guidances, Manuals, and the Like—Should Federal Agencies Use Them to Bind the Public?*, 41 DUKE L.J. 1311, 1315 (1992) (“While these nonlegislative rules by definition cannot *legally* bind, agencies often inappropriately issue them with the intent or effect of imposing a *practical* binding norm upon the regulated or benefited public.”); Yackee & Yackee, *supra* note 3, at 1432 (“[A]gencies may be able to regulate via non-rule rules with relative impunity.”); Cindy Skrzycki, *Finding a Way to Better Guidance*, WASH. POST, Dec. 20, 2005, at D1 (“Though not legally binding, guidance is sometimes considered practically binding by regulated industries, a sort of ‘backdoor’ rulemaking.”). Guidance documents represent a form of “soft law.” See Jacob E. Gersen & Eric A. Posner, *Soft Law: Lessons from Congressional Practice*, 61 STAN. L. REV. 573, 576–77 (2008).
10. Courts typically find challenges to nonlegislative rules unripe. See *Nat’l Park Hospitality Ass’n v. Dep’t of Interior*, 538 U.S. 803, 809–12 (2003); *Colwell v. HHS*, 558 F.3d 1112, 1123–29 (9th Cir. 2009); *Munsell v. USDA*, 509 F.3d 572, 585–87 (D.C. Cir. 2007); *Funk*, *supra* note 6, at 1335–41; Gwendolyn McKee, *Judicial Review of Agency Guidance Documents: Rethinking the Finality Doctrine*, 60 ADMIN. L. REV. 371, 385–91, 400–02, 407 (2008). If an agency uses a guidance document in the course of imposing a sanction or otherwise seeks to give it a binding effect, then a court would entertain a procedural or other objection to that announcement. See, e.g., *NRDC v. EPA*, 643 F.3d 311, 320–21 (D.C. Cir. 2011); *Manufactured Housing Inst. v. EPA*, 467 F.3d 391, 397–99 (4th Cir. 2006). So long as agencies take care and rely on indirection, however, courts generally will decline to review guidance documents. Pre-enforcement challenges might have a better chance of surmounting finality and ripeness obstacles if interested parties first filed a petition with the agency requesting the amendment or revocation of a nonlegislative rule and then seek judicial review of the denial. See Sean Croston, *The Petition Is Mightier Than the Sword: Rediscovering an Old Weapon in the Battles over “Regulation Through Guidance,”* 63 ADMIN. L. REV. 381, 394–99 (2011); see also *Fox Television Stations, Inc. v. FCC*, 280 F.3d 1027, 1037 (D.C. Cir. 2002) (“[D]enial of a petition to initiate a rulemaking for the repeal or modification of a rule is a final agency action subject to judicial review.”).
11. See Jennifer Nou, *Agency Self-Insulation Under Presidential Review*, 126 HARV. L. REV. 1755, 1784–86 (2013); see also Nina A. Mendelson & Jonathan B. Wiener, *Responding to Agency Avoidance of OIRA*, 37 HARV. J.L. & PUB. POL’Y 447, 485–89 (2014) (assessing this claim); Robert Pear, *Bush Directive Increases His Regulatory Sway*, N.Y. TIMES, Jan. 30, 2007, at A1 (“[OMB] already has an elaborate process for the review of proposed rules. But in recent years, many agencies have circumvented this process by issuing guidance documents . . .”). OMB reviews “significant” proposed and final rules before publication. See Exec. Order No. 12,866, *Regulatory Planning and Review*, §§ 3(f), 6(a)(3), 58 Fed. Reg. 51,735 (Oct. 4, 1993), amended by Exec. Order No. 13,563, *Improving Regulation and Regulatory Review*, 76 Fed. Reg. 3821 (Jan. 18, 2011), reprinted in 5 U.S.C. § 601

[B]y issuing a guidance document, an agency can obtain a rule-like effect while minimizing political oversight and avoiding the procedural discipline, public participation, and judicial accountability required by the APA. The prospect of “compliance for less” is almost certainly among the reasons that agencies use guidance documents rather than go through the effort of notice-and-comment rulemaking.<sup>12</sup>

This Part offers an in-depth look at the evolving use of guidance documents by the FDA.<sup>13</sup>

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app. (2012). OMB did, however, at one point insist on reviewing significant guidance documents, and it evidently (though informally) continues to do so. *See infra* notes 94–98 and accompanying text. The Office of Information and Regulatory Affairs (OIRA)—a division of OMB—carries out these functions. *See* Cass R. Sunstein, *The Office of Information and Regulatory Affairs: Myths and Realities*, 126 HARV. L. REV. 1838 (2013); Note, *OIRA Avoidance*, 124 HARV. L. REV. 994, 994–1003 (2011).

12. Nina A. Mendelson, *Regulatory Beneficiaries and Informal Agency Policymaking*, 92 CORNELL L. REV. 397, 408 (2007) (adding that, “[s]ince guidance documents are generally not published in the *Federal Register*, they are also less likely to be subject to congressional oversight or attention in the media” (footnote omitted)); *see also id.* at 410–13 (elaborating on the reasons why guidance documents largely escape executive, legislative, and judicial review); *id.* at 452 (“When an agency chooses to issue a policy in a guidance document rather than a rule, regulatory beneficiaries lose the crucial ability to participate in the agency decision and to obtain judicial review of it.”); *cf.* Anthony, *supra* note 9, at 1318; *id.* at 1379 (“[I]f an agency wants to bind the public, it . . . should not try to do it on the cheap or on the sly.”).
13. For similar case studies involving other agencies, see Jill E. Family, *Easing the Guidance Document Dilemma Agency by Agency: Immigration Law and Not Really Binding Rules*, 47 U. MICH. J.L. REFORM 1 (2013); Kristin E. Hickman, *Coloring Outside the Lines: Examining Treasury’s (Lack of) Compliance with Administrative Procedure Act Rulemaking Requirements*, 82 NOTRE DAME L. REV. 1727 (2007); Sam Kalen, *The Transformation of Modern Administrative Law: Changing Administrations and Environmental Guidance Documents*, 35 ECOLOGY L.Q. 657 (2008). In contrast, a recent empirical study confidently concluded that we have nothing to worry about. *See* Connor N. Raso, Note, *Strategic or Sincere? Analyzing Agency Use of Guidance Documents*, 119 YALE L.J. 782, 805–23 (2010); *see also id.* at 805 (including the FDA as one of five agencies surveyed for purposes of considering all guidance documents issued relative to legislative rules promulgated annually over a ten-year period). Even if his conclusion follows from the data that he reviewed, my unapologetically qualitative survey of the practice at one agency begs to differ. *Cf. id.* at 821–22 & n.170 (conceding that the FDA may represent a special case); *id.* at 811 n.140, 816 n.156 (finding no compilation of FDA guidance documents deemed “significant” under OMB’s criteria). For another seemingly tone-deaf empirical assessment of the issue, see Yackee & Yackee, *supra* note 3, at 1438–39, 1460–64 (offering an admittedly crude survey focusing on the Department of Interior (DOI) that generally echoed Raso’s conclusion); *id.* at 1474 (summarizing interviews with DOI employees about their utilization of nonlegislative rules). Remarkably, these authors searched for nonlegislative rules by identifying uncommented upon announcements in the “Rules and Regulations” section of the *Federal Register*. *See id.* at 1461 & n.229. That would pick up direct final rules, and technically it coincides with the categorization used by the Office of Federal Register, *see* 1 C.F.R. § 5.9(b) (2014), but in practice most announcements of nonlegislative rules appear in the separate “Notices” section, *see id.* § 5.9(d).

### A. The FDA's Struggles in Promulgating Regulations

The FDA was one of the first federal agencies to make extensive use of its initially unclear rulemaking powers. In lieu of bringing enforcement actions under the open-ended provisions of the Food, Drug, and Cosmetic Act (FDCA),<sup>14</sup> and generating adjudicatory precedent for future cases, the FDA began to promulgate more detailed rules to implement its statutory authority.<sup>15</sup> Although infractions still required individual enforcement proceedings, the agency would simplify its burden of proof in those cases,<sup>16</sup> which, coupled with the greater clarity of expectations, would help to promote improved compliance.

In the FDCA, Congress expressly granted the agency the authority to issue regulations governing certain subjects,<sup>17</sup> but it also required that interested parties be allowed to request a public hearing as part of the rulemaking process.<sup>18</sup> Until 2007, for instance, the FDA's power to promulgate prescription drug advertising regulations was subject to this "formal" rulemaking procedure.<sup>19</sup> In practice, these procedural requirements became a source of frustrating delays for the agency.<sup>20</sup>

The statute also included residual rulemaking authority.<sup>21</sup> After courts decided that this provision empowered the FDA to issue binding regulations on matters not specifically covered by the formal

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14. Pub. L. No. 75-717, 52 Stat. 1042 (1938) (codified as amended at 21 U.S.C. §§ 301-399d (2012)).

15. See Eric R. Claeys, *The Food and Drug Administration and the Command-and-Control Model of Regulation*, 49 ST. LOUIS U. L.J. 105, 117-21 (2004); Richard A. Merrill, *FDA and the Effects of Substantive Rules*, 35 FOOD DRUG COSM. L.J. 270, 271-72 (1980); Reuel E. Schiller, *Rulemaking's Promise: Administrative Law and Legal Culture in the 1960s and 1970s*, 53 ADMIN. L. REV. 1139, 1147-49 (2001).

16. See generally Charles C. Ames & Steven C. McCracken, *Framing Regulatory Standards to Avoid Formal Adjudication: The FDA as a Case Study*, 64 CAL. L. REV. 14 (1976).

17. See 21 U.S.C. § 371(e) (2012).

18. See *Pharm. Mfrs. Ass'n v. Gardner*, 381 F.2d 271, 278 (D.C. Cir. 1967).

19. See 21 U.S.C. § 352(n) (2006), amended by Food and Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, § 901(d)(6), 121 Stat. 823, 942. Evidently Congress had become frustrated by the agency's failure to undertake any rulemaking in this area since the late 1960s. See *infra* notes 105-06 and accompanying text.

20. See Robert W. Hamilton, *Rulemaking on a Record by the Food and Drug Administration*, 50 TEX. L. REV. 1132, 1142 (1972) ("[T]he FDA has conducted two major [formal rulemaking] proceedings that have been the subject of wide criticism. Both proceedings have taken (or will take) more than ten years from the formulation of the original proposal to the actual effective date of the regulation."); cf. Aaron L. Nielson, *In Defense of Formal Rulemaking*, 75 OHIO ST. L.J. 237 (bemoaning the fact that this procedure has fallen into disuse, and suggesting that the delays experienced by the FDA arose from its failure to manage the process efficiently).

21. See 21 U.S.C. § 371(a).

rulemaking provision,<sup>22</sup> the agency shifted to notice-and-comment procedures for the promulgation of rules. At the same time, courts allowed interested parties to bring pre-enforcement challenges to such regulations.<sup>23</sup> Although “informal” rulemaking avoided the cumbersome hearings required with formal rulemaking, searching judicial review on the merits,<sup>24</sup> coupled with increasing procedural demands added by all three branches of government, have made it increasingly difficult.<sup>25</sup> For instance, in the FDA’s largest rulemaking exercise underway at the moment (regulations to implement significant statutory amendments related to food safety), OMB apparently delayed issuance of the proposed rules for over one year.<sup>26</sup>

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22. See *Nat’l Ass’n Pharm. Mfrs. v. FDA*, 637 F.2d 877 (2d Cir. 1981); *Pharm. Mfrs. Ass’n v. FDA*, 634 F.2d 106, 108 (3d Cir. 1980) (per curiam); Thomas W. Merrill & Kathryn Tongue Watts, *Agency Rules with the Force of Law: The Original Convention*, 116 HARV. L. REV. 467, 557–65 (2002); see also *id.* at 513–16, 583–84, 586–87 (arguing that these decisions reflect a fundamental misinterpretation of the FDCA, though conceding that any effort now to correct this mistake would imperil many of the legislative rules issued by the FDA).
  23. See *Abbott Labs. v. Gardner*, 387 U.S. 136 (1967) (holding that an FDA drug labeling regulation was ripe for judicial review).
  24. For a classic illustration involving the FDA, see *United States v. Nova Scotia Food Prods. Corp.*, 568 F.2d 240, 249–53 (2d Cir. 1977).
  25. See U.S. GEN. ACCT. OFFICE, GAO/HRD-92-35, *FDA REGULATIONS: SUSTAINED MANAGEMENT ATTENTION NEEDED TO IMPROVE TIMELY ISSUANCE* (1992); Thomas J. Hwang et al., *Quantifying the Food and Drug Administration’s Rulemaking Delays Highlights the Need for Transparency*, 33 HEALTH AFF. 309, 313 (2014) (discussing “[t]he slow pace of FDA rulemaking”); see also *supra* note 3 (referencing the ossification literature).
  26. See Brady Dennis, *Sweeping Rules for Food Are Released*, WASH. POST, Jan. 5, 2013, at A1 (“The new proposals spent more than a year awaiting final approval from the OMB. That led some stakeholders to speculate that the administration might have been holding up the proposals until after the election.”); see also *Ctr. for Food Safety v. Hamburg*, 954 F. Supp. 2d 965, 970–72 (N.D. Cal. 2013) (finding that the FDA had violated deadlines for the issuance of seven different sets of regulations to implement the Food Safety Modernization Act); U.S. GOV’T ACCOUNTABILITY OFFICE, GAO-09-205, *FEDERAL RULEMAKING: IMPROVEMENTS NEEDED TO MONITORING AND EVALUATION OF RULES DEVELOPMENT AS WELL AS TO THE TRANSPARENCY OF OMB REGULATORY REVIEWS 82* (2009) (discussing the fate of an FDA regulation as one of several case studies examined); Sabrina Tavernise, *F.D.A. Sets a Standard on Labeling “Gluten Free.”*, N.Y. TIMES, Aug. 3, 2013, at A11 (reporting that the agency finally issued this regulation six years after first proposing it, and nine years after Congress had specifically demanded such rulemaking). Similarly, OMB evidently delayed the release of a final rule from the Centers for Medicare and Medicaid Services (CMS) to implement the so-called “sunshine” provisions of the Affordable Care Act, which require the disclosure of pharmaceutical and medical device industry gifts to physicians. See Editorial, *In the Dark on Doctor Perks*, L.A. TIMES, Feb. 1, 2013, at A16 (“[T]he regulations are 15 months overdue. As with the new food-safety act regulations—most of which were finally released in January, a full year past deadline—the sunshine rules . . . have been held up by [OMB].”).

The FDA has experimented with further short cuts for issuing rules. In 1997, expressing an interest in expediting the issuance of its routine or otherwise noncontroversial regulations, the agency published a guidance document to describe “direct final rulemaking,” which dispenses with the need to publish a proposal or invite public comment unless someone objects shortly after promulgation.<sup>27</sup> Direct final rulemaking has not, however, worked out as well as the agency had hoped. A survey conducted a little more than one year after issuance of the guidance found that “the FDA has issued thirteen direct final rules, five of which it has already withdrawn in whole or in part because of the receipt of some significant adverse comment.”<sup>28</sup> One decade later, a follow-up survey found a similar pattern,<sup>29</sup> and little has changed during the latest five-year period.<sup>30</sup>

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27. See Notice, Guidance for FDA and Industry: Direct Final Rule Procedures, 62 Fed. Reg. 62,466 (Nov. 21, 1997). The FDA announced that it would ordinarily provide a post-promulgation comment period of at least seventy-five days after publishing a direct final rule, and, no more than thirty days after the close of this period, it would publish a notice either confirming an effective date of thirty days thereafter or announcing the withdrawal of the rule because of the receipt of significant adverse comment. See *id.* at 62,468. In tandem with the initial publication of a direct final rule, the FDA promised to issue a companion notice of proposed rulemaking (NPRM), which would then provide the basis for proceeding with informal rulemaking in the event that the agency withdrew the direct final rule, and any comments previously received would be considered in the course of this parallel rulemaking proceeding. See *id.* at 62,469.
28. Lars Noah, *Doubts About Direct Final Rulemaking*, 51 ADMIN. L. REV. 401, 411 & n.47 (1999) (contrasting this initial pattern with the greater success experienced by the Environmental Protection Agency (EPA) and others, adding that “disparities in agency batting averages will affect their relative success in realizing the supposed efficiencies of direct final rulemaking”); see also *id.* at 412–28 (explaining why the procedure is unlawful); *id.* at 423 (suggesting that courts “might resist direct final rulemaking as an inappropriate dodge”); *id.* at 426 (“[T]o the extent that regulations promulgated through direct final rulemaking seem vulnerable to procedural or substantive challenges, this expedited process may actually backfire by increasing the odds of challenges to non-controversial rules that regulated entities would otherwise not bother assailing in court.”).
29. See Michael Kolber, *Rulemaking Without Rules: An Empirical Study of Direct Final Rulemaking*, 72 ALB. L. REV. 79 (2009). Excluding entries from his survey that I already had counted (i.e., through 3/15/99), Kolber’s Appendix showed that the FDA had issued twenty-five direct final rules and nine notices of withdrawal. See *id.* at 113–15.
30. During this period, the FDA issued twelve direct final rules and four notices of withdrawal. These numbers are based on a Lexis search (conducted 6/25/13) in the “Federal Register” library for “agency(FDA) and action(direct w/1 final) and date aft May 1, 2008” and exclude confirmation notices.

## B. Guidance-making as the New Rulemaking

As informal rulemaking became increasingly difficult, the FDA shifted from promulgating regulations to issuing guidance.<sup>31</sup> By the mid-1990s, “[w]ell over a thousand such documents exist[ed].”<sup>32</sup> This offered the agency a convenient short cut for communicating its expectations to regulated entities, but the FDA’s growing dependence on guidance documents presents a couple of problems. First, these informal announcements may operate as de facto rules but escape normal procedural safeguards for their promulgation or review.<sup>33</sup> Second, they allow the FDA to take positions that do not even constrain agency officials, which leaves regulated entities guessing about their rights and obligations.<sup>34</sup> Nonetheless, Congress largely has endorsed and even encouraged this development, though questions remain about whether the agency may have gone too far.

### 1. Evolution of the FDA’s Good Guidance Practices

The FDA has formalized its procedures for the issuance and use of guidance documents. In 1997, the agency announced its policy on “Good Guidance Practices” (GFPs).<sup>35</sup> The new policy called for uni-

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31. See Todd D. Rakoff, *The Choice Between Formal and Informal Modes of Administrative Regulation*, 52 ADMIN. L. REV. 159, 168 (2000). Actually, it had done so throughout its history, though the nomenclature has changed over time. See K.M. Lewis, *Informal Guidance and the FDA*, 66 FOOD & DRUG L.J. 507, 509–23 (2011) (tracing the evolution in the agency’s use of guidance); *id.* at 538–43 (summarizing the advantages and disadvantages of the FDA’s growing reliance on guidance documents, concluding that the practice is generally beneficial); *id.* at 546 (“The story of guidance at FDA is full of twists and turns. After a century of experimentation, FDA has stumbled upon a formula that reasonably accommodates the conflicting interests of stakeholders.”).
  32. Request for Comments, Guidance Documents; The Food and Drug Administration’s Development and Use, 61 Fed. Reg. 9181, 9182 (Mar. 7, 1996).
  33. See *Syncor Int’l Corp. v. Shalala*, 127 F.3d 90, 95–96 (D.C. Cir. 1997); *Cnty. Nutrition Inst. v. Young*, 818 F.2d 943, 948–49 (D.C. Cir. 1987) (per curiam); *Belarno Int’l, Ltd. v. FDA*, 678 F. Supp. 410, 414–16 (E.D.N.Y. 1988); Edward John Allera, *FDA’s Use of Guidelines, Notices of Proposed Rulemaking, and Compliance Policies as De Facto Rules: An Abuse of Discretion*, 36 FOOD DRUG COSM. L.J. 270, 274–77 (1981); Rakoff, *supra* note 31, at 167 (“If an agency . . . generates a set of detailed guidelines for its inspectors to enforce, it in effect still establishes the law for all those unwilling to pay the expense, or suffer the ill-will of challenging the agency in court.”); James Hunnicutt, Note, *Another Reason to Reform the Federal Regulatory System: Agencies’ Treating Nonlegislative Rules as Binding Law*, 41 B.C. L. REV. 153, 164, 175 (1999).
  34. See Lars Noah, *The FDA’s New Policy on Guidelines: Having Your Cake and Eating It Too*, 47 CATH. U. L. REV. 113, 140–42 (1997) (criticizing the agency’s practice of not taking definitive positions in guidance documents and, thereby, attempting to escape judicial review).
  35. See Notice, The Food and Drug Administration’s Development, Issuance, and Use of Guidance Documents, 62 Fed. Reg. 8961 (Feb. 27, 1997). Less than a year earlier, the FDA had published a notice of its proposed policy, inviting comments

formity in format, the use of standardized nomenclature, explicit language disavowing any binding legal effect, assurances of access to these documents by interested parties, limited opportunities for public input, and procedures for internal review.<sup>36</sup> This policy represented a response to complaints that the FDA inappropriately used guidance documents as if they constituted binding rules that regulated entities had to follow.<sup>37</sup>

Less than a year later, in the course of making sweeping amendments to the FDCA, Congress directed the agency to issue the GGP's as regulations no later than July 1, 2000.<sup>38</sup> Although it generally endorsed the FDA's growing reliance on guidance documents, Congress also took the opportunity to impose some restrictions on their development and use.<sup>39</sup> The amendment reiterated the nonbinding character

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and announcing a public meeting on the subject. *See* Request for Comments, Guidance Documents; The Food and Drug Administration's Development and Use, 61 Fed. Reg. 9181 (Mar. 7, 1996); Notice of Public Meeting, Guidance Documents; The Food and Drug Administration's Development and Use, 61 Fed. Reg. 15,080 (Apr. 4, 1996).

36. *See* 62 Fed. Reg. at 8968–70; *see also* Hunnicutt, *supra* note 33, at 179–85, 192 (describing and critiquing aspects of the FDA's original GGP's policy).
37. *See* 62 Fed. Reg. at 8961 (explaining that the policy represented a response to a citizen petition filed by an association of device manufacturers that had objected to the FDA's mandatory application of nonbinding guidelines); *id.* at 8963 (discussing comments alleging past misuses of guidance documents by agency employees); *see also* United States v. Bioclinical Sys., Inc., 666 F. Supp. 82, 83–84 (D. Md. 1987) (rejecting the FDA's effort to require that device manufacturers adhere to a sterility guideline that had not emerged from notice-and-comment rulemaking).
38. *See* Food and Drug Administration Modernization Act (FDAMA), Pub. L. No. 105-115, § 405 (FDCA § 701(h)(5)), 111 Stat. 2296, 2369 (1997) (codified at 21 U.S.C. § 371(h)(5) (2012)); *see also* S. REP. NO. 105-43, at 26 (1997) (explaining this provision). Fifteen years later, Congress made a minor amendment to this provision, adding that, “[w]ith respect to devices, if a notice to industry guidance letter, a notice to industry advisory letter, or any similar notice sets forth initial interpretations of a regulation or policy or sets forth changes in interpretation or policy, such notice shall be treated as a guidance document for purposes of this subparagraph.” Food and Drug Administration Safety and Innovation Act, Pub. L. No. 112-144, § 619(2), 126 Stat. 993, 1064 (2012) (codified at 21 U.S.C. § 371(h)(1)(C)(ii) (2012)).
39. *See* Lewis, *supra* note 31, at 537 (“[B]y enshrining the GGP's in the FDAMA, Congress has signaled that it expects and desires FDA to make policy through guidance, provided that FDA follows specified procedures.”). In an otherwise excellent general overview of federal agencies' freedom to select among rulemaking, adjudication, prosecution, and guidance (though seemingly oblivious to the use of threats and other means of exerting informal leverage that I discuss in Part III), the distinctiveness of the FDA's development and use of guidance documents gets essentially no attention. *See* M. Elizabeth Magill, *Agency Choice of Policymaking Form*, 71 U. CHI. L. REV. 1383, 1411 n.96 (2004) (suggesting incorrectly that the FDA's GGP's lack any statutory foundation); *id.* at 1445 (“Guidance is relatively cheap to produce; it does not require the [FDA] to present its view to the public for comment or to a court for evaluation.”); *cf. id.* at 1392 &

of guidance documents,<sup>40</sup> though it directed the agency to “ensure that employees of the [FDA] do not deviate from such guidances without appropriate justification and supervisory concurrence.”<sup>41</sup> The amendment also sought to ensure that the public have some opportunity to participate and get reasonable access to them.<sup>42</sup> Congress required that the FDA solicit comments before finalizing major guidance,<sup>43</sup> while the agency could wait to solicit public feedback on minor guidance until after the fact.<sup>44</sup> The amendment made no provision for judicial review, demanding only that the agency provide “an effective appeals mechanism” to address any complaints of noncompliance with these procedural requirements.<sup>45</sup>

Less than three months after the deadline imposed by Congress, the FDA promulgated its final GGPs rule.<sup>46</sup> In addition to reiterating

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n.20 (explaining that, “in contrast to the other policymaking forms examined here, guidance documents permit the agency to develop policy relatively cheaply,” adding that “an agency is not required to present its view to an administrative tribunal or court, and the agency does not have to solicit or respond to public comment,” while noting with no elaboration that the FDA “appears to be the most formalized”); Rakoff, *supra* note 31, at 170 (“[T]he creation by the FDA of a whole organized system of rules contained in guidance documents can be seen either as an example of thoughtful and balanced institutional creativity, or as a brazen attempt to subvert the APA as construed by the courts.”).

40. See 21 U.S.C. § 371(h)(1)(A) (2012) (“Such documents shall not create or confer any rights for or on any person, although they present the views of the Secretary on matters under the jurisdiction of the [FDA].”).
41. *Id.* § 371(h)(1)(B) (adding that the agency “shall provide training to employees in how to develop and use guidance documents and shall monitor the development and issuance of such documents”); see also *id.* § 371(h)(2) (“In developing guidance documents, the Secretary shall ensure uniform nomenclature for such documents and uniform internal procedures for approval of such documents. The Secretary shall ensure that guidance documents and revisions of such documents are properly dated and indicate the nonbinding nature of the documents.”).
42. See *id.* § 371(h)(1)(A) (“The Secretary shall develop guidance documents with public participation and ensure that information identifying the existence of such documents and the documents themselves are made available to the public both in written form and, as feasible, through electronic means.”); *id.* § 371(h)(3) (“All such documents shall be made available to the public.”).
43. See *id.* § 371(h)(1)(C)(i) (“For guidance documents that set forth initial interpretations of a statute or regulation, changes in interpretation or policy that are of more than a minor nature, complex scientific issues, or highly controversial issues, the Secretary shall ensure public participation prior to implementation of guidance documents . . .”). If, however, the agency “determines that such prior public participation is not feasible or appropriate,” then it “shall provide for public comment upon implementation and take such comment into account.” *Id.*
44. See *id.* § 371(h)(1)(D) (“For guidance documents that set forth existing practices or minor changes in policy, the Secretary shall provide for public comment upon implementation.”).
45. See *id.* § 371(h)(4); see also Lewis, *supra* note 31, at 539, 542 (discussing the inability to seek judicial review); *supra* note 10 (same).
46. See Final Rule, Administrative Practices and Procedures; Good Guidance Practices, 65 Fed. Reg. 56,477 (Sept. 19, 2000) (codified at 21 C.F.R. § 10.115 (2014)).

their nonbinding nature,<sup>47</sup> the agency committed itself to using guidance documents rather than other even less formal mechanisms for announcing policy.<sup>48</sup> The agency differentiated between “Level 1” and “Level 2” guidance documents,<sup>49</sup> defining the former category as those that “(i) Set forth initial interpretations of statutory or regulatory requirements; (ii) Set forth changes in interpretation or policy that are of more than a minor nature; (iii) Include complex scientific issues; or (iv) Cover highly controversial issues.”<sup>50</sup> Arguably, this definition describes subjects that the FDA in the past would have handled through notice-and-comment rulemaking, while only those less consequential matters viewed as appropriate for Level 2 guidance would have avoided APA requirements as interpretive rules or general statements of policy (or nowadays perhaps as candidates for direct final rulemaking).

Under the GGPs rule, Level 1 guidance documents must undergo a truncated notice-and-comment procedure,<sup>51</sup> while Level 2 guidance

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47. See 21 C.F.R. § 10.115(d)(1) (2014) (“Guidance documents do not establish legally enforceable rights or responsibilities. They do not legally bind the public or FDA.”); see also *id.* § 10.115(d)(2) (“You may choose to use an approach other than the one set forth in a guidance document. . . . FDA is willing to discuss an alternative approach with you to ensure that it complies with the relevant statutes and regulations.”); *id.* § 10.115(d)(3) (“Although guidance documents do not legally bind FDA, they represent the agency’s current thinking. Therefore, FDA employees may depart from guidance documents only with appropriate justification and supervisory concurrence.”); *id.* § 10.115(i)(1)(iv) (providing that guidance must “[p]rominently display a statement of the document’s nonbinding effect”); *id.* § 10.115(i)(2) (“Guidance documents must not include mandatory language such as ‘shall,’ ‘must,’ ‘required,’ or ‘requirement,’ unless FDA is using these words to describe a statutory or regulatory requirement.”).

48. See *id.* § 10.115(e) (“The agency may not use documents or other means of communication that are excluded from the definition of guidance document to informally communicate new or different regulatory expectations to a broad public audience for the first time. These GGPs must be followed whenever regulatory expectations that are not readily apparent from the statute or regulations are first communicated to a broad public audience.”); see also *id.* § 10.115(b)(3) (“Guidance documents do not include: Documents relating to internal FDA procedures, agency reports, general information documents provided to consumers or health professionals, speeches, journal articles and editorials, media interviews, press materials, warning letters, memoranda of understanding, or other communications directed to individual persons or firms.”); *id.* § 10.115(b)(2) (“Guidance documents include, but are not limited to, documents that relate to: The design, production, labeling, promotion, manufacturing, and testing of regulated products; the processing, content, and evaluation or approval of submissions; and inspection and enforcement policies.”).

49. *Id.* § 10.115(c); see also *id.* § 10.115(c)(2) (adding that “Level 2 guidance documents include all guidance documents that are not classified as Level 1”).

50. *Id.* § 10.115(c)(1).

51. See *id.* § 10.115(g)(1); see also *id.* § 10.115(g)(2)–(3) (explaining that, when pre-issuance comment is deemed “not feasible or appropriate” for Level 1 guidance documents, the agency will invite post-publication comments and consider revis-

documents only provide an opportunity for post-publication comment.<sup>52</sup> The agency promised to make guidance documents available in hard copy and electronic form,<sup>53</sup> and members of the public can, “at any time, suggest that FDA revise or withdraw an already existing guidance document.”<sup>54</sup> The FDA called upon its various units to ensure compliance with GGPs,<sup>55</sup> and persons who believe that an employee has failed to follow these procedures may appeal the issue up the internal chain of command and, if necessary, to the agency’s ombudsman.<sup>56</sup>

Thus, the FDA’s GGPs contemplate a “lite” form of informal rulemaking, at least for Level 1 guidance documents.<sup>57</sup> In some respects, the procedures parallel those associated with notice-and-com-

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ing the guidance); *id.* § 10.115(g)(5) (adding that post-publication comments are always welcome).

52. *See id.* § 10.115(g)(4); *see also* Lewis, *supra* note 31, at 543 (“The GGPs therefore provide the public a sufficient forum to voice their concerns regarding politically salient issues, while granting the agency the necessary flexibility to inexpensively formulate policies on important topics that are either (1) too technical, complex and esoteric for the general public to understand and comment on, or (2) too mundane to generate much outcry.”).
53. *See* 21 C.F.R. § 10.115(m). Announcements of the availability of Level 1 guidance documents also would appear in the *Federal Register*, *see id.* § 10.115(g)(1)(ii)(A), (g)(1)(iv)(B), (g)(3)(i)(A), while Level 2 guidance documents simply appear on the agency’s website, *see id.* § 10.115(g)(4)(i)(A), though they also would get included in the comprehensive lists of guidance documents periodically published in the *Federal Register*, *see id.* § 10.115(n)(2). For more on APA requirements for the publication of nonlegislative rules, *see supra* notes 6 & 8.
54. 21 C.F.R. § 10.115(f)(4); *see also id.* § 10.115(f)(2)–(3) (inviting suggestions for guidance to develop); *id.* § 10.115(k)(1) (“The agency will periodically review existing guidance documents to determine whether they need to be changed or withdrawn.”); *id.* § 10.115(k)(2) (“When significant changes are made to the statute or regulations, the agency will review and, if appropriate, revise guidance documents relating to that changed statute or regulation.”).
55. *See id.* § 10.115(l)(2) (“FDA centers and offices will monitor the development and issuance of guidance documents to ensure that GGPs are being followed.”); *see also id.* § 10.115(j) (“Each center and office must have written procedures for the approval of guidance documents. Those procedures must ensure that issuance of all documents is approved by appropriate senior FDA officials.”); *id.* § 10.115(l)(1) (“All current and new FDA employees involved in the development, issuance, or application of guidance documents will be trained regarding the agency’s GGPs.”).
56. *See id.* § 10.115(o). For a discussion of a similar internal appeal mechanism, *see* Karen M. Becker et al., *Scientific Dispute Resolution: First Use of Provision 404 of the Food and Drug Administration Modernization Act of 1997*, 58 *FOOD & DRUG L.J.* 211, 212–13 (2003).
57. *See* Lewis, *supra* note 31, at 536 (“The GGPs and the FDAMA established unprecedented opportunities for public participation in the guidance-making and guidance-revising process, and imposed procedural requirements akin to notice-and-comment rulemaking, albeit slightly more lenient.”); *id.* at 544 (“[T]he GGPs subject FDA proposals to a probing review process that approximates the rigor of notice-and-comment rulemaking and provides opportunities for public participation.”); *cf.* Hunnicutt, *supra* note 33, at 180 (“[I]f the agency is going to accept

ment rulemaking.<sup>58</sup> In other respects, however, the procedures demand far less of the FDA, especially the absence of any need to offer detailed responses to public comments.<sup>59</sup> Then again, the APA's requirement for a "concise general statement of the [rule's] basis and purpose"<sup>60</sup> plainly never meant to impose such a requirement for legislative rules though courts later so interpreted it.<sup>61</sup> In short, Level 1 guidance documents produced consistent with the GGPs—coupled with the absence of routine opportunities for "pre-enforcement" judicial review (technically, of course, a misnomer in this context) or close scrutiny by the other two branches of government—may reflect something of a throwback to informal rulemaking as originally conceived.<sup>62</sup>

Congress instructed the FDA "periodically" to publish a list of guidance documents in the *Federal Register*,<sup>63</sup> and the GGPs rule com-

commentary prior to implementing a [Level 1 guidance], why not simply employ informal notice-and-comment rulemaking as defined in the APA?").

58. *See, e.g.*, 21 C.F.R. § 10.115(g)(1)(v) (noting that the agency may decide to issue a revised draft for another round of comments); *see also id.* § 10.115(g)(1)(iii)(B) (explaining that it may invite advisory committee review).
59. *See id.* § 10.115(g)(1)(iv)(A) (providing only that it will "[r]eview any comments received and prepare the final version of the guidance document that incorporates suggested changes, when appropriate"); *see also id.* § 10.115(h)(3) (explaining that comments submitted to the Division of Dockets Management remain available for public inspection); Lewis, *supra* note 31, at 522 ("Level 1 guidance does not require the agency to respond to significant comments it receives . . . . This frees FDA from one of the major procedural burdens associated with notice-and-comment rulemaking."). *But cf.* Johnson, *supra* note 7, at 541 n.322 ("[T]he FDA has committed to full notice-and-comment procedures for 'Level 1 guidance documents.' . . . For guidance documents that are not Level 1, the FDA posts the guidance documents on the Internet and gives the public an opportunity to comment, but the FDA does not need to reply to those comments.").
60. 5 U.S.C. § 553(c) (2012).
61. *See* Lars Noah, *Divining Regulatory Intent: The Place for a "Legislative History" of Agency Rules*, 51 HASTINGS L.J. 255, 308–10 (2000); Rakoff, *supra* note 31, at 163–65; Peter L. Strauss, *From Expertise to Politics: The Transformation of American Rulemaking*, 31 WAKE FOREST L. REV. 745, 753, 757, 760 (1996).
62. *See* Rakoff, *supra* note 31, at 169 ("It would not be far-fetched to rephrase these [GGPs for Level 1 guidance documents] by saying that the FDA now proposes to issue its important regulations mostly in accordance with the notice-and-comment rulemaking procedure set forth in the APA, as it was understood before 1970. The only difference is that, at least in the agency's view, the entire matter will be beyond the purview of the courts."); *see also* Jessica Mantel, *Procedural Safeguards for Agency Guidance: A Source of Legitimacy for the Administrative State*, 61 ADMIN. L. REV. 343, 398–405 (2009) (favoring a requirement that both major and minor guidance allow for pre-adoption public comment and include a concise explanatory statement to accompany the final guidance but without any need to respond to particular comments); *id.* at 403–04 ("[M]y proposed limited notice-and-comment process parallels the notice-and-comment process followed by agencies from enactment of the APA through the 1960s.").
63. *See* 21 U.S.C. § 371(h)(3) (2012); *see also id.* § 371(h)(2) ("The Secretary shall periodically review all guidance documents and, where appropriate, revise such documents.").

mitted to doing so annually.<sup>64</sup> In practice, however, these lists have appeared somewhat irregularly.<sup>65</sup> The latest version reveals almost two thousand guidance documents, in both draft and final form,<sup>66</sup> and in recent years the FDA has produced more than a hundred new ones annually,<sup>67</sup> easily outpacing the frequency of notice-and-comment rulemaking.<sup>68</sup>

It did not take long for complaints to surface about ossification of the FDA's guidance-making process.<sup>69</sup> Perhaps that explains why

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64. See 21 C.F.R. § 10.115(n)(2); see also *id.* § 10.115(f)(5) (“Once a year, FDA will publish, both in the FEDERAL REGISTER and on the Internet, a list of possible topics for future guidance document development or revision during the next year.”); Notice, Annual Guidance Agenda, 75 Fed. Reg. 76,011 (Dec. 7, 2010).
65. See Notice, Comprehensive List of Current Guidance Documents at the Food and Drug Administration, 63 Fed. Reg. 9795 (Feb. 26, 1998); Notice, Annual Comprehensive List of Guidance Documents at the Food and Drug Administration, 64 Fed. Reg. 31,228 (June 10, 1999); Notice, Annual Comprehensive List of Guidance Documents at the Food and Drug Administration, 65 Fed. Reg. 45,428 (July 21, 2000); Notice, Annual Comprehensive List of Guidance Documents at the Food and Drug Administration, 66 Fed. Reg. 53,836 (Oct. 24, 2001); Notice, Annual Comprehensive List of Guidance Documents at the Food and Drug Administration, 70 Fed. Reg. 824 (Jan. 5, 2005); Notice, Annual Comprehensive List of Guidance Documents at the Food and Drug Administration, 71 Fed. Reg. 15,422 (Mar. 28, 2006).
66. See Notice, Comprehensive List of Guidance Documents at the Food and Drug Administration, 75 Fed. Reg. 48,180 (Aug. 9, 2010). Current lists (divided by subject matter) also appear on the agency’s website, see REGULATORY INFORMATION, *Guidances*, <http://www.fda.gov/RegulatoryInformation/Guidances/default.htm> (last visited July 5, 2013), archived at <http://perma.unl.edu/5NTR-4FAY>, which should reflect new guidance documents within 30 days of issuance, see 21 C.F.R. § 10.115(n)(1).
67. See Notice of Availability, Food and Drug Administration Report on Good Guidance Practices: Improving Efficiency and Transparency, 76 Fed. Reg. 82,311, 82,312 (Dec. 30, 2011) (“In fiscal year (FY) 2009, the Agency issued approximately 124 guidance documents. Since that time, its issuance of guidance documents has been trending upward, with the Agency issuing approximately 133 guidance documents in FY 2010 and approximately 144 guidance documents in FY 2011.”); see also Lewis, *supra* note 31, at 549–50 fig.5 (enumerating the annual production of guidance at the FDA over the last quarter of a century); *id.* at 537 (“[S]tatistics suggest its annual output of guidance has increased regularly since the formulation of the GGPs.”).
68. See Erica Seiguer & John J. Smith, *Perception and Process at the Food and Drug Administration: Obligations and Trade-Offs in Rules and Guidances*, 60 FOOD & DRUG L.J. 17, 25–26 (2005) (finding more than twice as many Level 1 guidance documents as regulations issued by the FDA between 2001 and 2003).
69. See *id.* at 24 (“[T]he development of guidances has come to resemble rulemaking in terms of the extent of clearance and time required to develop and implement them.”); *id.* at 27 (“Several individuals involved in both rulemaking and guidance development and implementation voiced concern about the increased layers of review . . . [and] worried that the additional scrutiny of guidances may detract from their utility as they become less flexible and responsive. . . . For some, this is a by-product of the formalization of the guidancemaking process in the GGPs . . . .”); *id.* at 32 (“Some agency officials and stakeholders suggest that in-

Level 1 guidance often remain in draft form,<sup>70</sup> which makes the procedures for their issuance (as drafts) essentially the same as those used for Level 2 guidance. For instance, the FDA recently has attracted criticism for its failure to finalize a draft guidance on mobile health applications issued in 2011.<sup>71</sup> In any case, and in spite of their explicitly “nonbinding” character, draft or final guidance still often operate

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creasing formality in the creation of guidances and more extensive oversight may hinder the speed and flexibility of their development. To the extent that rulemaking and guidance development are approximating each other in terms of time and resources required, some of the advantages of guidances may be diluted.”); see also Michael Asimow, *Guidance Documents in the States: Toward a Safe Harbor*, 54 ADMIN. L. REV. 631, 647 (2002) (describing a similar trajectory in California); *id.* at 632 (“[A]n agency should be permitted to adopt guidance documents without any pre-adoption procedures.”); Peter L. Strauss, *The Rulemaking Continuum*, 41 DUKE L.J. 1463, 1481 (1992) (“[I]t would be unreasonable to expect that any significant portion of today’s publication rules would appear if notice-and-comment rulemaking were required for their adoption.”).

70. See Seiguer & Smith, *supra* note 68, at 31 (“Another aspect of the concern over timeliness was voiced concerning the existence and persistence of draft guidances, often for years after an NOA [notice of availability] is published in the *Federal Register*. These documents, although in draft form and not issued as final documents, come to represent final guidances.”); see also Noah, *supra* note 34, at 127 & n.56 (discussing this tendency prior to adoption of the GGP’s policy). This may happen when the FDA gets inundated with comments, as happened after it issued a draft (and not yet finalized) guidance document on unorthodox treatments more than six years ago. See Notice of Availability, Draft Guidance for Industry on Complementary and Alternative Medicine Products and Their Regulation by the Food and Drug Administration, 72 Fed. Reg. 29,337, 29,338 (May 25, 2007) (noting the receipt of “a large volume of comments”); see also Notice of Availability, Draft Guidance for Industry: Voluntary Labeling Indicating Whether Foods Have or Have Not Been Developed Using Bioengineering, 66 Fed. Reg. 4839 (Jan. 18, 2001) (noting the receipt of more than 50,000 written comments). Conversely, the agency may invoke the power to skip the draft (and comment) stage on questionable grounds. See, e.g., Notice of Availability, Compliance Policy Guide: Compounding of Drugs for Use in Animals, 68 Fed. Reg. 134 (July 14, 2003) (explaining the failure to first solicit public comment on this Level 1 guidance document because the agency needed to revise its policy in response to a Supreme Court decision issued more than a year earlier). Recently, one FDA Center recognized that it had dozens of drafts that were more than three years old. See Notice, Retrospective Review of Draft Guidance Documents Issued Before 2010, 78 Fed. Reg. 48,175 (Aug. 7, 2013) (promising to either withdraw or finalize them).
71. See Hayley Tsukayama, *Lawmakers Press for Medical-App Rules*, WASH. POST, Mar. 13, 2013, at A14; see also *GOP Senators Criticize FDA Delays in Finalizing Draft Guidances*, DRUG INDUS. DAILY, May 9, 2014, available at 2014 WLNR 12430760 (discussing a letter sent by members of an oversight committee to the Commissioner objecting that “draft guidances are becoming default FDA policy”). Previously, a pair of Senators had sponsored an amendment to a pending bill designed to delay finalization of this draft. See Dina ElBoghady, *Feeling Sick? There’s an App for That*, WASH. POST, June 24, 2012, at G1. The agency eventually did issue a final version. See Notice of Availability, Mobile Medical Applications; Guidance for Industry and Food and Drug Administration Staff, 78 Fed. Reg. 59,038 (Sept. 25, 2013); Thomas M. Burton, *FDA Updates Its Guidance on*

as de facto requirements.<sup>72</sup> In recognition of this fact, some commentators have recommended—though without focusing on the FDA specifically—that courts entertain pre-enforcement challenges,<sup>73</sup> which no doubt would serve to bring guidance-making full circle back to legislative rulemaking with all of the difficulties that process has entailed for agencies.

## 2. Congressional Demands for FDA Guidance

Congress did not simply endorse the FDA's GGP's in 1997; in that same legislation, it also called for the issuance of guidance related to a few specific subjects.<sup>74</sup> Increasingly over the last decade, Congress

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*Mobile-Software Apps*, WALL ST. J., Sept. 24, 2013, at B4 (reporting that it had received 130 comments on the draft, which prompted substantial changes).

72. See, e.g., *Hood v. Wholesoy & Co.*, No. 12-cv-5550-YGR, 2013 WL 3553979, at \*2–3 (N.D. Cal. July 12, 2013) (noting a pair of 2012 FDA warning letters that referenced a 2009 draft guidance on use of the term “evaporated cane juice” (ECJ) on food labels); *id.* at \*5 (“[T]he Draft ECJ Guidance on which Plaintiff [in this consumer fraud action] relies says expressly that it is not a ‘legally enforceable’ standard, but only a suggestion. Given that statement, it is unclear why FDA subsequently has issued two warning letters citing that guidance. At a minimum, this indicates to the Court that the FDA’s position is not settled.”); *BBK Tobacco & Foods, LLP v. FDA*, 672 F. Supp. 2d 969, 974–76 (D. Ariz. 2009); see also *Seiguer & Smith*, *supra* note 68, at 29 (“While the enforcement implications differ for rules and guidances, in practice most of those interviewed said that industry treats guidances no differently than rules.”); *infra* Part III (elaborating on some of the reasons for this).
73. See Mark Seidenfeld, *Substituting Substantive for Procedural Review of Guidance Documents*, 90 TEX. L. REV. 331, 373–94 & n.265 (2011) (favoring substantive review of these “pragmatically binding” documents even while recognizing the risk of ossifying the process); see also Robert A. Anthony & David A. Codevilla, *Pro-Ossification: A Harder Look at Agency Policy Statements*, 31 WAKE FOREST L. REV. 667, 676–92 (1996) (urging more stringent judicial review under the arbitrary and capricious standard); *id.* at 669 (conceding that this might ossify nonlegislative rulemaking); *id.* at 672–73 n.21, 677 n.35 (discussing, without suggesting changes to, ripeness doctrine).
74. See Food and Drug Administration Modernization Act, Pub. L. No. 105-115, § 112(b), 111 Stat. 2296, 2310 (1997) (requiring that, within one year of enactment, the agency issue guidance describing the policies and procedures for “fast track” drug approvals); *id.* §§ 119(a) (FDCA § 505(b)(4)(A)), 119(b)(1)(B) (FDCA § 505(j)(3)(A)), 111 Stat. at 2316–17 (codified at 21 U.S.C. §§ 355(b)&(j) (2012)) (calling for the issuance of guidance for reviewers of biologic product applications); *id.* § 206(c)(2) (FDCA § 513(i)(1)(F)), 111 Stat. at 2340 (codified at 21 U.S.C. § 360c(i)(1)(F) (2012)) (requiring that, within 270 days of enactment, the agency issue guidance relating to intended use determinations for purposes of making judgments about the substantial equivalence of medical devices); *id.* § 403(b), 111 Stat. at 2367 (requiring that, within 180 days of enactment, the agency issue guidance to industry to clarify the requirements for applications seeking supplemental product approvals); see also *id.* § 116(a) (FDCA § 506A(c)(2)), 111 Stat. at 2314 (codified at 21 U.S.C. § 356a(c)(2) (2012)) (allowing the agency to issue either “regulation or guidance” to implement new requirements governing major manufacturing changes for approved drugs).

has directed the FDA to publish guidance documents on a number of other subjects that it wants the agency to address.<sup>75</sup> In 2006, for instance, it gave the agency approximately nine months to issue guidance on “minimum data elements that should be included in a

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75. *See, e.g.*, Drug Quality and Security Act, Pub. L. No. 113-54, § 202 (FDCA § 582(a)(2)), 127 Stat. 587, 605–06 (2013) (to be codified at 21 U.S.C. § 360eee-1(a)(2)) (requiring, within one year of enactment, draft guidance to establish standards for the exchange of drug transaction information but issued only after first providing a 60 day public comment period); *id.* § 202 (FDCA § 582(a)(3), (a)(5)(A)), 127 Stat. at 606–07 (to be codified at 21 U.S.C. § 360eee-1(a)(3), (a)(5)(A)) (requiring, within two years of enactment, guidance governing waivers, exceptions, and exemptions from these standards); *id.* § 203 (FDCA § 582(h)), 127 Stat. at 626–28 (to be codified at 21 U.S.C. § 360eee-1(h)) (requiring several types of guidance related to drug tracing requirements, specifying procedures for their issuance and revision that seem somewhat more demanding than GMPs for Level 1 guidance, and providing that these nonbinding pronouncements not take effect for one year); Pandemic and All-Hazards Preparedness Reauthorization Act of 2013, Pub. L. No. 113-5, § 304(3), 127 Stat. 161, 187 (to be codified at 21 U.S.C. § 360bbb-4(c)) (requiring that, within one year of enactment, the agency issue final guidance regarding acceptable animal models for the licensing of countermeasures); Food and Drug Administration Safety and Innovation Act, Pub. L. No. 112-144, § 806, 126 Stat. 993, 1082 (2012) (requiring, by Dec. 31, 2014, final Level 1 guidance about “pathogen-focused antibacterial drug development”); *id.* § 901(c), 126 Stat. at 1085–86 (requiring that, within two years of enactment, the FDA issue a final Level 1 guidance document on accelerated drug approval); *id.* § 1121, 126 Stat. at 1112 (requiring, within two years of enactment, guidance on Internet promotion); FDA Food Safety Modernization Act, Pub. L. No. 111-353, § 113(b), 124 Stat. 3885, 3921 (2011) (calling for the issuance of guidance within 180 days of enactment to clarify the meaning of and requirements for new dietary supplement ingredients); Family Smoking Prevention and Tobacco Control Act, § 101(b) (FDCA § 911(l)(1)), 123 Stat. 1776, 1818 (2009) (codified at 21 U.S.C. § 387k(l)(1) (2012)) (“Not later than 2 years after the date of enactment . . . , the Secretary shall issue regulations or guidance (or any combination thereof) on the scientific evidence required for assessment and ongoing review of modified risk tobacco products.”); *id.* § 101(q)(1), 123 Stat. at 1838 (calling for guidance about enforcement against retailers); *id.* § 101(q)(3), 123 Stat. at 1840 (providing that certain amendments related to penalties only become effective upon the issuance of such guidance); Food and Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, § 303(c), 121 Stat. 823, 862–63 (requiring that, within 180 days of enactment, the agency issue guidance to clarify the humanitarian device exemption); *id.* § 701(a) (FDCA § 712(f)), 121 Stat. at 903 (codified at 21 U.S.C. § 379d-1(f) (2012)) (“Not less than once every 5 years, the Secretary shall review guidance of the [FDA] regarding conflict of interest waiver determinations with respect to advisory committees and update such guidance as necessary.”); *id.* § 911 (FDCA § 511), 121 Stat. at 951 (codified at 21 U.S.C. § 360a (2012)) (requiring that, within one year of enactment, the agency issue (and, within five years, review and update) guidance for the conduct of clinical trials with respect to antibiotic drugs); *id.* § 1005(f), 121 Stat. at 969 (requiring that, within 270 days of enactment, the agency issue guidance to the industry about submitting reports to a new electronic portal identifying food safety problems); Medical Device User Fee and Modernization Act of 2002, Pub. L. No. 107-250, § 213, 116 Stat 1588, 1614–15 (requiring that, within 270 days of enactment, the agency issue guidance regarding pediatric devices).

serious adverse event report” for nonprescription drugs and dietary supplements.<sup>76</sup> In contrast, when decades earlier it gave the FDA power to require such reporting for prescription drugs and medical devices, Congress required that the agency use notice-and-comment rulemaking to spell out such details.<sup>77</sup> In 2010, when Congress created an approval pathway for generic biologics (so-called “biosimilars”), it directed the agency to produce implementing guidance, though only after first soliciting public comment—in effect, calling for the issuance of Level 1 guidance.<sup>78</sup> In contrast, when it codified an approval pathway for generic versions of conventional pharmaceutical products a quarter of a century earlier, Congress demanded that the FDA engage in notice-and-comment rulemaking to craft implementing regulations.<sup>79</sup>

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76. See Dietary Supplement and Nonprescription Drug Consumer Protection Act, Pub. L. No. 109-462, §§ 2(e)(3), 3(d)(3), 120 Stat. 3469, 3472, 3475 (2006).
77. See Drug Amendments of 1962, Pub. L. No. 87-781, § 103(a) (FDCA § 505(j)(1)), 76 Stat. 780, 782–83 (codified as amended at 21 U.S.C. § 355(k)(1) (2012)) (calling for general regulations or specific orders to define what reports manufacturers of approved drugs must submit); Medical Device Amendments of 1976, Pub. L. No. 94-295, § 2 (FDCA § 519(a)), 90 Stat. 539, 564–65 (codified as amended at 21 U.S.C. § 360i(a) (2012)) (calling for regulations to define what reports device manufacturers, importers, and distributors must submit); *cf.* Safe Medical Devices Act of 1990, Pub. L. No. 101-629, § 5(a)(2) (FDCA § 513(a)(1)(B)), 104 Stat. 4511, 4517–18 (codified at 21 U.S.C. § 360c(a)(1)(B) (2012)) (directing the FDA to develop and disseminate guidelines for Class II medical devices). Of course, the FDA uses guidance documents to elaborate on its regulations implementing these statutory provisions. See, e.g., Notice of Availability, Draft Guidance: Medical Device Reporting for Manufacturers, 78 Fed. Reg. 41,069 (July 9, 2013).
78. See Biologics Price Competition and Innovation Act, Pub. L. No. 111-148, § 7002(a)(2) (PHSA § 351(k)(8)), 124 Stat. 119, 808 (2010) (codified at 42 U.S.C. § 262(k)(8) (2012)) (cross-referencing 21 U.S.C. § 371(h)); see also Notice of Public Hearing, Draft Guidances Relating to the Development of Biosimilar Products, 77 Fed. Reg. 12,853, 12,854 (Mar. 2, 2012) (requesting comments on three draft guidance documents that it had issued a few weeks earlier); Katie Thomas, *Generic Drug Makers See a Drought Ahead*, N.Y. TIMES, Dec. 4, 2012, at B1 (reporting that “the F.D.A. was not expected to issue guidelines for approving biosimilars anytime soon”). This exercise will provoke serious controversy, and the choices that the FDA ultimately makes will have tremendous financial consequences.
79. See Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, § 105(a), 98 Stat. 1585, 1597 (imposing a one year deadline for doing so); see also 21 C.F.R. pts. 314(C), 320 (2014) (implementing rules). Of course, the FDA has further elaborated on these regulations with guidance. See, e.g., Notice of Availability, Draft Guidance for Industry on Abbreviated New Drug Applications: Stability Testing of Drug Substances and Products, 77 Fed. Reg. 58,999 (Sept. 25, 2012); Notice of Availability, Guidance for Industry on Abbreviated New Drug Applications: Impurities in Drug Substances, 74 Fed. Reg. 34,359 (July 15, 2009); Notice of Availability, Draft Guidance for Industry on the Submission of Summary Bioequivalence Data for Abbreviated New Drug Applications, 74 Fed. Reg. 17,872 (Apr. 17, 2009); see also *In re Flonase Antitrust Litig.*, 795 F. Supp. 2d 300, 304–05, 312 (E.D. Pa. 2011) (explaining the agency’s ten-

The sweeping food safety amendments enacted in 2011 are littered with congressional demands for the issuance of guidance. A central provision of this legislation called for the use of an approach based on a strategy previously known as hazard analysis and critical control points (HACCP), and it included a requirement that the FDA issue implementing regulations within eighteen months,<sup>80</sup> coupled with several requirements for the issuance of related guidance documents.<sup>81</sup> The very next section of the new law called on the agency to issue (and periodically revise as necessary) “performance standards” related to specific food contaminants either as guidance documents or as regulations,<sup>82</sup> a peculiar concession about their interchangeability that had appeared occasionally in earlier legislation.<sup>83</sup> Congress also

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agency to rely on draft guidance documents to outline its expectations for the testing of generic drugs).

80. See FDA Food Safety Modernization Act, Pub. L. No. 111-353, § 103(a) (FDCA § 418(n)), 124 Stat. 3885, 3895 (2011) (codified at 21 U.S.C. § 350g(n) (2012)). Congress separately included details about the intended scope of this rulemaking process. See *id.* § 103(c), 124 Stat. at 3896–98.
81. See *id.* § 103(b), 124 Stat. at 3896 (calling for guidance related to this rulemaking though without specifying any particular time frame); *id.* § 103(d), 124 Stat. at 3898 (calling for the issuance of a compliance policy guide for small entities within 180 days of promulgation of implementing regulations); *id.* § 103(h), 124 Stat. at 3898 (calling for updates of existing guidance on HACCP for fish within 180 days of enactment). A similar pattern—namely, required rulemaking plus the issuance of affiliated guidance—appears in several other new provisions: (1) standards for produce safety, see *id.* § 105(a) (FDCA § 419(a)–(c)), 124 Stat. at 3899–902 (codified at 21 U.S.C. § 350h(a)–(c) (2012)) (rulemaking within two years); *id.* (FDCA § 419(e)), 124 Stat. at 3902–03 (codified at 21 U.S.C. § 350h(e)) (guidance within one year); *id.* § 105(b), 124 Stat. at 3904 (calling for the issuance of a compliance policy guide for small entities within 180 days of promulgation of implementing regulations); (2) protection against terrorist attacks on the food supply, see *id.* § 106(a) (FDCA § 420(b)), 124 Stat. at 3905 (codified at 21 U.S.C. § 350i(b) (2012)) (rulemaking within eighteen months); *id.* § 106(b), 124 Stat. at 3906 (guidance within one year); *id.* § 106(c) (calling for periodic review of both the implementing regulations and guidance documents); and (3) foreign supplier verification, see *id.* § 301(a) (FDCA § 805(c)), 124 Stat. at 3953 (codified at 21 U.S.C. § 384a(c) (2012)) (rulemaking within one year); *id.* (FDCA § 805(b)) (codified at 21 U.S.C. § 384a(b)) (guidance within one year); see also *id.* § 302 (FDCA § 806(a)(2)), 124 Stat. at 3955 (codified at 21 U.S.C. § 384b(a)(2) (2012)) (calling for guidance within eighteen months about participation in a voluntary qualified importer program).
82. See *id.* § 104(b), (d), 124 Stat. at 3899; see also Drug Quality and Security Act, Pub. L. No. 113-54, § 102(a)(2) (FDCA § 503B(b)(5)), 127 Stat. 587, 591 (2013) (to be codified at 21 U.S.C. § 353b(b)(5)) (formatting requirements for reports of compounded drugs produced by registered outsourcing facilities); *id.* § 102(a)(2) (FDCA § 503B(b)(2)(B)), 127 Stat. at 592 (to be codified at 21 U.S.C. § 353b(b)(2)(B)) (adverse event reporting by such facilities).
83. See Family Smoking Prevention and Tobacco Control Act, § 101(b) (FDCA § 911(l)(1)), 123 Stat. 1776, 1818 (2009) (codified at 21 U.S.C. § 387k(l)(1) (2012)); Food and Drug Administration Modernization Act, Pub. L. No. 105-115, § 116(a) (FDCA § 506A(c)(2)), 111 Stat. 2296, 2314 (1997) (codified at 21 U.S.C. § 356a (2012)).

demanded that the FDA submit certain guidance documents to particular subcommittees for prior review.<sup>84</sup>

In short, statutory amendments enacted during the last couple of decades include more than thirty separate provisions that invite or require guidance-making by the FDA. In light of this recent legislative tendency to call for the issuance of guidance by the agency, which may reflect an effort by Congress to insulate the FDA's policymaking from White House review,<sup>85</sup> little doubt remains about the legitimacy

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84. See FDA Food Safety Modernization Act, § 114(a), 124 Stat. at 3921 (requiring that a pair of congressional committees get at least ninety days advance notice of any FDA guidance document or regulation relating to post harvest processing of raw oysters); see also Food and Drug Administration Safety and Innovation Act, Pub. L. No. 112-144, § 1143(a), 126 Stat. 993, 1130 (2012) (requiring that a pair of congressional committees get at least sixty days advance notice of any FDA guidance document expressing an intent to regulate laboratory-developed tests); *United States v. Franck's Lab, Inc.*, 816 F. Supp. 2d 1209, 1229–30, 1252 (M.D. Fla. 2011) (discussing congressional frustration with the FDA's failure to revise its guidance on compounding of veterinary drugs); S. REP. NO. 113-164, at 81 (2014) ("The Committee [on Appropriations] is concerned that the Food and Drug Administration is not meeting any stakeholders before publicly releasing further guidance [on pharmacy compounding] for public comment."); cf. Food and Drug Administration Modernization Act, Pub. L. No. 105-115, § 121(d), 111 Stat. 2296, 2321–22 (1997) (requiring that, within thirty days of enactment, the agency withdraw a pair of guidance documents published in 1995 that related to positron emission tomography (PET) radiopharmaceutical drug products).

85. Cf. *Nou*, *supra* note 11, at 1835 ("Congress could dictate specific policymaking forms that are more likely, as a class, to bypass presidential review; for example, prohibiting rulemaking would channel policymaking to other forms such as guidance documents."). See generally McGarity, *supra* note 3, at 1397 ("[I]nformal rulemaking has evolved in an environment of intense institutional competition. Congress and the President have been vying for control over this important policymaking tool."); Sidney A. Shapiro, *Political Oversight and the Deterioration of Regulatory Policy*, 46 ADMIN. L. REV. 1, 4 (1994) (discussing "the 'negative-sum' nature of presidential and legislative competition concerning oversight"). It also might serve to reduce the involvement of meddling courts, thereby arguably making the FDA relatively more responsive to Congress—which engages in admittedly sporadic review but without differentiating between binding and non-binding rules—than the other two branches of government. Contrary to the claims of some commentators, see, e.g., Mendelson, *supra* note 12, at 411, the Congressional Review Act (CRA), 5 U.S.C. §§ 801–808 (2012), does apply to guidance documents, see *id.* § 804(3); Strauss, *supra* note 61, at 769 ("Every action an agency takes that fits the APA's definition of 'rule,' not only legislative rules but also the much larger volume of interpretive rules, statements of policy and other forms of guidance, must be provided to Congress for consideration under the disapproval procedure."); see also Morton Rosenberg, CONG. RESEARCH SERV., RL30116, CONGRESSIONAL REVIEW OF AGENCY RULEMAKING: AN UPDATE AND ASSESSMENT OF THE CONGRESSIONAL REVIEW ACT AFTER A DECADE 25–28 (2008), archived at <http://perma.unl.edu/89ES-QM74> (same, but recognizing that agencies generally have not been sending their nonlegislative rules to Congress); *supra* notes 71 & 84 (identifying instances of congressional review of FDA guidance documents, including an order to withdraw a pair related to PET drugs,

of this general development.<sup>86</sup> It poses, however, a curious question. Several commentators have discussed the degree of deference owed by courts when evaluating agency interpretations of ambiguous statutory language that appear in guidance documents instead of regulations.<sup>87</sup> No one appears to have considered the extent to which an explicit congressional order to issue guidance on a particular matter should factor into the analysis, but it seems that such a delegation of authority might justify granting an agency interpretation significant deference even if the guidance document emerged without the exact procedures required for binding rules (though Level 1 comes close).<sup>88</sup> If granted significant deference by the courts, however, then nonbinding guidance documents would have an even stronger de facto binding effect on regulated entities.<sup>89</sup>

### 3. *Extending GGP's to Other Agencies?*

If the shift to guidance struck it as salutary, then it seems at least mildly curious that Congress did not amend the APA so that the same procedures would apply to other federal agencies when they use guidance documents. Partly, of course, it reflected the fact that Congress had to reauthorize the soon-to-sunset drug user fee legislation in 1997,<sup>90</sup> and that happened just as the FDA had begun to structure its guidance development process. It also may have reflected a prefer-

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which represents twice the number of rules issued by any agency that Congress has ever overridden using the CRA).

86. Cf. Raso, *supra* note 13, at 814 & n.144 (pointing out that “Congress occasionally requires agencies to issue guidance documents,” and noting that critics “often neglect [to recognize] th[is] fact,” but citing only one largely inapt illustration). Unlike Mr. Raso, I have tried to document the extent to which this happens at least with regard to one agency. I have no idea whether Congress acts similarly with regard to other agencies, which it has not made subject to GGPs, *see infra* note 92, though I have come across one other illustration of this phenomenon mentioned in the scholarly literature, *see* The Energy Independence and Security Act of 2007, Pub. L. No. 110-140, § 433(d), 121 Stat. 1492, 1614 (2007) (cited by Kalen, *supra* note 13, at 716 & n.350).
87. *See, e.g.*, Kristin E. Hickman, *Unpacking the Force of Law*, 66 VAND. L. REV. 465, 484–90, 511–25 (2013); John F. Manning, *Nonlegislative Rules*, 72 GEO. WASH. L. REV. 893, 937–44 (2004).
88. Cf. *Barnhart v. Walton*, 535 U.S. 212, 222 (2002) (enumerating relevant factors); *United States v. Mead Corp.*, 533 U.S. 218, 229 (2001) (asking whether Congress gave the agency “the responsibility to implement a particular provision or fill a particular gap”); Funk, *supra* note 6, at 1347–48 (explaining that agencies do not need any specific delegated authority to issue nonlegislative rules).
89. *See* Randolph J. May, *Ruling Without Real Rules—or How to Influence Private Conduct Without Really Binding*, 53 ADMIN. L. REV. 1303, 1308–09 (2001); Thomas J. Fraser, Note, *Interpretive Rules: Can the Amount of Deference Accorded Them Offer Insight into the Procedural Inquiry?*, 90 B.U. L. REV. 1303, 1325–26 (2010).
90. *See* Prescription Drug User Fee Act of 1992, Pub. L. No. 102-571, § 105, 106 Stat. 4491, 4498 (codified as amended at 21 U.S.C. §§ 379g–379h (2012)). In addition,

ence for experimenting with these hybridized procedures before imposing them across the board,<sup>91</sup> but, more than fifteen years later, Congress has shown no real interest in broadening the reach of GGPs.<sup>92</sup>

Instead, in 2007, OMB took this additional step by calling on Executive branch agencies to adopt GGPs loosely modeled on the FDA's approach.<sup>93</sup> In addition, one week earlier, the White House had issued an Executive Order to clarify, among other things, that these same agencies (including the FDA) should seek OMB clearance of any "economically significant" guidance documents.<sup>94</sup> The suggestion that

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of course, the APA rarely gets amended. See Peter L. Strauss, *Changing Times: The APA at Fifty*, 63 U. CHI. L. REV. 1389, 1391-92 (1996).

91. See Rakoff, *supra* note 31, at 172 ("While a judgment as to the success of the precise procedures the FDA has chosen to use in establishing its organized system of half-formal, half-informal 'guidance' must await the test of time, it seems to me experiments of this sort are well worth pursuing.")
92. See Mendelson, *supra* note 12, at 401 & n.25 (explaining that, notwithstanding various proposals previously introduced in Congress and "extensive oversight in 2000," FDAMA remains the only statute addressing the development and use of guidance documents); see also McKee, *supra* note 10, at 380 ("The FDA is unusual among federal agencies in that it has codified statutory provisions addressing guidance documents."); Hunnicutt, *supra* note 33, at 185 ("The GGPs, however, apply to only one agency. To establish greater efficiency and consistency in the use of nonlegislative rules throughout the federal government, Congress ought to revise nonlegislative rules for all agencies."); *id.* at 190-91 (elaborating); cf. William Funk, *Legislating for Nonlegislative Rules*, 56 ADMIN. L. REV. 1023 (2004) (offering proposed amendments to the APA, but geared toward facilitating substantive judicial review rather than modeled on the GGPs). For a recent bill that would do so, see the Clearing Unnecessary Regulatory Burdens Act, S. 602, 112th Cong. (2011).
93. See Notice, Final Bulletin for Agency Good Guidance Practices, 72 Fed. Reg. 3432, 3439-40 (Jan. 25, 2007) [hereinafter OMB Bulletin] (covering only "significant" guidance documents, and calling for pre-issuance comment opportunity only for a subset deemed "economically significant," though agencies would have to prepare and make available a response to any public comments on the latter); *id.* at 3438 (explaining that agencies "must prepare a robust response-to-comments document," conceding that "these procedures are similar to APA notice-and-comment requirements"); *id.* at 3433 ("The provisions of the FDAMA and FDA's implementing regulations . . . informed the development of this government-wide Bulletin."); *id.* at 3434 (explaining differences between its definition of "significant" guidance documents and the FDA's "Level 1" category); see also Stephen M. Johnson, *Good Guidance, Good Grief!*, 72 MO. L. REV. 695, 722-26, 732-33 (2007) (describing and critiquing this initiative); Mendelson, *supra* note 12, at 447-50 (discussing limitations with OMB's call for other agencies to adopt GGPs); Paul R. Noe & John D. Graham, *Due Process and Management for Guidance Documents: Good Governance Long Overdue*, 25 YALE J. ON REG. 103 (2008) (providing a brief defense of the OMB Bulletin penned by its authors); Cindy Skrzycki, *Bush Order Limits Agencies' 'Guidance'*, WASH. POST, Jan. 30, 2007, at D1 (discussing some of the initial reactions). Strangely, OMB did not expressly exempt the FDA from the Bulletin.
94. See Exec. Order No. 13,422, Further Amendment to Executive Order 12866 on Regulatory Planning and Review, 72 Fed. Reg. 2763 (Jan. 18, 2007) (revoked

guidance documents could have a significant economic impact represents an uncharacteristically candid admission about how such technically nonbinding announcements may operate in practice.<sup>95</sup> In any case, the requirement for limited OMB review of economically significant guidance was revoked at the outset of the Obama administration,<sup>96</sup> only to get informally resurrected just a couple of months later,<sup>97</sup> which seemed fairly dubious insofar as the Executive Order on regulatory review originally issued at the outset of the Clinton administration had (unlike its predecessor) applied solely to genuinely binding rules.<sup>98</sup>

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2009). Several members of Congress took issue with this development, though most of their criticism focused on other aspects of the Executive Order. See Cindy Skrzycki, *Fighting for the Right to the Rules*, WASH. POST, July 17, 2007, at D2 (reporting that it triggered three oversight hearings and an appropriations rider approved by the House to block implementation by OMB).

95. See OMB Bulletin, 72 Fed. Reg. at 3435 (elaborating on “situations in which it may reasonably be anticipated that a guidance document could lead parties to alter their conduct in a manner that would have such an economically significant impact”); *id.* at 3434 (recognizing that “the impacts of guidance often will be more indirect and attenuated than binding legislative rules”); see also Notice, Draft Report to Congress on the Costs and Benefits of Federal Regulations, 67 Fed. Reg. 15,014, 15,034–35 (Mar. 28, 2002) (including an OMB request for public comments on “problematic guidance documents”). I wonder whether a reviewing court would credit such an OMB designation to counter an agency’s ripeness objection if a party pursued a judicial challenge to a guidance document.
96. See Exec. Order No. 13,497, Revoking Executive Orders 13258 and 13422 Concerning Regulatory Planning and Review, 74 Fed. Reg. 6113 (Jan. 30, 2009); see also Presidential Memorandum on Regulatory Review, 74 Fed. Reg. 5977 (Jan. 30, 2009) (soliciting agency comments on possible amendments to Pres. Clinton’s Executive Order 12,866); OMB Notice, Federal Regulatory Review, 74 Fed. Reg. 8819 (Feb. 26, 2009) (inviting public comment on the same).
97. See Peter R. Orszag, *Memorandum for the Heads and Acting Heads of Executive Departments and Agencies*, OMB (Mar. 4, 2009), archived at <http://perma.unl.edu/XX8M-5GBR>; see also Sunstein, *supra* note 11, at 1853–54 (elaborating). At least one FDA draft guidance document apparently went unnoticed until an advisor to the President caught a news item and demanded that the agency withdraw it immediately. See Gardiner Harris, *White House and the F.D.A. Often at Odds*, N.Y. TIMES, Apr. 3, 2012, at A1 (describing an incident involving posted calorie counts for movie theater popcorn); see also Notice of Availability, Draft Guidance for Industry: Questions and Answers Regarding Implementation of the Menu Labeling Provisions of Section 4205 of the Patient Protection and Affordable Care Act of 2010, 75 Fed. Reg. 52,426 (Aug. 25, 2010), *withdrawn*, 76 Fed. Reg. 4360 (Jan. 25, 2011) (reflecting the formal resolution of this episode).
98. See Noe & Graham, *supra* note 93, at 105. When the Obama administration amended Executive Order 12,866, it apparently did not alter this provision or otherwise suggest any review of guidance documents. See Exec. Order No. 13,563, Improving Regulation and Regulatory Review, 76 Fed. Reg. 3821 (Jan. 18, 2011). Even so, under the Paperwork Reduction Act (PRA), 44 U.S.C. §§ 3501–3520 (2012), information collection requests must go through their own version of a notice-and-comment process even if unconnected to a rulemaking proceeding, see 5 C.F.R. §§ 1320.5, 1320.10 (2014); Jeffery S. Lubbers, *Paperwork Redux: The (Stronger) Paperwork Reduction Act of 1995*, 49 ADMIN. L. REV. 111,

### C. Too Much of a Good Thing at the FDA?

The FDA does not reserve guidance documents for narrow and technical facets of its work. Large swaths of important agency activities depend entirely on such nonbinding pronouncements,<sup>99</sup> and in areas other than those where Congress has expressly invited or demanded guidance-making. As elaborated below, these include such non-trivial issues as direct-to-consumer advertising of prescription products, indirect advertising to physicians, pharmacy compounding, and everything having to do with genetically engineered foods. In other areas, the FDA uses guidance to update regulations promulgated long ago.<sup>100</sup> Occasionally, it will issue regulations that invite/encourage parties to access existing or anticipated future guidance on a particular subject,<sup>101</sup> even though such an arrangement arguably

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114–17 (1997). Under this law, some guidance documents always have required OMB review. *See* Seiguer & Smith, *supra* note 68, at 24 (“If a new guidance has any paperwork burdens (e.g., additional forms to be filed with FDA), the PRA demands the same oversight for the guidance as that which applies to a rule, including oversight by OMB. While a guidance cannot impose a burden or require a form because technically it is voluntary, it can trigger a paperwork burden to the extent that information must be reported to FDA.”); *see also* Notice of Availability, Guidance for Industry: Guide to Minimize Food Safety Hazards for Fresh-Cut Fruits and Vegetables, 73 Fed. Reg. 10,037 (Feb. 25, 2008) (“This document was issued as a ‘draft final’ guidance [almost one year ago] pending OMB approval of the collection of information.”). *But cf.* Mendelson, *supra* note 12, at 411 n.80 (asserting incorrectly that the PRA does not apply to guidance documents); Raso, *supra* note 13, at 788 & n.16 (making the same mistake).

99. *See* Rakoff, *supra* note 31, at 167–68 (“What the FDA did [with its GGPs] was to take the APA’s lenient attitude toward interpretative rules and policy statements and convert it into a wholly alternative system of regulation. . . . [G]uidance documents are meant to be statements of no legal consequence but immense practical consequence about virtually everything the agency regulates.”).
100. *See infra* notes 103–06 and accompanying text; *see also* Noah, *supra* note 61, at 294–99 (discussing the practice of interpreting rather than amending rules). Conversely, rather than going to the trouble of revising a recently finalized guidance, the FDA may issue a draft guidance further explaining it. *See, e.g.*, Notice of Availability, Draft Guidance for Industry on Abbreviated New Drug Applications: Stability Testing of Drug Substances and Products, Questions and Answers, 78 Fed. Reg. 52,931 (Aug. 27, 2013).
101. *See, e.g.*, 21 C.F.R. § 101.9(b)(7)(vi) (2014) (serving sizes for nutrition labeling); *id.* § 170.39(h) (substances that migrate from food-contact articles); *id.* § 310.501(e) (patient labeling for oral contraceptives); *id.* § 310.515(d) (patient labeling for drug products containing estrogen); *id.* § 314.50 (format and content of applications for new drug approval); *id.* § 500.80(a) (carcinogens in food-producing animals); *id.* § 530.13(c) (compounding of veterinary drugs); *id.* § 822.12 (postmarket surveillance for medical devices); *see also* *Henley v. FDA*, 77 F.3d 616, 618, 621 (2d Cir. 1996) (rejecting a challenge to the FDA’s revised regulation for patient labeling to accompany oral contraceptives, finding merit to the asserted need for flexibility in updating such information); *infra* note 138 (listing more general codified cross-references). References to specific guidance documents appear throughout the FDA’s medical device classification regulations, *see* 21 C.F.R. pts. 862–892 (2014), but these are unobjectionable insofar as Congress

conflicts with a pair of rules that the Office of the Federal Register imposes on agency regulations that use incorporation by reference.<sup>102</sup> Nowadays, it seems, legislative rulemaking only happens when Congress insists on that course of action.

For instance, rather than go to the trouble of amending its then 25-year-old regulations delineating “current” good manufacturing practices (cGMPs) for drugs, the FDA decided to issue guidance for the adoption of innovative quality control technologies by the pharmaceutical industry.<sup>103</sup> Similarly, even as prescription drug advertising has become increasingly sophisticated,<sup>104</sup> reflecting greater ingenuity and the emergence of brand new media such as the Internet, the FDA has not revised regulations that it issued during the 1960s,<sup>105</sup> relying instead on various guidance documents.<sup>106</sup> At the same time, the Office of the Inspector General (OIG) of the Department of Health and Human Services (HHS), acting under its authority to investigate fraud and abuse involving the Medicare and Medicaid programs, is-

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expressly authorized the use of such guidelines as “special controls” for Class II devices, *see* 21 U.S.C. § 360c(a)(1)(B) (2012).

102. *See* 1 C.F.R. § 51.1(f) (2014) (requiring that the cross-referenced material already exist); *id.* § 51.7(b) (barring incorporation by reference of materials published by the agency itself); *see also* Emily S. Bremer, *Incorporation by Reference in an Open-Government Age*, 36 HARV. J.L. & PUB. POL’Y 131, 142 (2012) (“This rule prevents agencies from pulling regulations out of the CFR, publishing them elsewhere (for example, in a pamphlet or on the agency’s website), and then incorporating them by reference.”); *id.* at 184–86 (discussing prohibitions on “dynamic” as opposed to static incorporations by reference).
103. *See* Leila Abboud & Scott Hensley, *Factory Shift: New Prescription for Drug Makers*, WALL ST. J., Sept. 3, 2003, at A1.
104. *See* Lars Noah, *Medicine’s Epistemology: Mapping the Haphazard Diffusion of Knowledge in the Biomedical Community*, 44 ARIZ. L. REV. 373, 430–34 (2002).
105. *See* Lars Noah, *Advertising Prescription Drugs to Consumers: Assessing the Regulatory and Liability Issues*, 32 GA. L. REV. 141, 146 n.21 (1997) (“[A]fter originally promulgating its advertising regulations in the 1960s, . . . the Agency has preferred to issue technically nonbinding policy statements and guidelines . . .”). The sole exception responded to an explicit congressional directive to issue implementing rules for a new statutory provision. *See* Final Rule, Dissemination of Information on Unapproved/New Uses for Marketed Drugs, Biologics, and Devices, 63 Fed. Reg. 64,556 (Nov. 20, 1998) (codified at 21 C.F.R. pt. 99 (2006)), *rescinded*, 73 Fed. Reg. 9342 (Feb. 20, 2008); *see also infra* note 112 and accompanying text (discussing a still pending NPRM to implement a 2007 statutory amendment on direct-to-consumer advertising of prescription products).
106. *See, e.g.*, Notice of Availability, Draft Guidances for Industry on Improving Information About Medical Products and Health Conditions, 69 Fed. Reg. 6308 (Feb. 10, 2004); Notice of Availability, Guidance for Industry on Consumer-Directed Broadcast Advertisements, 64 Fed. Reg. 43,197 (Aug. 9, 1999); Request for Comments, Prescription Drug Advertising and Promotional Labeling; Development and Use of FDA Guidance Documents, 62 Fed. Reg. 14,912, 14,913–16 (Mar. 28, 1997); *infra* notes 116–28 (discussing guidance documents that address industry distribution of textbooks and article reprints to physicians as well as sponsorship of continuing medical education programs).

sued guidelines to restrict drug and device industry marketing practices.<sup>107</sup>

Direct-to-consumer advertising (DTCA) of prescription drugs and medical devices has expanded over the last quarter of a century.<sup>108</sup> In 1995, in the course of soliciting public feedback, the FDA conceded that “[t]here are no regulations that pertain specifically to consumer-directed promotional materials.”<sup>109</sup> Almost two decades later, that statement remains true, though numerous guidance documents now address different aspects of the practice.<sup>110</sup> In 2007, in addition to lifting the burdensome formal rulemaking requirements that had applied to prescription drug advertising regulations for almost half a century, Congress granted the agency greater authority in this area, though only after the FDA issues binding rules,<sup>111</sup> which it has proposed but not yet finalized.<sup>112</sup> In contrast, after the agency repeatedly

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107. See Notice, *OIG Compliance Program Guidance for Pharmaceutical Manufacturers*, 68 Fed. Reg. 23,731 (May 5, 2003); Robert Pear, *Drug Industry Is Told to Stop Gifts to Doctors*, N.Y. TIMES, Oct. 1, 2002, at A1; see also CAL. HEALTH & SAFETY CODE § 119402 (2012) (requiring adoption of compliance programs that satisfy the OIG guidelines).
108. See Request for Comment, *Healthcare Professional Survey of Prescription Drug Promotion*, 77 Fed. Reg. 61,761, 61,762 (Oct. 11, 2012); Keith J. Winstein & Suzanne Vranica, *Drug Firms' Spending on Consumer Ads Fell 8% in '08, a Rare Marketing Pullback*, WALL ST. J., Apr. 16, 2009, at B2 (“U.S. spending on such drug ads hit a peak of \$4.8 billion in 2007 . . .”).
109. Notice of Public Hearing, *Direct-to-Consumer Promotion*, 60 Fed. Reg. 42,581, 42,583 (Aug. 16, 1995).
110. See Notice of Availability, *Draft Guidance for Industry on Presenting Risk Information in Prescription Drug and Medical Device Promotion*, 74 Fed. Reg. 25,245 (May 27, 2009); Notice of Public Hearing, *Consumer-Directed Promotion of Regulated Medical Products*, 70 Fed. Reg. 54,054 (Sept. 13, 2005) (summarizing milestones in the agency’s supervision of the practice); Notice of Availability, *Draft Guidances for Industry on Improving Information About Medical Products and Health Conditions*, 69 Fed. Reg. 6308 (Feb. 10, 2004), *comment period reopened*, 69 Fed. Reg. 30,945 (June 1, 2004); Notice of Availability, *Guidance for Industry on Consumer-Directed Broadcast Advertisements*, 64 Fed. Reg. 43,197 (Aug. 9, 1999); see also Lars Noah, *This Is Your Products Liability Restatement on Drugs*, 74 BROOK. L. REV. 839, 902 n.275 (2009) (“More than a decade has passed since the FDA announced plans to issue a notice of proposed rulemaking to address the issue.”).
111. See Food and Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, § 901(d)(2), 121 Stat. 823, 939 (codified at 21 U.S.C. § 353b(a) (2012)) (authorizing advance review of broadcast DTCA); see also *id.* § 901(d)(6), 121 Stat. at 942 (codified at 21 U.S.C. § 352(n) (2012)) (eliminating the formal rulemaking procedures previously applicable to drug advertising regulations).
112. See Notice of Proposed Rulemaking, *Direct-to-Consumer Prescription Drug Advertisements; Presentation of the Major Statement in Television and Radio Advertisements in a Clear, Conspicuous, and Neutral Manner*, 75 Fed. Reg. 15,376 (proposed Mar. 29, 2010) (to be codified at 21 C.F.R. § 202.1(e)), *comment period reopened*, 77 Fed. Reg. 16,973 (Mar. 23, 2012).

failed to tackle online promotional efforts,<sup>113</sup> Congress recently demanded that it issue guidance dealing with that subject.<sup>114</sup>

More than twenty years ago, the FDA became concerned about efforts by pharmaceutical and medical device manufacturers to promote “off-label” uses to health care professionals in the guise of educational outreach—primarily through the distribution of textbooks and reprints of articles (so-called “enduring materials”) and sponsorship of continuing medical education (CME) programs.<sup>115</sup> In 1992, the agency issued a “draft policy statement” to inform the industry that it might regard such activities as unlawful product promotions unless certain steps were taken to ensure editorial independence.<sup>116</sup> Although characterized at the time as a “safe harbor,”<sup>117</sup> these announcements were part of a crackdown on perceived industry excesses rather than an enlightened effort to liberalize existing prohibitions that seemed unduly restrictive.

The FDA formulated its off-label promotion policies in a manner designed to evade normal administrative law constraints. The draft policy statement evolved into a pair of draft guidance documents on

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113. See Notice of Hearing, Promotion of Food and Drug Administration-Regulated Medical Products Using the Internet and Social Media Tools, 74 Fed. Reg. 48,083 (Sept. 21, 2009); Randy Gray, Note, *One Click Is Enough: Satisfying FDA’s Fair Balance in the Highly-Regulated Marketplace*, 39 RUTGERS COMPUTER & TECH. L.J. 95, 98 (2013) (“Despite contemplating social media regulations since 1996, the FDA . . . has not issued any specific regulations for the industry to follow regarding social media. Instead, it has been the FDA’s policy to attempt to regulate the industry’s use of the social media through letters complaining of their promotional activity.” (footnote omitted)); *id.* at 103, 106–08 (discussing several of these warning letters); *id.* at 111, 113–15 (noting repeated failures by the FDA to issue a promised guidance document); Christian Torres, *Citing Risks, Drug Firms Going Offline*, WASH. POST, Aug. 14, 2011, at A3 (same).
114. See Food and Drug Administration Safety and Innovation Act, Pub. L. No. 112-144, § 1121, 126 Stat. 993, 1112 (2012); see also Notice of Availability, Draft Guidance for Industry on Fulfilling Regulatory Requirements for Postmarketing Submissions of Interactive Promotional Media for Prescription Human and Animal Drugs and Biologics, 79 Fed. Reg. 2449 (Jan. 14, 2014) (responding to this directive).
115. See Lars Noah, *Truth or Consequences?: Commercial Free Speech vs. Public Health Promotion (at the FDA)*, 21 HEALTH MATRIX 31, 69–70 (2011).
116. See Notice, Draft Policy Statement on Industry-Supported Scientific and Educational Activities, 57 Fed. Reg. 56,412 (Nov. 27, 1992). In the wake of strong industry reaction to the *Draft Policy Statement*, the FDA twice extended the comment deadline. See Extension of Comment Period, Draft Policy Statement on Industry-Supported Scientific and Educational Activities, 58 Fed. Reg. 6126 (Jan. 26, 1993); Request for Comments, Citizen Petition Regarding the Food and Drug Administration’s Policy on Promotion of Unapproved Uses of Approved Drugs and Devices, 59 Fed. Reg. 59,820 (Nov. 18, 1994).
117. See David G. Adams, *FDA Regulation of Communications on Pharmaceutical Products*, 24 SETON HALL L. REV. 1399, 1409–17 (1994) (describing the origins of this policy, and defending its constitutionality).

enduring materials published in 1995,<sup>118</sup> which were finalized one year later,<sup>119</sup> and into a final guidance document on CME programs published in 1997.<sup>120</sup> Although not formally binding, even in their final form,<sup>121</sup> these various FDA announcements unmistakably sought to alter the behavior of pharmaceutical and medical device companies. A federal district court understood these realities when, in the first phase of constitutional litigation brought by the Washington Legal Foundation (WLF), it rejected the agency's claim that the challenge to the draft policy statement was not ripe for judicial review; Judge Lamberth speculated that the FDA would "threaten[] (but never actually initiat[e]) enforcement procedures against companies which failed to comply with the agency's *de facto* policy."<sup>122</sup>

Only after Congress intervened in 1997, by enacting a provision that required the issuance of implementing regulations,<sup>123</sup> did the FDA bother to undertake notice-and-comment rulemaking to promulgate formally binding requirements to control industry dissemination of enduring materials describing off-label uses of drugs and medical devices.<sup>124</sup> Although the WLF litigation continued,<sup>125</sup> the agency ultimately managed to prevail on appeal by offering a somewhat contrived interpretation of its policies.<sup>126</sup> When the statutory provision

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118. See Notice, Advertising and Promotion; Draft Guidances, 60 Fed. Reg. 62,471 (Dec. 6, 1995).

119. See Notice, Advertising and Promotion; Guidances, 61 Fed. Reg. 52,800 (Oct. 8, 1996).

120. See Notice, Final Guidance on Industry-Supported Scientific and Educational Activities, 62 Fed. Reg. 64,074 (Dec. 3, 1997). The agency had received more than two hundred comments on the 1992 draft policy statement and a related citizen petition, see *id.* at 64,074, and the preamble accompanying this guidance document, which offered fairly detailed responses to these comments, occupied almost twenty pages in the *Federal Register*, see *id.* at 64,074–92.

121. See, e.g., *id.* at 64,094 n.1 ("This guidance . . . does not operate to bind FDA or the industry . . .").

122. Wash. Legal Found. v. Kessler, 880 F. Supp. 26, 34 (D.D.C. 1995); see also *id.* at 36 ("[F]ew if any companies are willing to directly challenge the FDA in this manner. . . . [M]anufacturers are most reluctant to arouse the ire of such a powerful agency.").

123. See Pub. L. No. 105-115, § 401(a), 111 Stat. 2296, 2356–64 (1997) (codified at 21 U.S.C. § 360aaa (2006)).

124. See Final Rule, Dissemination of Information on Unapproved/New Uses for Marketed Drugs, Biologics, and Devices, 63 Fed. Reg. 64,556 (Nov. 20, 1998) (codified at 21 C.F.R. pt. 99 (2006)).

125. See Wash. Legal Found. v. Friedman, 13 F. Supp. 2d 51 (D.D.C. 1998), amended by 36 F. Supp. 2d 16 (D.D.C. 1999), amended sub nom. Wash. Legal Found. v. Henney, 56 F. Supp. 2d 81 (D.D.C. 1999), vacated in part and appeal dismissed, 202 F.3d 331 (D.C. Cir. 2000).

126. See Lars Noah, *What's Wrong with "Constitutionalizing Food and Drug Law"?*, 75 TUL. L. REV. 137, 146–48 (2000); see also Notice, Decision in Washington Legal Foundation v. Henney, 65 Fed. Reg. 14,286 (Mar. 16, 2000) (memorializing the position that the agency had taken on appeal). Although the appellate court had left parts of the district court's injunction in place, see Wash. Legal Found. v.

sunset in 2006, the FDA opted to rescind rather than amend the implementing regulation,<sup>127</sup> which it then replaced with a substantially similar (though, of course, technically nonbinding) guidance document.<sup>128</sup> It seems at least mildly curious that the agency would think it appropriate to use a guidance document to address a complex and contentious issue of this sort after the matter previously had required a special (though temporary) legislative amendment coupled with implementing regulations.<sup>129</sup>

In connection with the compounding of drug products, the FDA has struggled to draw the line between the permissible practice of pharmacy and impermissible efforts to flout federal licensing requirements, eventually announcing its approach to enforcement in a 1992 “Compliance Policy Guide” (CPG).<sup>130</sup> Proponents of compounding failed in mounting a procedural challenge to this announcement.<sup>131</sup>

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Henney, 202 F.3d 331, 334 n.4 & 337 n.7 (D.C. Cir. 2000), on remand Judge Lamberth concluded that nothing remained of his original order, *see* Wash. Legal Found. v. Henney, 128 F. Supp. 2d 11, 15 (D.D.C. 2000); *cf. id.* (“[T]he issue remains 100% unresolved, and the country’s drug manufacturers are still without clear guidance as to their permissible conduct. To say that FDA’s March 16, 2000 Notice finally clarifies the situation is a farce; the Notice specifically invites a constitutional challenge to each and every one of its enforcement actions.”). A First Amendment challenge to a prosecution for off-label promotion recently succeeded. *See* United States v. Caronia, 703 F.3d 149 (2d Cir. 2012).

127. *See* Notice of Availability, Draft Guidance for Industry on Good Reprint Practices for the Distribution of Medical Journal Articles and Medical or Scientific Reference Publications on Unapproved New Uses of Approved Drugs and Approved or Cleared Medical Devices, 73 Fed. Reg. 9342 (Feb. 20, 2008); *see also* Notice of Availability, Draft Guidance for Industry on Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices, 76 Fed. Reg. 82,303 (Dec. 30, 2011) (issuing a related guidance).
128. *See* Notice of Availability, Guidance for Industry on Good Reprint Practices for the Distribution of Medical Journal Articles and Medical or Scientific Reference Publications on Unapproved New Uses of Approved Drugs and Approved or Cleared Medical Devices, 74 Fed. Reg. 1694 (Jan. 13, 2009); *see also* Noah, *supra* note 115, at 80–81 (discussing this guidance); *id.* at 70 n.169, 77–80 (explaining that the 1997 guidance document on CME programs had remained unchanged during this time). Five years later, the FDA further diminished the authoritative status of its policy. *See* Notice of Availability, Revised Draft Guidance for Industry on Distributing Scientific and Medical Publications on Unapproved New Uses—Recommended Practices, 79 Fed. Reg. 11,793 (Mar. 3, 2014).
129. *See* Michael Jon Andersen, Note, *Bound Guidance: FDA Rulemaking for Off-Label Pharmaceutical Drug Marketing*, 60 CASE W. RES. L. REV. 531, 547 (2010); *see also id.* at 542–44 (explaining that the draft guidance document had elicited several adverse comments, including from at least one member of Congress, and that the agency partly took these into account in the final version).
130. *See* Notice of Availability, Compliance Policy Guide: Manufacture, Distribution, and Promotion of Adulterated, Misbranded, or Unapproved New Drugs for Human Use by State-Licensed Pharmacies, 57 Fed. Reg. 10,906 (Mar. 31, 1992).
131. *See* Prof’ls & Patients for Customized Care v. Shalala, 56 F.3d 592, 599 (5th Cir. 1995); *see also* Takhar v. Kessler, 76 F.3d 995, 1002 (9th Cir. 1996) (rejecting procedural challenge to CPG on off-label use of veterinary drugs).

Five years later, Congress codified much of the agency's existing informal policy, though with some modifications.<sup>132</sup> Five years after enactment, the Supreme Court invalidated the provision on First Amendment grounds,<sup>133</sup> leaving the agency to issue a revised version of its older CPG.<sup>134</sup> In 2012, after a nationwide outbreak of fungal meningitis led to numerous deaths in patients who had received injections of a steroid compounded by a pharmacy in Massachusetts, members of Congress pressed FDA officials to explain the agency's somewhat indeterminate policy.<sup>135</sup>

Responsiveness to scientific advances represents a common justification for guidance.<sup>136</sup> At one level, the FDA wants to specify details about how it will evaluate the safety and effectiveness of regulated products. For instance, the agency has used guidance to define appropriate forms of toxicity testing for food and color additives.<sup>137</sup> Simi-

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132. Pub. L. No. 105-115, § 127(a), 111 Stat. 2296, 2328 (codified at 21 U.S.C. § 353a (2012)).

133. *See* *Thompson v. W. States Med. Ctr.*, 535 U.S. 357, 372–77 (2002); *see also* Noah, *supra* note 115, at 53–65 (critiquing the decision).

134. *See* Notice of Availability, Pharmacy Compounding Compliance Policy Guide, 67 Fed. Reg. 39,409 (June 7, 2002); *see also* *Wedgewood Vill. Pharmacy, Inc. v. United States*, 421 F.3d 263, 272–73 (3d Cir. 2005) (granting deference to this CPG even though not promulgated through notice-and-comment rulemaking); *cf.* *Med. Ctr. Pharmacy v. Mukasey*, 536 F.3d 383, 390–91, 401–06 (5th Cir. 2008) (concluding that the unconstitutional advertising restriction was severable from the remainder of FDAMA's compounding limitations, rendering the CPG irrelevant).

135. *See* Michael Snow, Note, *Seeing Through the Murky Vial: Does the FDA Have the Authority to Stop Compounding Pharmacies from Pirate Manufacturing?*, 66 VAND. L. REV. 1609, 1613, 1636–37 (2013); Timothy W. Martin et al., *Outbreak Spurs Calls for New Controls*, WALL ST. J., Oct. 9, 2012, at A1. For a vaguely parallel trajectory involving another guideline, *see* Amy Gaither, Comment, *Over the Counter, Under the Radar: How the Zicam Incident Came About Under FDA's Historic Homeopathic Exception*, 62 ADMIN. L. REV. 487, 502–09 (2010) (discussing the 1988 CPG that largely exempted homeopathic remedies from regulation as new drugs). Recently the FDA also has used guidance documents to address a problem that partly explains the upsurge in pharmacy compounding. *See, e.g.*, Notice of Availability, Guidance for Industry on Planning for the Effects of High Absenteeism to Ensure Availability of Medically Necessary Drug Products, 76 Fed. Reg. 14,025 (Mar. 15, 2011); Notice of Availability, Product Shortage Report, 76 Fed. Reg. 68,770 (Nov. 7, 2011). *See generally* Lars Noah, *Triage in the Nation's Medicine Cabinet: The Puzzling Scarcity of Vaccines and Other Drugs*, 54 S.C. L. REV. 741 (2003).

136. *See* Seiguer & Smith, *supra* note 68, at 23 (“In many cases, guidances are used to communicate very detailed—often scientific—information to FDA’s constituencies. Those interviewed agreed that due to the rapid pace of scientific advancement, guidances—with their less rigorous review and clearance process . . . and their nonbinding nature—provide the best means of providing information to assist industry in understanding and complying with regulatory requirements.”).

137. *See* Notice of Availability, Draft Revised “Toxicological Standards for Food and Color Additive Safety Evaluation,” 58 Fed. Reg. 16,536 (Mar. 29, 1993); *Simpson v. Young*, 854 F.2d 1429, 1435 (D.C. Cir. 1988) (holding that the FDA need not

larly, it has issued guidance to describe how to conduct acceptable clinical trials of particular classes of drugs and devices.<sup>138</sup>

At another level, profound scientific advances may confront the FDA with difficult regulatory questions that require some time to resolve, and, at least initially, it may prefer a flexible response.<sup>139</sup> Over the last quarter of a century, for instance, the agency has relied exclusively on guidance documents to address the various issues that have arisen with genetically engineered (GE) plants,<sup>140</sup> animals,<sup>141</sup> and ap-

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demand adherence to these guidelines given the “permissive language in the manual”); Edward F. Bouchard, *The Food and Drug Administration’s Redbook: The Practical Implications for Business Practices*, 39 FOOD DRUG COSM. L.J. 211 (1984).

138. *See, e.g.*, *Berlex Labs., Inc. v. FDA*, 942 F. Supp. 19, 26–27 (D.D.C. 1996) (rejecting a procedural challenge to a guidance document on the acceptability of clinical trials with comparable products); Notice of Availability, Guidance for Industry on Residual Drug in Transdermal and Related Drug Delivery Systems, 76 Fed. Reg. 51,038 (Aug. 17, 2011); *see also* 21 C.F.R. § 312.23(a)(8) (2014) (“Guidance documents are available from FDA that describe ways in which these [preclinical drug testing] requirements may be met.”); *id.* § 314.105(c) (“FDA makes its views on drug products and classes of drugs available through guidance documents, recommendations, and other statements of policy.”); *id.* § 314.445(a) (“FDA has made available guidance documents . . . to help you to comply with certain requirements of this part [governing new drug approval].”); *id.* § 316.50 (same, for orphan drugs); *id.* § 601.29 (same, for biologics); *id.* § 814.20(g) (premarket approval applications for medical devices); Christopher L. Hagenbush, *How the Food and Drug Administration and Industry Use Guidelines in Defining and Interpreting Statutory Requirements*, 38 FOOD DRUG COSM. L.J. 177, 178–79 (1983) (describing the FDA’s decision to issue guidelines rather than regulations concerning clinical testing); Richard A. Merrill, *The Architecture of Government Regulation of Medical Products*, 82 VA. L. REV. 1753, 1778–81, 1779 n.79, 1848 (1996) (discussing the importance to applicants of reliable FDA guidance on acceptable clinical study designs). For a recent example, *see* Notice of Availability, Draft Guidance for Industry on Alzheimer’s Disease: Developing Drugs for the Treatment of Early Stage Disease, 78 Fed. Reg. 9396 (Feb. 8, 2013); Gina Kolata, *F.D.A. Plans to Loosen Rules on Alzheimer’s Drug Approval*, N.Y. TIMES, Mar. 14, 2013, at A1.
139. *See* Seiguer & Smith, *supra* note 68, at 22 (“[I]n circumstances where the science or technology may be evolving rapidly, such that more speed and flexibility are needed, guidances are likely to be considered the best solution.”).
140. *See, e.g.*, Notice, Guidance on Consultation Procedures: Foods Derived from New Plant Varieties, 76 Fed. Reg. 9020 (Feb. 16, 2011); Notice of Availability, Guidance for Industry; Recommendations for the Early Food Safety Evaluation of New Non-Pesticidal Proteins Produced by New Plant Varieties Intended for Food Use, 71 Fed. Reg. 35,688 (June 21, 2006); Notice of Availability, Draft “Guidance for Industry: Drugs, Biologics, and Medical Devices Derived from Bioengineered Plants for Use in Humans and Animals,” 67 Fed. Reg. 57,828 (Sept. 12, 2002); Notice, Statement of Policy: Foods Derived from New Plant Varieties, 57 Fed. Reg. 22,984 (May 29, 1992); *see also* *Alliance for Bio-Integrity v. Shalala*, 116 F. Supp. 2d 166 (D.D.C. 2000) (rejecting procedural and substantive challenges to the FDA’s 1992 policy statement); Lars Noah, *Managing Biotechnology’s [R]evolution: Has Guarded Enthusiasm Become Benign Neglect?*, 11 VA. J.L. & TECH. 4, ¶¶ 31–35 (2006) (discussing this statement); *id.* ¶ 42 (explaining that a

propriate labeling of food products derived from these sources.<sup>142</sup> The FDA has responded in a similar fashion to advances in pharmacogenomics,<sup>143</sup> nanotechnologies,<sup>144</sup> and xenotransplantation.<sup>145</sup> At some

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set of regulations proposed at the very end of the Clinton administration went nowhere).

141. See Notice of Availability, Guidance for Industry on Regulation of Genetically Engineered Animals Containing Heritable Recombinant DNA Constructs, 74 Fed. Reg. 3057 (Jan. 16, 2009); Lars Noah, *Whatever Happened to the “Frankenfish”?: The FDA’s Foot-dragging on Transgenic Salmon*, 65 ME. L. REV. 606, 611–12 (2013); cf. David Pierson, *FDA to Phase out Antibiotic Use by Farms; Employing the Drugs for Boosting Animal Growth Will Be Curbed to Fight Increasing Resistance in Humans*, L.A. TIMES, Dec. 12, 2013, at A1 (reporting that the agency finalized a guidance calling for the voluntary cessation of non-therapeutic uses of antimicrobials in livestock within three years); Editorial, *FDA Moves Timidly Against Antibiotic Use on Farms*, USA TODAY, Dec. 26, 2013, at 10A (criticizing this effort as woefully inadequate).
142. See Notice of Availability, Draft Guidance for Industry: Voluntary Labeling Indicating Whether Foods Have or Have Not Been Developed Using Bioengineering, 66 Fed. Reg. 4839 (Jan. 18, 2001); Notice of Availability, Interim Guidance on the Voluntary Labeling of Milk and Milk Products from Cows that Have Not Been Treated with Recombinant Somatotropin, 59 Fed. Reg. 6279 (Feb. 10, 1994); Lars Noah, *Genetic Modification and Food Irradiation: Are Those Strictly on a Need-to-Know Basis?*, 118 PENN. ST. L. REV. (forthcoming June 2014); see also Ariana Eunjung Cha, *New Salvo Launched in GMO Labeling Debate*, WASH. POST, Oct. 20, 2013, at A3 (“The FDA has yet to finalize a 12-year-old draft guidance document outlining the labeling of foods that contain genetically modified ingredients.”); cf. 21 C.F.R. § 101.29 (1996) (addressing kosher food labeling), *revoked*, Food and Cosmetic Labeling; Revocation of Certain Regulations, 62 Fed. Reg. 43,071, 43,072–73 (Aug. 12, 1997) (explaining that this rule never provided anything beyond general guidance in the first place and would be replaced with a CPG).
143. See, e.g., Notice of Availability, Guidance for Industry on Clinical Pharmacogenomics: Premarket Evaluation in Early-Phase Clinical Studies and Recommendations for Labeling, 78 Fed. Reg. 5816 (Jan. 28, 2013); Notice of Availability, Companion to Guidance for Industry on Pharmacogenomic Data, 72 Fed. Reg. 49,722 (Aug. 29, 2007); Notice of Availability, Guidance for Industry on Pharmacogenomic Data Submissions, 70 Fed. Reg. 14,698 (Mar. 23, 2005). See generally Lars Noah, *The Coming Pharmacogenomics Revolution: Tailoring Drugs to Fit Patients’ Genetic Profiles*, 43 JURIMETRICS J. 1 (2002).
144. See, e.g., Notice of Availability, Draft Guidance for Industry: Safety of Nanomaterials in Cosmetic Products, 77 Fed. Reg. 24,722 (Apr. 25, 2012); Notice of Availability, Draft Guidance for Industry: Considering Whether an FDA-Regulated Product Involves the Application of Nanotechnology, 76 Fed. Reg. 34,715 (June 14, 2011).
145. See, e.g., Notice of Availability, Medical Devices Containing Materials Derived from Animal Sources (Except for In Vitro Diagnostic Devices); Draft Guidance for Industry and Food and Drug Administration Staff, 79 Fed. Reg. 3826 (Jan. 23, 2014); Notice of Availability, Guidance for Industry: Source Animal, Product, Preclinical, and Clinical Issues Concerning the Use of Xenotransplantation Products in Humans, 68 Fed. Reg. 16,542 (Apr. 4, 2003); Notice of Availability, Draft Guidance for Industry: Precautionary Measures to Reduce the Possible Risk of Transmission of Zoonoses by Blood and Blood Products from Xenotransplantation Product Recipients and Their Intimate Contacts, 67 Fed. Reg. 6266 (Feb. 11, 2002); Notice of Availability, Guidance for Industry: Public Health Issues Posed

point, the steep learning curve should begin to plateau, and a maturing industry might benefit from the greater clarity provided by binding and more stable pronouncements from the agency.<sup>146</sup> So long as guidance documents manage to communicate the FDA's evolving expectations reasonably well and secure voluntary adherence, however, the agency may have little reason to formalize its policies and subject them to unwelcome external scrutiny.

### III. SECURING ADHERENCE TO ANNOUNCED (AND UNANNOUNCED) POLICIES

If guidance documents technically do not bind anyone, then why do regulated entities not simply ignore these announcements? Moreover, if the FDA communicates its expectations privately rather than through guidance,<sup>147</sup> then why would regulated entities pay any attention whatsoever? As explained in this Part, companies subject to the agency's jurisdiction ignore such informal expressions of policy—whether or not announced in a public document—at their peril.

Congress originally granted the FDA only limited and procedurally cumbersome mechanisms for securing compliance with the statute: product seizures, injunctions, and criminal penalties.<sup>148</sup> Apart from procedural hurdles, formal agency enforcement actions face a form of Executive branch scrutiny; instead of having to run things by OMB, the FDA must secure the concurrence of the Department of Justice (DOJ) because the agency lacks any independent litigation author-

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by the Use of Nonhuman Primate Xenografts in Humans, 64 Fed. Reg. 16,743 (Apr. 6, 1999).

146. See Martha J. Carter, *The Ability of Current Biologics Law to Accommodate Emerging Technologies*, 51 FOOD & DRUG L.J. 375, 376 (1996) (“While the FDA has made a good faith effort to provide guidance to industry and to solicit industry’s feedback, it is disquieting to note that the entire field of biotechnology is being regulated without notice and comment rulemaking.”); *id.* at 377 (noting that “[g]uidelines are much easier to change than regulations”); Noah, *supra* note 140, ¶ 43 (“Although flexibility in dealing with an emerging technology has obvious advantages, there is a case to be made for establishing clearer rules for bioengineered food products.”); Andrew Pollack, *Without U.S. Rules, Biotech Food Lacks Investors*, N.Y. TIMES, July 30, 2007, at A1.
147. Cf. 21 C.F.R. § 10.115(b)(3) (2014) (excluding from GGP’s “warning letters . . . or other communications directed to individual persons or firms”).
148. See 21 U.S.C. §§ 332–334 (2012). The FDA enjoys largely unreviewable discretion in deciding whether and how to exercise its enforcement powers. See *Heckler v. Chaney*, 470 U.S. 821, 831–32 (1985); see also *United States v. Sage Pharm., Inc.*, 210 F.3d 475, 480 (5th Cir. 2000) (holding that the FDA could target one firm for selling unapproved new drugs even though it had not yet acted against others who distributed substantially similar products); *Schering Corp. v. Heckler*, 779 F.2d 683, 685–87 (D.C. Cir. 1985) (rejecting as unreviewable a pharmaceutical company’s challenge to a settlement between the FDA and a competitor).

ity.<sup>149</sup> Separately, Congress has delegated to the agency increasingly elaborate licensing powers, but these also came with demanding procedures.<sup>150</sup> The FDA has, however, deployed these various tools in creative ways: for instance, the agency may threaten to impose a sanction or withhold a license in the hopes of encouraging “voluntary” compliance with a request that the agency would find difficult to impose directly on a regulated entity.<sup>151</sup>

Such “arm-twisting” succeeds, and evades judicial or other scrutiny, in part because companies in pervasively regulated industries believe that they cannot afford to resist agency demands.<sup>152</sup> For instance, some critics have accused the FDA of retaliating against firms that fail to cooperate.<sup>153</sup> Whether or not such charges are accurate,

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149. See *United States v. Gel Spice Co.*, 773 F.2d 427, 429 (2d Cir. 1985); Charles R. McConachie, *The Role of the Department of Justice in Enforcing the Federal Food, Drug and Cosmetic Act*, 31 FOOD DRUG COSM. L.J. 333 (1976); Vandya Swaminathan & Matthew Avery, *FDA Enforcement of Criminal Liability for Clinical Investigator Fraud*, 4 HASTINGS SCI. & TECH. L.J. 325, 350 (2012); see also Neal Devins & Michael Herz, *The Uneasy Case for Department of Justice Control of Federal Litigation*, 5 U. PA. J. CONST. L. 558, 570 (2003) (noting the following common justification for this arrangement: “[B]ecause the Attorney General sees the big picture—and sees it with the same eyes as the President—centralization will ensure that representation is consistent with the broader policy concerns of the Administration.”); *id.* at 577–83 (elaborating on and critiquing this claim); *id.* at 566 (explaining “that one reason for agencies’ strong preference for administrative enforcement is freedom from DOJ oversight and control”).
150. See Merrill, *supra* note 138, at 1757–58, 1762, 1764–66; *cf. id.* at 1864 (“Nor are FDA’s decisions—to grant, withhold, or delay approval—commonly challenged in court. . . . The FDA product approval system is, in short, remarkably free from conventional legal constraint.”).
151. See Lars Noah, *Administrative Arm-Twisting in the Shadow of Congressional Delegations of Authority*, 1997 WIS. L. REV. 873, 874; *cf. Novel Procedures in FCC License Transfer Proceedings: Hearing Before the Subcomm. on Commercial & Administrative Law of the H. Comm. on the Judiciary*, 106th Cong. 29 (2000) (statement of Professor Lars Noah, University of Florida College of Law). The agency has long relied on such techniques. See H. Thomas Austern, *Expertise in Vivo*, 15 ADMIN. L. REV. 46, 50, 56 (1963) (discussing informal enforcement by the FDA through “jaw-boning” and “lifted eyebrow” techniques, which succeed because of the ever-present threat of criminal sanctions); *id.* at 52 (“[M]ost of those regulated do not often dare to challenge an informal assertion of power.”).
152. See, e.g., *Chamber of Commerce v. U.S. Dep’t of Labor*, 174 F.3d 206, 210 (D.C. Cir. 1999) (OSHA “is intentionally using the leverage it has by virtue solely of its power to inspect. The Directive is therefore the practical equivalent of a rule that obliges an employer to comply or to suffer the consequences; the voluntary form of the rule is but a veil for the threat it obscures.”); *id.* at 212–13 (holding therefore that this announcement was not exempt from notice-and-comment rulemaking requirements). See generally Brigham Daniels, *When Agencies Go Nuclear: A Game Theoretic Approach to the Biggest Sticks in an Agency’s Arsenal*, 80 GEO. WASH. L. REV. 442 (2012).
153. See, e.g., *Se. Minerals, Inc. v. Harris*, 622 F.2d 758, 761, 767 (5th Cir. 1980) (criticizing the agency’s “bureaucratic hubris that confuses abuse of power with reason,” adding that “the FDA’s abuse of its statutory rights of entry and inspection so as to harass and threaten [the parties] can in no way be condoned”); *Allega-*

the perception leads companies to accede to the agency's wishes even though they may lack any basis in law or fact.<sup>154</sup> Whatever the reason, the FDA has managed to accomplish its goals more efficiently using what amount to back channels.<sup>155</sup> In this manner, as explained in the sections that follow, the agency has successfully exercised a recall power not delegated by Congress. In addition, and without the need to allege any wrongdoing or threaten formal enforcement action, the agency has conditioned the granting of licenses on various postapproval restrictions either not contemplated in the enabling statute or without abiding by procedural prerequisites for their imposition.

### A. Threats/Offers in the Enforcement Context

During the early 1990s, the FDA negotiated consent decrees with pharmaceutical companies that it had accused of unlawfully promoting certain prescription drugs. In one of these cases, a manufacturer agreed to undertake an extensive corrective advertising campaign and also to preclear all of its promotional materials with the agency for a

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*tions of FDA Abuses of Authority: Hearings Before the Subcomm. on Oversight and Investigations of the H. Comm. on Commerce*, 104th Cong. 2 (1995) (statement of Hon. Joe Barton) (suggesting that "these stories are not rare exceptions," and adding that "the FDA never forgets who its enemies are"); *id.* at 9 (statement of Hon. Thomas J. Bliley, Jr.) (suggesting that "the threat of retaliation is deeply embedded in the culture of this Agency"). *But see id.* at 6 (statement of Hon. Henry A. Waxman) (warning that we should "not base our policy decisions on anecdotes and hyperbole"); *id.* at 83 (statement of Hon. John D. Dingell) (noting that, "upon a fuller review of the five case studies selected by the Majority, claims of FDA retaliation were decidedly premature").

154. *See, e.g., Hearings, supra* note 153, at 70 (testimony of Ronald C. Jankelson, Myotronics, Inc.) (describing pressures to enter into a consent decree); *see also* Elizabeth C. Price, *Teaching the Elephant to Dance: Privatizing the FDA Review Process*, 51 *FOOD & DRUG L.J.* 651, 653 (1996) ("The natural response to such alleged abusive tactics would be to bring suit against the agency, but such a response might not be in the best interests of the affected company."); Peter Brimelow & Leslie Spencer, *Food and Drugs and Politics*, *FORBES*, Nov. 22, 1993, at 115 (citing the results of a survey which found that 84% of respondents failed to press potentially legitimate complaints against the FDA for fear of retaliation).
155. Recently, one commentator partially endorsed this type of behavior: "Threat regimes . . . are important and are best justified when the industry is undergoing rapid change—under conditions of 'high uncertainty.' . . . Examples include periods surrounding a newly invented technology or business model, or a practice about which little is known." Tim Wu, *Agency Threats*, 60 *DUKE L.J.* 1841, 1842 (2011) ("Conversely, in mature, settled industries, use of informal procedures is much harder to justify."); *see also id.* at 1848–57 (elaborating, and conceding the need to guard against abuse). This passage invokes the same rationales that the Supreme Court long ago credited when allowing agencies to eschew rulemaking in favor of *formal* adjudication! *See SEC v. Chenery Corp.*, 332 U.S. 194, 202–03 (1947). For an excellent rebuttal of Professor Wu's essay, *see* Jerry Brito, "Agency Threats" and the Rule of Law: An Offer You Can't Refuse, 37 *HARV. J.L. & PUB. POL'Y* 553 (2014).

period of two years,<sup>156</sup> even though the statute generally prohibits mandatory preclearance of pharmaceutical advertising.<sup>157</sup> In another case, a company agreed to establish an FDA-approved training program for its pharmaceutical sales representatives,<sup>158</sup> even though the agency does not appear to have the power to regulate such communications.<sup>159</sup> In these and other cases, explicit FDA threats of especially burdensome product seizures or injunctions prompted the companies to accept these unprecedented requirements.<sup>160</sup>

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156. *See Syntex Will Run Naprosyn Corrective Ads in 18 Medical Journals and on "Lifetime" TV in Court-Filed Consent Decree to Halt Arthroprotective Claims*, F-D-C REP., THE PINK SHEET, Oct. 14, 1991, at 6, 7 [hereinafter *Syntex Will Run Corrective Ads*], archived at <http://perma.unl.edu/4F35-KRGP> (reporting that "[t]he comprehensive scope and breadth of FDA scrutiny set out in the consent agreement are unprecedented"); see also *Bristol Oncology Promotions Will Be Precleared by FDA for Two Years*, F-D-C REP., THE PINK SHEET, June 3, 1991, at 6, archived at <http://perma.unl.edu/6FP-8T7K> (describing a preclearance requirement covering a dozen products in a consent decree negotiated with Bristol-Myers Squibb, and adding that "[t]he agency has extracted similar agreements in recent years").
157. *See* 21 U.S.C. § 352(n) (2012) (providing that, "except in extraordinary circumstances, no regulation issued under this subsection shall require prior approval by the Secretary of the content of any advertisement"); see also 21 C.F.R. § 202.1(j) (2014) (implementing regulations that call for FDA preclearance of proposed advertisements only if unexpected fatalities or other serious side effects come to light); Request for Comments, Direct-to-Consumer Promotion, 61 Fed. Reg. 24,314, 24,315 (May 14, 1996) (disavowing any intent to require routine preclearance of prescription drug ads); cf. Food and Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, § 901(d)(2), 121 Stat. 823, 939 (codified at 21 U.S.C. § 353b(a) (2012)) (authorizing the adoption of regulations for the advance review of broadcast DTCA).
158. *See Kabi Pharmacia's Dipentum Consent Decree Requires FDA-Approved Training Program for Sales Reps*, F-D-C REP., THE PINK SHEET, Aug. 9, 1993, at 17, archived at <http://perma.unl.edu/8ALK-T3UV> (noting that the "FDA's involvement in developing a training program is unprecedented"). Other provisions of this consent decree required corrective advertising, preclearance of all promotional materials for one year, and reimbursement of the costs of the FDA's investigation. *See id.* at 18.
159. *See* Lars Noah, *Death of a Salesman: To What Extent Can the FDA Regulate the Promotional Statements of Pharmaceutical Sales Representatives?*, 47 FOOD & DRUG L.J. 309, 322-26 (1992).
160. *See, e.g., Syntex Will Run Corrective Ads*, *supra* note 156, at 7 ("To get the Syntex agreement, FDA is understood to have threatened to seize all of the company's stocks of Naprosyn."); see also Richard M. Cooper, *The Need for Oversight of Agency Policies for Settling Enforcement Actions*, 59 ADMIN. L. REV. 835, 840-41 (2007) ("The FDA has no written statement of general policy for its consent decrees. . . . Common provisions of an FDA consent decree include . . . a grant to FDA of authority, not otherwise provided by the FDCA, to order the company to take certain types of action if FDA determines that the company has not complied with the decree . . ."); *id.* at 843 ("Organizations commonly view the prospect of civil litigation against the government and administrative sanctions as far worse than settling on the government's terms. . . . Because organizations almost always accept such settlements rather than litigate, it is reasonable to infer that they have little bargaining power."); cf. *id.* at 840 ("As part of the price for avoid-

The FDA routinely issues “warning letters” that allege some regulatory infraction and provide the recipient with a limited period of time to take corrective action (coupled with a threat of formal enforcement proceedings).<sup>161</sup> In the case of drugs and medical devices, the agency used to go further and explain that government purchasing entities had been advised to stop dealing with the firm in the meantime.<sup>162</sup> Because the federal government represents the single largest purchaser of prescription drugs in this country, few manufacturers could afford to lose these contracts.<sup>163</sup> If a company dared to disagree with the agency’s allegations and chose to pursue a judicial

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ing prosecution, [one major drug] company also agreed to endow a chair at Seton Hall University Law School, which happened to be the alma mater of the U.S. Attorney.”); Hunnicutt, *supra* note 33, at 174 (explaining that one FDA consent decree obligated the regulated entity to abide by nonbinding guidance).

161. See Rebecca Boxhorn, Note, *FDA Goes Loko with Warning Letters*, 12 MINN. J.L. SCI. & TECH. 749, 750 (2011) (“Warning Letters generally contain: (1) a determination that the regulated party is in violation of the FDCA, (2) a demand for corrective action, (3) a request for response within fifteen days, and (4) a warning that the receipt of a Warning Letter may hinder future government contracting opportunities.”). Congress clearly authorized precisely such informal action by the FDA. See 21 U.S.C. § 336 (2012) (“Nothing in this chapter shall be construed as requiring the Secretary to report for prosecution, or for the institution of libel or injunction proceedings, minor violations of this chapter whenever he believes that the public interest will be adequately served by a suitable written notice or warning.”). The latest enforcement numbers reveal the issuance of 4,882 warning letters and just 25 seizure or injunction actions. See FDA, ENFORCEMENT STATISTICS SUMMARY (2012), archived at <http://perma.unl.edu/XB6S-GWVJ>; Andrew Zajac, *Under Obama, a Renewed FDA: The Agency Steps up Its Regulatory Activity, and the Activism Is Likely to Increase*, L.A. TIMES, Oct. 10, 2010, at A11.
162. See Noah, *supra* note 151, at 886 n.47. Nowadays the agency uses milder language to get the same point across. See FDA, REGULATORY PROCEDURES MANUAL ch. 4, at 4-17 (2011), archived at <http://perma.unl.edu/QA38-EHCV> (providing that letters sent to manufacturers of medical devices should include the following language: “Federal agencies are advised of all Warning Letters about devices so that they may take this information into account when considering the award of contracts.”); *id.* at 4-18 (providing that letters sent to drug manufacturers should include the following language: “Other federal agencies may take this Warning Letter into account when considering the award of contracts.”). In contrast to its silence in the FDCA, Congress included procurement freeze provisions in a pair of prominent environmental statutes. See 33 U.S.C. § 1368 (2012); 42 U.S.C. § 7606 (2012).
163. See Boxhorn, *supra* note 161, at 768 (“Threats by the FDA to inform other government agencies . . . of the presence of an outstanding Warning Letter present a real risk to those pharmaceutical companies that consistently contract with the government for the sale of their products to Medicare and Medicaid patients.”); see also Scott Hensley, *Big Buyers Push for Steep Price Cuts from Drug Makers*, WALL ST. J., June 22, 2006, at B1 (explaining that, as the health insurer for over five million individuals, the Department of Veterans Affairs can exercise significant leverage in procurement deals); cf. Daniels, *supra* note 152, at 493 (discussing the Department of Labor’s successful use of threats to debar firms from federal contracts in order to secure compliance with equal employment opportunity requirements).

challenge rather than accede to its demands, the FDA invariably argued that the controversy was not ripe for review.<sup>164</sup> If a company voluntarily corrected the violations of federal law alleged in a warning letter, whether or not accompanied by a threatened procurement freeze, then it lost any chance to challenge the legal basis for the FDA's objections.

Historically, the FDA lacked the statutory authority to order a recall of potentially dangerous products subject to its regulatory jurisdiction.<sup>165</sup> Over the last few decades, Congress gradually has expanded the agency's authority to demand such corrective actions,<sup>166</sup> though still not with regard to drugs.<sup>167</sup> In the absence of delegated power, the agency has had to encourage voluntary recalls, and long ago it promulgated detailed regulations setting forth its recall procedures and policies.<sup>168</sup>

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164. See, e.g., *Dietary Supplement Coalition, Inc. v. Kessler*, 978 F.2d 560, 563 (9th Cir. 1992); *Prof'ls & Patients for Customized Care v. Shalala*, 847 F. Supp. 1359, 1365 (S.D. Tex. 1994), *aff'd*, 56 F.3d 592, 599 (5th Cir. 1995); *Estee Lauder, Inc. v. FDA*, 727 F. Supp. 1, 5 (D.D.C. 1989); see also *Boxhorn*, *supra* note 161, at 759–62 (discussing these and more recent decisions). *But see* *Wash. Legal Found. v. Kessler*, 880 F. Supp. 26, 29–30, 34–36 (D.D.C. 1995) (holding that a challenge to the FDA's unofficial policy against drug industry sponsorship of scientific symposia was ripe for review based in part on warning letters alleging the unlawful promotion of off-label uses at such meetings). Only once did a court hold that such a challenge was justiciable on the basis of an interim procurement freeze. See *Den-Mat Corp. v. United States*, 1992 U.S. Dist. LEXIS 12233, at \*13 (D. Md. Aug. 17, 1992) (“Such action by the FDA would effectively ‘seize’ all products that normally would be sold to federal agencies.”). The court also expressed concern that “the FDA may have targeted Den-Mat . . . for a publicity campaign designed to coerce Den-Mat (and others) into complying with the agency's decision.” *Id.* at \*14.
165. See *Nat'l Confectioners Ass'n v. Califano*, 569 F.2d 690, 694–95 (D.C. Cir. 1978); *United States v. Superpharm Corp.*, 530 F. Supp. 408, 410 (E.D.N.Y. 1981); *United States v. C.E.B. Prods., Inc.*, 380 F. Supp. 664, 667–72 (N.D. Ill. 1974). *But cf.* *United States v. K-N Enter., Inc.*, 461 F. Supp. 988, 990–91 (N.D. Ill. 1978) (reading the FDCA broadly as authorizing a court-ordered recall of adulterated drugs). In recent years, however, courts have construed the FDA's power to request injunctive relief more broadly to include remedies not delineated in the statute. See, e.g., *United States v. Rx Depot, Inc.*, 438 F.3d 1052, 1058–63 (10th Cir. 2006); *United States v. Lane Labs-USA Inc.*, 427 F.3d 219, 233–36 (3d Cir. 2005) (upholding a district court order that the seller of unapproved new drugs pay restitution to consumers).
166. See, e.g., *FDA Food Safety Modernization Act*, Pub. L. No. 111-353, § 206, 124 Stat. 3885, 3940–44 (2011) (codified at 21 U.S.C. § 350l (2012)); *Safe Medical Devices Act of 1990*, Pub. L. No. 101-629, § 8, 104 Stat. 4520 (codified at 21 U.S.C. § 360h(e) (2012)).
167. See Eleanor G. Tennyson, Note, *A “Phantom Recall” Does Not Comport with FDA's Regulatory Practice—or Does It?: The Need for More Stringent Mandatory Reporting in FDA Matters*, 97 IOWA L. REV. 1839, 1843–44, 1852–53 (2012).
168. See *Final Rule, Recalls (Including Product Corrections)—Guidelines on Policy, Procedures, and Industry Responsibilities*, 43 Fed. Reg. 26,202, 26,218 (June 16, 1978) (codified at 21 C.F.R. pt. 7(c) (2014)); see also 21 C.F.R. § 7.40(a) (“This

This strategy has succeeded because firms know that a failure to cooperate with an agency request would invite more draconian enforcement measures authorized by statute.<sup>169</sup> Because, however, these necessitate judicial proceedings (and DOJ concurrence), the issuance of adverse publicity may represent a still more effective way of prompting action.<sup>170</sup> Companies often prefer a voluntary recall because it allows them to exercise greater control over the nature and extent of public notification about any hazards associated with their particular product.<sup>171</sup>

The FDCA expressly authorizes the issuance of adverse publicity, though only in limited circumstances.<sup>172</sup> Even then, targets of a negative information campaign often have no meaningful opportunity to

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- [subpart] recognize[s] the voluntary nature of recall by providing guidelines so that responsible firms may effectively discharge their recall responsibilities.”).
169. See 21 C.F.R. § 7.40(c) (“Seizure, multiple seizure, or other court action is indicated when a firm refuses to undertake a recall requested by the FDA.”); Proposed Rule, Recall Policy and Procedures, 41 Fed. Reg. 26,924, 26,924 (June 30, 1976) (“While the act does not specifically mention recalls, the statutory sanctions available to FDA have a vital role in a firm’s willingness to recall and support the development of recall as a major FDA regulatory tool.”); see also Daniels, *supra* note 152, at 449 (“[A]gencies often use regulatory nukes by aiming the nuke instead of launching it, . . . mak[ing] regulatory nukes much more powerful than their launch rate would suggest.”).
170. See Ernest Gellhorn, *Adverse Publicity by Administrative Agencies*, 86 HARV. L. REV. 1380, 1408 (1973) (“Since [recalls] cannot be required by law, the FDA ensures compliance by threatening seizure, injunction, and the issuance of publicity. Of these, the threat of publicity is usually the most potent persuader.”); *id.* at 1415 (noting that the FDA apparently “cannot resist the temptation of using [public] warnings to operate an extrastatutory recall program”). In effect, the government threatens to engage in product disparagement in order to shame the seller into altering its behavior. Cf. Lars Noah, *The Imperative to Warn: Dismantling the “Right to Know” from the “Need to Know” About Consumer Product Hazards*, 11 YALE J. ON REG. 293, 398 (1994) (“[W]arning requirements occasionally represent a surreptitious form of regulation, for instance, to encourage design modifications or product reformulations without directly mandating the desired changes.”). For an excellent recent treatment of this issue, see Nathan Cortez, *Adverse Publicity by Administrative Agencies in the Internet Era*, 2011 BYU L. REV. 1371.
171. See Mary Olson, *Substitution in Regulatory Agencies: FDA Enforcement Alternatives*, 12 J.L. ECON. & ORG. 376, 385–86 (1996); see also *id.* at 390 (noting concerns about FDA retaliation against uncooperative firms).
172. See 21 U.S.C. § 375(b) (2012) (“The Secretary may also cause to be disseminated information regarding food, drugs, devices, or cosmetics in situations involving, in the opinion of the Secretary, imminent danger to health or gross deception of the consumer.”); see also *Ajay Nutrition Foods, Inc. v. FDA*, 378 F. Supp. 210, 216–19 (D.N.J. 1974) (refusing to enjoin adverse publicity issued by the FDA), *aff’d mem.*, 513 F.2d 625 (3d Cir. 1975); *Hoxsey Cancer Clinic v. Folsom*, 155 F. Supp. 376, 377–78 (D.D.C. 1957) (same). For a recent example of an undoubtedly defensible use of this power, see Denise Grady, *F.D.A. Discourages Procedure in Uterine Surgery*, N.Y. TIMES, Apr. 18, 2014, at A13 (“The devices, known as morcellators, have been widely used in laparoscopic operations to remove fibroid tumors from the uterus . . . . The action on Thursday does not take them off the

respond to the charges or seek judicial review.<sup>173</sup> In recognition of the risk of improper use, the FDA once proposed a rule to limit the issuance of such publicity.<sup>174</sup> The agency never finalized this proposal, and it continues to rely on explicit or implicit threats of disseminating bad press as a method of encouraging voluntary compliance with its recall and other demands.<sup>175</sup> For instance, although the FDA has no business trying to influence decisions about what price companies charge for products subject to its jurisdiction,<sup>176</sup> the agency recently used public threats to do just that after a manufacturer introduced a new drug at what seemed like an exorbitant price.<sup>177</sup>

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market or ban their use, but ‘discourages’ doctors from using them in hysterectomies or fibroid surgery.”)

173. See Cortez, *supra* note 170, at 1383–84, 1386–87, 1441–54; *id.* at 1453 (concluding that agencies “enjoy virtually boundless discretion to brandish adverse publicity”); Gellhorn, *supra* note 170, at 1424 (“Publicity is quicker and cheaper; it is not presently subject to judicial review or other effective legal control; and it involves the exercise of pure administrative discretion.”); *id.* at 1426 (“Because adverse publicity is usually a deprivation not subject to effective judicial control, it should usually be a sanction of last, not first, resort.”); *id.* at 1441 (“Adverse agency publicity is a powerful and often unruly nonlegal sanction.”); Wu, *supra* note 155, at 1856–57 (discussing the hazards of “conviction by press release”).
174. See Proposed Rule, Publicity Policy, 42 Fed. Reg. 12,436, 12,440–41 (Mar. 4, 1977), *withdrawn*, 56 Fed. Reg. 67,440, 67,446 (Dec. 30, 1991); see also 45 C.F.R. pt. 17 (2013) (HHS policy governing the use of publicity); *cf.* 21 C.F.R. § 10.115(b)(3) (2014) (excluding from GGP’s “agency reports, general information documents provided to consumers or health professionals, speeches, journal articles and editorials, media interviews, [and] press materials”). Instead, the FDA has issued guidance governing its use of adverse publicity. See Cortez, *supra* note 170, at 1406–07.
175. See Cortez, *supra* note 170, at 1375–76, 1381–82, 1409–15; *id.* at 1413 (finding that “the FDA issued 1542 press announcements between 2004 and 2010, equating to almost one every business day” and that 30% of these qualified as individualized, negative, and preliminary).
176. “One may well ask how far an agency might go in conditioning licenses. In addition to postmarketing studies and the waiver of hearing rights, for example, could the FDA condition product approvals on agreements not to engage in broadcast advertising or not to raise drug prices faster than the rate of inflation?” Noah, *supra* note 151, at 883; see also *id.* (“Could the Agency demand waivers of patent rights or promises to contribute some percentage of profits to a public health agency (or perhaps the Republican National Committee)?”); *id.* at 933 (“[T]he FDA presumably understands that it cannot condition product approvals on voluntary price controls or charitable contributions, even though Congress has not expressly prohibited such demands.”).
177. After it received FDA approval for the preterm labor drug Makena® (hydroxyprogesterone caproate), which came with seven years of market exclusivity as an “orphan” drug, K-V Pharmaceutical attracted sharp criticism for deciding to charge \$1,500 per dose (approximately \$30,000 total during the course of a pregnancy) because previously available compounded versions had sold for no more than \$20 per dose. See Rob Stein, *Price Tag Soars on Preterm Birth Drug*, WASH. POST, Mar. 29, 2011, at A1 (adding that an FDA official suggested that it might approve a generic version of the same drug for a different indication, which would then allow physicians to use it off-label). In a thinly veiled effort to pressure the

## B. Offers/Threats in the Licensing Context

Product licensing gives the FDA even greater leverage for extracting concessions from sellers.<sup>178</sup> In 1996, for instance, the agency approved Procter & Gamble's food additive petition for the non-caloric fat substitute olestra for use in certain snack foods.<sup>179</sup> Nearly twenty-five years had elapsed between the company's initial contacts with agency officials and final approval, and Procter & Gamble spent more than \$200 million in the product development process.<sup>180</sup> Indeed, the FDA approved olestra just days before the expiration of the company's previously extended patents.<sup>181</sup> The final regulation conditioned use of the additive on special labeling, vitamin fortification, and the submission of follow-up reports to allow for further review.<sup>182</sup>

The requirement for postmarket surveillance represented one of the most curious features of the approval. The regulation itself did not mandate further testing by the petitioner; it only provided that the FDA "will review and evaluate all data and information bearing on the safety of olestra received by the agency."<sup>183</sup> In the preamble accompanying the regulation, however, the agency explained that "as a

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manufacturer to lower its price, the agency issued a press release indicating that it would continue to tolerate pharmacy compounding of the drug. See Rob Stein, *FDA Won't Obstruct Cheap Alternative to Makena*, WASH. POST, Mar. 31, 2011, at A5; see also *K-V Pharm. Co. v. FDA*, 889 F. Supp. 2d 119, 132–40 (D.D.C. 2012) (dismissing as unreviewable a challenge to this exercise of enforcement discretion); Harris, *supra* note 97, at A1 (reporting that the White House had forced the FDA to issue this statement); Andrew Zajac, *Pregnancy Drug's Price Reduced*, L.A. TIMES, Apr. 2, 2011, at AA2 (reporting a revised but still controversial price of \$690 per dose); cf. Lars Noah, *Treat Yourself: Is Self-Medication the Prescription for What Ails American Health Care?*, 19 HARV. J.L. & TECH. 359, 385–86 & n.141 (2006) (hypothesizing this sort of a stunt).

178. It certainly provides agencies with a powerful mechanism for securing adherence to nonbinding announcements. See Anthony, *supra* note 9, at 1340, 1372; Robert A. Anthony, "Well, You Want the Permit, Don't You?" *Agency Efforts to Make Non-legislative Documents Bind the Public*, 44 ADMIN. L. REV. 31 (1992).
179. See Food Additives Permitted for Direct Addition to Food for Human Consumption; Olestra, 61 Fed. Reg. 3118, 3172 (Jan. 30, 1996) (codified as amended at 21 C.F.R. § 172.867(c) (2014)) [hereinafter *Olestra Rule*]; see also Lars Noah & Richard A. Merrill, *Starting from Scratch?: Reinventing the Food Additive Approval Process*, 78 B.U. L. REV. 329, 413–21 (1998) (elaborating on this case study).
180. See Marian Burros, *Intensifying Debate on a Fat Substitute*, N.Y. TIMES, Jan. 17, 1996, at C1.
181. See Sally Squires, *FDA Decision Nears on Fat Substitute*, WASH. POST, Jan. 23, 1996, at F8. Upon approval, the company became eligible for limited patent term restoration. See Notice, Determination of Regulatory Review Period for Purposes of Patent Extension; Olean, 62 Fed. Reg. 763 (Jan. 6, 1997); Raju Narisetti, *Anatomy of a Food Fight: The Olestra Debate*, WALL ST. J., July 31, 1996, at B1.
182. See 21 C.F.R. § 172.867(d)–(f) (2014).
183. *Id.* § 172.867(f) (adding that the FDA "will present such data, information, and evaluation to the agency's Food Advisory Committee within 30 months of the effective date of this regulation," and then "will initiate any appropriate regulatory proceedings"). Eight years later, after conducting this further review, the agency

condition of approval, Procter and Gamble is to conduct the studies that it has identified in its letter to FDA,<sup>184</sup> and it warned that, “if Procter and Gamble does not conduct the identified studies and does not conduct them according to the articulated timetable, FDA will consider the approval set forth in this document to be void *ab initio* and will institute appropriate proceedings.”<sup>185</sup>

This threat was remarkable insofar as it treated the food additive approval as a private license rather than a public regulation available (subject only to patent limitations) to any firm wishing to manufacture and sell the additive.<sup>186</sup> The FDA’s threat also seemingly ignored the procedures specified by Congress for withdrawing an approval.<sup>187</sup> The agency responded that its postmarket surveillance condition was “not without precedent,” citing the more limited data collection requirement imposed fifteen years earlier on the manufacturer of the food additive aspartame,<sup>188</sup> but this also had reflected a nominally voluntary undertaking by the sponsor.<sup>189</sup>

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amended the rule. *See* Final Rule, Food Additives Permitted for Direct Addition to Food for Human Consumption; Olestra, 69 Fed. Reg. 29,432 (May 24, 2004).

184. Olestra Rule, 61 Fed. Reg. at 3168 (“Procter and Gamble has notified FDA that the company will be conducting additional studies of olestra exposure (both amounts consumed and patterns of consumption) and the effects of olestra consumption . . . .”); *see also* U.S. GEN. ACCT. OFFICE, GAO/RCED-93-142, FOOD SAFETY AND QUALITY: INNOVATIVE STRATEGIES MAY BE NEEDED TO REGULATE NEW FOOD TECHNOLOGIES 61 (1993) [hereinafter GAO FOOD ADDITIVE REPORT] (According to one official, the “FDA may try to negotiate requirements for firms to conduct postmarket surveillance, including the collection and reporting of data on dietary use and on any adverse effects, as a condition for approving novel macro-ingredients as food additives.”).
185. Olestra Rule, 61 Fed. Reg. at 3169. The preamble provided little information about the nature of this correspondence, though the letter from the company referenced by the agency—dated one month after the close of the public comment period and less than one week before publication of the approval—suggested last minute negotiations had taken place.
186. *See* GAO FOOD ADDITIVE REPORT, *supra* note 184, at 27 (“Unlike approvals for new drugs, food additives regulations are not licenses. Once FDA has issued a regulation specifying the uses and conditions of use for a food additive, any company is free to market the additive as long as the additive is in compliance with the regulation and is not patented.”).
187. *See* 21 U.S.C. § 348(h) (2012); 21 C.F.R. § 171.130 (2014).
188. Olestra Rule, 61 Fed. Reg. at 3169. The final decision approving aspartame included the following additional condition: “Searle is to monitor the actual use levels of aspartame and to provide such information on aspartame’s use to the Bureau of Foods as the Bureau may deem necessary by an order, in the form of a letter, to Searle.” Notice, Aspartame: Commissioner’s Final Decision, 46 Fed. Reg. 38,285, 38,303 (July 24, 1981).
189. *See* GAO FOOD ADDITIVE REPORT, *supra* note 184, at 61 (“In at least one instance, FDA has been able to obtain *voluntary* postmarket surveillance for a food additive (Aspartame, an artificial sweetener) as part of the approval process for this substance. However, FDA does not have the statutory authority to *require* surveillance for food products, as it does for human drugs . . . .”).

Even more so than it does in the case of food additives, the FDA carefully reviews all new drug products prior to marketing. Until recently, the FDCA made no mention of postmarket (so-called “Phase IV”) study requirements,<sup>190</sup> but the agency long ago issued regulations governing such clinical trials.<sup>191</sup> As a condition of product approval, the FDA often has encouraged applicants to undertake postapproval research,<sup>192</sup> though it has done a poor job of holding pharmaceutical manufacturers to these promises.<sup>193</sup> In 1997, Congress authorized such requirements, though only for drugs eligible for “fast track” review.<sup>194</sup> Ten years later, it amended the statute to allow for the routine imposition of postapproval study requirements.<sup>195</sup>

In 1992, in response to complaints about excessive delays in approving AIDS drugs, the agency promulgated regulations to establish an accelerated approval procedure for new drugs and biologics intended to treat serious or life-threatening illnesses.<sup>196</sup> Before approving a new drug, the FDA must find that it is both safe and effective, but, under the accelerated approval procedures, it accepted weaker evidence of effectiveness than normally required.<sup>197</sup> If a pharmaceutical

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190. See Robert L. Fleshner, *Post-Marketing Surveillance of Prescription Drugs: Do We Need to Amend the FDCA?*, 18 HARV. J. ON LEGIS. 327 (1981).

191. See Final Rule, Approved New Drugs That Require Continuation of Long-Term Studies, Records, and Reports; Listing of Levodopa, 37 Fed. Reg. 201 (Jan. 7, 1972) (codified as amended at 21 C.F.R. § 310.303(a) (2014)).

192. See Charles Steenburg, *The Food and Drug Administration’s Use of Postmarketing (Phase IV) Study Requirements: Exception to the Rule?*, 61 FOOD & DRUG L.J. 295, 325–27 (2006). The Centers for Medicare and Medicaid Services (CMS) have twisted different arms to encourage postapproval studies. See Lars Noah, *Coerced Participation in Clinical Trials: Conscripting Human Research Subjects*, 62 ADMIN. L. REV. 329, 331–35 & n.7, 342–66 (2010) (criticizing CMS for using its leverage to persuade Medicare beneficiaries to “volunteer” for medical research); *id.* at 331–32 & nn.10–11 (explaining that the agency used guidance documents to announce this policy).

193. See Gardiner Harris, *Drug Makers Remain Years Behind on Testing Approved Medicines, Report Finds*, N.Y. TIMES, Oct. 27, 2009, at A18.

194. See Food and Drug Administration Modernization Act, Pub. L. No. 105-115, § 112(a) (FDCA § 506(b)(2)(A)), 111 Stat. 2296, 2309 (1997) (codified at 21 U.S.C. § 356(b)(2)(A) (2012)).

195. See Food and Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, § 901(a) (FDCA § 505(o)), 121 Stat. 823, 923 (codified at 21 U.S.C. § 355(o) (2012)); see also *infra* note 214 and accompanying text (summarizing restrictions on exercising this new power).

196. See Final Rule, New Drug, Antibiotic, and Biological Drug Product Regulations; Accelerated Approval, 57 Fed. Reg. 58,942, 58,958 (Dec. 11, 1992) (codified at 21 C.F.R. pts. 314(H), 601(E) (2014)) [hereinafter Accelerated Approval Rule].

197. For instance, the FDA will accept evidence of drug effectiveness in attaining “surrogate endpoints” (e.g., reductions in CD4 cell counts or tumor shrinkage) in lieu of the more difficult to prove “clinical endpoints” (e.g., improved survival). See 21 C.F.R. §§ 314.510, 601.41 (2014); Accelerated Approval Rule, 57 Fed. Reg. at 58,943–44. Approval predicated on surrogate endpoints requires that the applicant agree to conduct postmarketing studies relating to the clinical endpoints.

company wanted to utilize this expedited licensing procedure, it had to agree to several conditions on approval not originally authorized by Congress. For example, an applicant would have to accept any necessary postmarketing restrictions, including distribution only through certain medical facilities or by specially-trained physicians, distribution conditioned on the performance of specified medical procedures, and advance submission of all promotional materials for FDA review.<sup>198</sup> At the time that the agency issued the rule, however, the governing statute did not authorize the imposition of any of these conditions.<sup>199</sup>

Moreover, the FDA demanded that a company waive its statutory right to demand an evidentiary hearing in the event that the agency later chose to withdraw the approval.<sup>200</sup> In response to industry complaints about such conditions, the FDA explained that any “applicants objecting to these procedures may forego approval under these regulations and seek approval under the traditional approval process.”<sup>201</sup> With potentially millions of dollars in revenue foregone for each additional month awaiting approval,<sup>202</sup> however, eligible drug companies

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198. See 21 C.F.R. §§ 314.520(a), 314.550, 601.42(a), 601.45.

199. See *supra* note 157 (describing limits on the power to preclear advertising); *infra* note 206 (discussing limits on the power to restrict distribution). The FDA responded that the statute provided it with sufficient flexibility to impose these various conditions for accelerated approvals. See Accelerated Approval Rule, 57 Fed. Reg. at 58,949, 58,951 (alluding to the “spirit” of the statute); *id.* at 58,953–54 (citing its broad rulemaking authority); see also Jeffrey E. Shuren, *The Modern Regulatory Administrative State: A Response to Changing Circumstances*, 38 HARV. J. ON LEGIS. 291, 308–15 (2001) (defending these initiatives).

200. See 21 C.F.R. §§ 314.530, 601.43 (providing the applicant with only an informal hearing prior to revocation).

201. Accelerated Approval Rule, 57 Fed. Reg. at 58,955. The FDA also explained that no court had interpreted the statute as requiring a formal evidentiary hearing before withdrawing approval, but that its own regulations provided for such a hearing. See *id.* Although the agency may utilize a summary judgment procedure to deny hearing requests when it withdraws its approval for a new drug approval, see *Weinberger v. Hynson, Westcott & Dunning, Inc.*, 412 U.S. 609, 620–22 (1973), it must provide a hearing when genuine issues are in dispute, see *id.* at 623; *Edison Pharm. Co. v. FDA*, 513 F.2d 1063, 1072 (D.C. Cir. 1975); *Sterling Drug, Inc. v. Weinberger*, 503 F.2d 675, 680–83 (2d Cir. 1974). The FDA also argued that the less formal hearing procedure that it provided for withdrawals of accelerated approvals would give the applicant adequate notice and opportunity to be heard. See Accelerated Approval Rule, 57 Fed. Reg. at 58,955.

202. See *User Fees for Prescription Drugs: Hearing Before the Subcomm. on Health and the Environment of the H. Comm. on Energy and Commerce*, 102d Cong. 10 (1992) (statement of David A. Kessler, Commissioner, FDA) (“For a drug that raises \$200 million a year in annual sales, assuming an 80 percent gross margin, every additional month of delay the Agency takes to review an application would cost the company about \$10 million in lost opportunity.”); Joseph A. DiMasi et al., *The Price of Innovation: New Estimates of Drug Development Costs*, 22 J. HEALTH ECON. 151 (2003); Peter Landers, *Cost of Developing a New Drug Increases to About \$1.7 Billion*, WALL ST. J., Dec. 8, 2003, at B4.

could not afford to decline the invitation to make use of these accelerated procedures, and the industry never challenged the rules in court. To its credit, the agency used rulemaking to create this mechanism, and, five years later, Congress belatedly authorized these special procedures for what it called “fast track” review.<sup>203</sup>

The FDA also has shown growing interest in developing more tailored risk management strategies for non-critical pharmaceuticals. These efforts might include restricting distribution to certain specialists,<sup>204</sup> patient informed consent requirements, structured postmarket surveillance, and mandatory concomitant therapy or monitoring.<sup>205</sup> In addition, the agency might seek to prohibit certain off-label uses, perhaps in those situations where the labeling specifically contraindicates a use. Before 2007, serious questions existed about the FDA’s power to impose such restrictions,<sup>206</sup> but the agency often managed to encourage pharmaceutical manufacturers to accept such limitations as a condition of product approval.<sup>207</sup> Congress subse-

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203. See Food and Drug Administration Modernization Act, Pub. L. No. 105-115, § 112(a) (FDCA § 506), 111 Stat. 2296, 2309 (1997) (codified at 21 U.S.C. § 356 (2012)). This seems like a recurring pattern over the last few decades: the FDA tries something that arguably exceeds the bounds of its delegated authority, and Congress later endorses the effort by granting the agency explicit authority that it previously lacked though subject to limitations.

204. See, e.g., Lars Noah, *Assisted Reproductive Technologies and the Pitfalls of Unregulated Biomedical Innovation*, 55 FLA. L. REV. 603, 654 (2003) (suggesting that only reproductive endocrinologists enjoy access to fertility drugs); Scott B. Markow, Note, *Penetrating the Walls of Drug-Resistant Bacteria: A Statutory Prescription to Combat Antibiotic Misuse*, 87 GEO. L.J. 531, 546–47 (1998) (suggesting that only infectious disease specialists in hospitals be permitted to use the latest antibiotics).

205. See Notice of Availability, Guidances for Industry on Premarketing Risk Assessment; Development and Use of Risk Minimization Action Plans; and Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment, 70 Fed. Reg. 15,866 (Mar. 29, 2005).

206. See *Am. Pharm. Ass’n v. Weinberger*, 377 F. Supp. 824, 831 (D.D.C. 1974) (invalidating FDA restrictions on the distribution of methadone as a condition of approval), *aff’d*, 530 F.2d 1054 (D.C. Cir. 1976) (per curiam); Mark A. Hurwitz, Note, *Bundling Patented Drugs and Medical Services: An Antitrust Analysis*, 91 COLUM. L. REV. 1188, 1192–95 (1991); see also Anna Wilde Mathews & Leila Aboud, *FDA Approves Generic OxyContin*, WALL ST. J., Mar. 24, 2004, at A3 (“[T]he FDA has never limited any opioid to certain pharmacies, and agency officials say they don’t have the authority to block certain physicians from prescribing a drug.”).

207. See Lars Noah, *Ambivalent Commitments to Federalism in Controlling the Practice of Medicine*, 53 U. KAN. L. REV. 149, 153, 188–91 (2004). One former FDA official (who had just left his post as a deputy commissioner) explained that risk-management plans “already guide the use of about 30 marketed drugs as part of ‘voluntary’ arrangements with drug companies.” Scott Gottlieb, Op-Ed., *Prescription for Trouble*, WALL ST. J., Mar. 6, 2007, at A19; see also Scott Gottlieb, *Drug Safety Proposals and the Intrusion of Federal Regulation into Patient Freedom and Medical Practice*, 26 HEALTH AFF. 664, 666 (2007) (elaborating); Lars Noah, *Challenges in the Federal Regulation of Pain Management Technologies*, 31 J.L.

quently did authorize the imposition of many such restrictions,<sup>208</sup> though subject to various constraints that continue to make the old voluntary approach attractive to the agency.

In some cases, physicians must register with the manufacturer—attesting that they understand the risks and benefits of a particular drug—before they may prescribe it.<sup>209</sup> For instance, when it approved Thalomid<sup>®</sup> (thalidomide) for the treatment of leprosy patients, the FDA conditioned approval on extremely strict marketing controls because of the serious risk of birth defects: distribution only through specially registered physicians and pharmacists, and tracking of patients who must agree to use two forms of contraception and undergo frequent pregnancy tests.<sup>210</sup> The agency secured comparable distri-

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MED. & ETHICS 55, 63 (2003) (noting that, in trying to encourage the manufacturer of OxyContin<sup>®</sup> to restrict distribution to pain management specialists, the Drug Enforcement Administration (DEA) “threatened to slash the company’s annual production quota by approximately 95 percent”). The DEA has used threats against physicians in an attempt to undermine state laws that liberalized access to controlled substances. See Interpretive Rule, Dispensing of Controlled Substances to Assist Suicide, 66 Fed. Reg. 56,607, 56,608 (Nov. 9, 2001); Notice, Administration Response to Arizona Proposition 200 and California Proposition 215, 62 Fed. Reg. 6164, 6164 (Feb. 11, 1997) (threatening the withdrawal of prescribing licenses, exclusion from participation in Medicare and Medicaid, and criminal prosecution of physicians who merely recommended marijuana to their patients as authorized under state law). In both instances, courts invalidated these efforts. See *Gonzales v. Oregon*, 546 U.S. 243, 272–75 (2006); *Conant v. Walters*, 309 F.3d 629, 639 (9th Cir. 2002).

208. See Food and Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, tit. IX, 121 Stat. 823, 922. In implementing this authority, the agency announced that previously accepted voluntary restrictions thereafter would be considered to comply with this provision. See Identification of Drug and Biological Products Deemed to Have Risk Evaluation and Mitigation Strategies for Purposes of the Food and Drug Administration Amendments Act of 2007, 73 Fed. Reg. 16,313, 16,314 tbl.1 (Mar. 27, 2008) (identifying sixteen such products).
209. See Francesca Lunzer Kritz, *Still Irritable, Still Waiting: After Return to Market, Lotronex Can Be Hard to Get*, WASH. POST, Feb. 11, 2003, at F1 (discussing restrictions on access to a drug used for the treatment of irritable bowel syndrome, and explaining that similar physician registration requirements apply to felbamate (used for epilepsy) and clozapine (used for schizophrenia)).
210. See Rita Rubin, *Thalidomide Could Guide Use of Drugs That Risk Birth Defects*, USA TODAY, July 22, 1998, at 7D; see also Sheryl Gay Stolberg, *Thalidomide Approved to Treat Leprosy, with Other Uses Seen*, N.Y. TIMES, July 17, 1998, at A1 (“If any doctors or pharmacists refuse to comply with the distribution rules, their privileges to prescribe or dispense the drug might be revoked.”); Jamie Talan, *Thalidomide’s Legacy*, WASH. POST, Jan. 4, 2000, at F10 (reporting that physicians who prescribe the drug receive from the manufacturer an “education kit, including a consent form to be signed by both doctor and patient”).

bution restrictions in connection with Accutane<sup>®</sup> (isotretinoin)<sup>211</sup> and Mifeprex<sup>®</sup> (mifepristone).<sup>212</sup>

When Congress has, however, empowered the FDA to impose particular requirements but subject them to various procedural and substantive restrictions, the agency should not sidestep these limitations through the simple expedient of encouraging the voluntary acceptance of such conditions on approval. For instance, the authority granted to the FDA in 2007 to adopt various distribution controls—called “risk evaluation and mitigation strategy” (REMS) requirements—provided, among other things, for advisory committee review, issuance of guidance, posting of approval letters or orders that impose REMS, elaborate dispute resolution procedures, and public meetings.<sup>213</sup> Similarly, under the postapproval studies provision added in 2007, the agency cannot demand such trials unless, among other things, it determines that less intensive risk surveillance methods will not suffice, the sponsor is granted an opportunity to seek resolution of any disputes about

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211. See Lars Noah, *Too High a Price for Some Drugs?: The FDA Burdens Reproductive Choice*, 44 SAN DIEGO L. REV. 231, 233–39 (2007); see also *id.* at 240–58 (questioning the constitutionality of mandatory contraception as a condition of access to teratogenic drugs).

212. See Lars Noah, *A Miscarriage in the Drug Approval Process?: Mifepristone Embroils the FDA in Abortion Politics*, 36 WAKE FOREST L. REV. 571, 583–86 (2001); *id.* at 581–82 (“Mifepristone’s eligibility to use such [accelerated review] procedures remains something of a mystery: the drug did not provide the type of therapeutic benefit over existing treatments for a serious illness that the regulations contemplated as justifying an expedited approval process. . . . Apparently the agency took this route so that it could better justify imposing otherwise unauthorized restrictions on the use and distribution of the drug . . . .”); Gina Kolata, *U.S. Approves Abortion Pill*, N.Y. TIMES, Sept. 29, 2000, at A1 (“A woman will be given written instructions . . . , and her doctor must sign a statement saying they have read the instructions and will comply with them exactly.”). For the most part, however, these restrictions have not been enforced. See Marc Kaufman, *Death After Abortion Pill Reignites Safety Debate*, WASH. POST, Nov. 3, 2003, at A3.

213. See Food and Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, § 901(b) (FDCA § 505-1(f)–(h)), 121 Stat. 823, 930–37 (codified at 21 U.S.C. § 355-1(f)–(h) (2012)); Jennifer L. Bragg & Maya P. Florence, *Life with a REMS: Challenges and Opportunities*, 13 J. HEALTH CARE L. & POL’Y 269, 269–75 (2010); Andrew Wilson & Christopher-Paul Milne, *FDA’s Risk Evaluation and Mitigation Strategies (REMS): Effective and Efficient Safety Tools or Process Poltergeist*, 66 FOOD & DRUG L.J. 569, 570–71, 578 tbl.2, 583–85 (2011). For instance, the FDA initiated such a process for narcotic analgesics. See Notice of Availability, Draft Blueprint for Prescriber Education for Long-Acting/Extended-Release Opioid Class-Wide Risk Evaluation and Mitigation Strategy, 76 Fed. Reg. 68,766 (Nov. 7, 2011). Evidently based on some of the feedback that it received, the agency decided not to proceed with this idea. See Barry Meier, *F.D.A. Won’t Order Doctors to Get Pain-Drug Training*, N.Y. TIMES, July 10, 2012, at B2; see also Hilary Homenko, Note, *Rehabilitating Opioid Regulation: A Prescription for the FDA’s Next Proposal of an Opioid Risk Evaluation and Mitigation Strategy (REMS)*, 22 HEALTH MATRIX 273, 275–76, 294–96 (2012) (explaining that an earlier proposal had fared poorly at an advisory committee meeting); *id.* at 292–94 (noting that the FDA has imposed REMS for narcotic analgesics on an ad hoc basis instead).

the imposition of such a requirement, and the necessary determinations are made only by division directors or higher-level officials.<sup>214</sup> Arm-twisting would improperly allow the FDA to secure voluntary distribution controls or postapproval studies without abiding by the limitations crafted by Congress. At the very least, the agency should announce its policies openly rather than leave them to ad hoc negotiations largely hidden from external scrutiny.<sup>215</sup>

#### IV. CONCLUSION

For a relatively small agency with a lot on its plate,<sup>216</sup> the FDA's reliance on procedural short cuts should come as no great surprise. Guidance documents clearly have a place in the portfolio of any agency, but the FDA has used this format for policy announcements that previously would have emerged after notice-and-comment rulemaking. In some respects, Congress has endorsed and further encouraged this development, but it also has sought to proceduralize and put the brakes on guidance-making at the FDA,<sup>217</sup> leading the agency to look for ways to escape even these limited constraints. Moreover,

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214. See Food and Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, § 901(a) (FDCA § 505(o)(3)(D), (F), (o)(5)), 121 Stat. 823, 923–24, 926 (codified at 21 U.S.C. § 355(o)(3)(D), (F), (o)(5) (2012)).

215. See Noah, *supra* note 151, at 938–40; see also Cooper, *supra* note 160, at 843 (“Even when enforcement officials may very well be exceeding their statutory authority or invading constitutionally protected rights (e.g., commercial free speech), organizations almost always prefer to settle. In doing so, they give up an opportunity to obtain a judicial ruling on the agency’s enforcement theories.”); *id.* at 844–47 (explaining why agency consent decrees and settlement policies evade scrutiny by both the judicial and executive branch); *id.* at 846 (“Judicial review, therefore, appears not to be an effectual restraint on the power of enforcement officials to extract concessions in settlements. Moreover, what is needed much more than case-by-case post hoc review of individual settlements is advance review of the policies and forms of agreement that shape an enforcement agency’s settlements generally.”). For instance, the agency did issue a guidance document to explain how it would exercise its new authority to require postapproval studies. See Notice of Availability, Guidance for Industry on Postmarketing Studies and Clinical Trials—Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act, 76 Fed. Reg. 18,226 (Apr. 1, 2011).

216. See Noah, *supra* note 1, at 902.

217. Cf. Anthony, *supra* note 9, at 1317 (warning of “the tendency to overregulate that is nurtured when the practice of making binding law by guidances, manuals, and memoranda is tolerated”); *id.* at 1374 (arguing that “the APA rulemaking requirements impose a salutary discipline . . . [which] deters casual and sloppy action, and . . . reduces tendencies toward overregulation or bureaucratic overreaching”); Matthew D. McCubbins et al., *Structure and Process, Politics and Policy: Administrative Arrangements and the Political Control of Agencies*, 75 VA. L. REV. 431, 442 (1989) (“Administrative procedures erect a barrier against an agency carrying out such a [policy change as a] fait accompli by forcing the agency to move slowly and publicly, giving politicians (informed by their constituents) time to act before the status quo is changed.”); *id.* at 481 (same).

guidance documents represent only the tip of the iceberg, with the FDA making use of any number of even less formal tools and techniques in order to accomplish its ends. Perhaps that is neither unexpected nor invariably worrisome, but those who keep tabs on this agency must remain vigilant to guard against the possibility that it will overuse and abuse these procedural short cuts.