



# Informal Guidance and the FDA

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**Informal Guidance and the FDA**  
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Harvard Law School, Class of 2012  
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## *Abstract*

This article discusses how the Food and Drug Administration has come to adopt informal guidance (agency advice that influences regulated entities but does not carry the force and effect of law) as its primary method of policymaking, as opposed to more formalized procedures like notice-and-comment rulemaking or case-specific adjudication. Using major developments in administrative law and modifications to the FDA's regulatory regime as milestones, I trace how and why the FDA's use of informal guidance to fulfill its statutory mandate has changed over the past century. Along the way, I identify important doctrinal questions that persist today, namely (1) whether informal advisory opinions bind the FDA and (2) the degree of judicial deference guidance documents should receive under the Supreme Court's decisions in *Chevron* and *Mead*. I attempt to resolve these doctrinal ambiguities. I then undertake a normative analysis of the FDA's increasing reliance on informal guidance, and conclude that, on the whole, this development has benefited the FDA's major stakeholders: regulated entities, the general public, and the agency itself. I close with modest proposals for reform and suggestions for further research. The article features an appendix with several tables illustrating the FDA's output of informal guidance documents by year, to facilitate further study.

## Introduction

In the modern U.S. administrative state, Congress delegates a great deal of interpretive and regulatory authority to administrative agencies by enacting broad, open-ended statutes with the expectation that the agencies will fill in the gaps.<sup>2</sup> Agencies use a variety of policymaking tools to fill these gaps, including (1) rulemaking,<sup>3</sup> (2) adjudication, and (3) informal guidance.<sup>4</sup> Rulemaking is a policymaking process akin to congressional legislation in which the agency is required to "provide notice of the proposed [policy] and to accept public comments;"<sup>5</sup> adjudication is the administrative equivalent of case-specific judicial enforcement;<sup>6</sup> and guidance constitutes informal agency advice that influences regulated entities but does not carry the force and effect of law.<sup>7</sup> Guidance documents include "enforcement guidelines, policy statements, interpretive rules (explicating a statute or regulation), and the like."<sup>8</sup> Informal guidance

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<sup>2</sup> *E.g.*, *Chevron, U.S.A., Inc. v. Nat'l Res. Def. Council*, 467 U.S. 837, 843-44 (1984) (quoting *Morton v. Ruiz*, 415 U.S. 199, 231 (1974)); James Hunnicutt, *Another Reason to Reform the Federal Regulatory System: Agencies' Treating Nonlegislative Rules as Binding Law*, 41 B.C. L. REV. 153, 155-56 (1999); Cass R. Sunstein, *Chevron Step Zero*, 92 VA. L. REV. 187, 188-198 (2006); Antonin Scalia, *Judicial Deference to Administrative Interpretations of Law*, 1989 DUKE L.J. 511, 516-17 ("Congress now knows that the ambiguities it creates, whether intentionally or unintentionally, will be resolved, within the bounds of permissible interpretation, not by the courts but by a particular agency, whose policy biases will ordinarily be known."). *But see generally* Mark Seidenfeld, *Chevron's Foundation*, 86 NOTRE DAME L. REV. 273 (2011) (rejecting the notion of "congressional intent to delegate interpretive primacy to agencies").

<sup>3</sup> Policies promulgated through rulemaking are known as "regulations," "legislative rules," or just "rules." *See* Hunnicutt, *supra* note 2, at 153. Rulemaking is in turn split into two categories: informal and formal rulemaking. *Id.* at 159 (citing 5 U.S.C. §§ 553, 556-57 (1994)). Because the overwhelming majority of regulations are promulgated through informal rulemaking, *id.*, the reader may safely assume that every instance of the word "rulemaking" in this article refers to informal rulemaking.

<sup>4</sup> *See generally* M. Elizabeth Magill, *Agency Choice of Policymaking Form*, 71 U. CHI. L. REV. 1383, 1386 (2004); *see also* 5 U.S.C. §§ 553-57 (2011).

<sup>5</sup> The rulemaking process imposes other procedural requirements as well. For an excellent summary, *see, e.g.*, Connor N. Raso, *Strategic or Sincere? Analyzing Agency Use of Guidance Documents*, 119 YALE L.J. 782, 788 (2010); Anne Joseph O'Connell, *Political Cycles of Rulemaking: An Empirical Portrait of the Modern Administrative State*, 94 VA. L. REV. 889, 900-02 (2008). Rules promulgated by agencies are "legally binding, generally applicable, and nonretroactive." Raso, *supra* at 788.

<sup>6</sup> Magill, *supra* note 4, at 1386.

<sup>7</sup> *Id.* Guidance documents are also often referred to as "nonlegislative rules," "interpretative rules," "statements of policy," or "guidelines," as well as "innumerable" other synonyms. Hunnicutt, *supra* note 2, at 153, 177. For an excellent and extensive definition of guidance, *see* Raso, *supra* note 5, at 785 n.1.

<sup>8</sup> Magill, *supra* note 4, at 1386; *see also* Raso, *supra* note 5, at 785 n.1.

lacks many of the procedural safeguards of rulemaking and adjudication that protect both regulated entities and regulatory beneficiaries;<sup>9</sup> "[a]s a consequence, [an] agency cannot base an enforcement action solely on a regulated entity's noncompliance with a guidance document."<sup>10</sup> In other words, guidance does not bind regulated entities. Despite guidance's non-binding status, however, "guidance documents often have rule-like effects on regulated entities"<sup>11</sup> because they "supply valuable information to regulated entities regarding how an agency will implement a program."<sup>12</sup> While agencies have been using guidance since the dawn of the administrative state, only recently have agencies aggressively used guidance as their predominant mode of policymaking.<sup>13</sup>

An agency's choice of policymaking process "is strategic. An agency must weigh the costs and benefits of various procedures" available to it.<sup>14</sup> As a result of the diversity between agencies, different agencies utilize these three tools in different proportions to

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<sup>9</sup> Hunnicutt, *supra* note 2, at 157-76 (citing 5 U.S.C. § 553(b)(A) (1994)).

<sup>10</sup> Nina A. Mendelson, *Regulatory Beneficiaries and Informal Agency Policymaking*, 92 CORNELL L. REV. 397, 406-07 (2007).

<sup>11</sup> *Id.* at 407. Some scholars have decried this aspect of informal guidance. *See, e.g.*, 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."); JAMES T. O'REILLY, *FOOD AND DRUG ADMINISTRATION* § 4:24 4-87 (3d ed. 2007) (quoting Byerly, *FDA Administrative Procedures: The Myth and the Reality* in *FOOD, DRUG, AND COSMETIC INDUSTRY* 43 (V. Kleinfeld ed. 1972)); *see generally* Hunnicutt, *supra* note 2. Others have viewed the rule-like effects of guidance more charitably. Lars Noah, *The FDA's New Policy on Guidelines: Having Your Cake and Eating it Too*, 47 CATH. U. L. REV. 113, 120-142 (1997); Todd D. Rakoff, *The Choice Between Formal and Informal Modes of Administrative Regulation*, 52 ADMIN L. REV. 159 (2000).

<sup>12</sup> Mendelson, *supra* note 10, at 397. *See also* Erica Seiguer and John J. Smith, *Perception and Process at the Food and Drug Administration: Obligations and Tradeoffs in Rules and Guidances*, 60 FOOD & DRUG L.J. 17, 29-30 (2005) ("[I]n practice[,] . . . industry treats guidances no differently than rules . . . Most business people don't know the difference between a regulation passed through rulemaking] and a guidance, so by and large the business field does not care. All they want is clarity [and consistency].").

<sup>13</sup> Stephen M. Johnson, *Good Guidance, Good Grief!*, 72 MO. L. REV. 695, 695 (2007). Guidance in its current form is such a new phenomenon that, as late as 2000, neither the leading Administrative Law treatise nor eminent administrative law casebooks listed "guidance" in their indexes. Rakoff, *supra* note 11, at 160. Indeed, when the FDA issued its "Good Guidance Practices," which will be described *infra* Section I.H.2, "the FDA had to devote the first part of its statement simply to defining what it was talking about." *Id.* at 159-60.

<sup>14</sup> *Cf.* O'Connell, *supra* note 5, at 917 (discussing different types of policymaking, including nonlegislative rulemaking, *i.e.* guidance).

fulfill their statutory mandates. For instance, whereas the National Labor Relations Board and the Federal Trade Commission rely heavily on case-by-case adjudication to create policy, the Federal Communications Commission primarily utilizes rulemaking to fulfill its regulatory agenda.<sup>15</sup> Similarly, over time, individual agencies may adjust their interpretive method of choice in response to changing circumstances.<sup>16</sup> For example, although formal adjudication was the predominant mode of administrative policymaking in the 1950s and 60s, many agencies shifted to rulemaking in the 1960s to conserve administrative resources and establish clear, generally applicable regulatory standards.<sup>17</sup>

The Federal Food and Drug Administration ("FDA") is no exception to the foregoing discussion. Over time, the FDA has experimented with all three policymaking forms to achieve its regulatory objectives, but has ultimately settled on informal guidance as its policymaking weapon of choice.<sup>18</sup> While administrative law scholars have published excellent articles documenting the recent explosion of guidance at the FDA,<sup>19</sup> to the best of my knowledge none have told the story of the evolution of guidance at the FDA from its humble beginnings at the turn of the twentieth century.

In this article, I trace the historical development of guidance at the FDA. Using watershed administrative law cases and modifications to the FDA's regulatory regime as milestones, I demonstrate how and why the FDA has settled upon guidance as its preferred mode of policymaking. Throughout, I identify doctrinally unsettled questions regarding the FDA's administrative and policymaking practice, namely (1) which

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<sup>15</sup> Magill, *supra* note 4, at 1399.

<sup>16</sup> *Id.* at 1398-99.

<sup>17</sup> Rakoff, *supra* note 11, at 163.

<sup>18</sup> *Id.* at 168; John C. Carey, *Is Rulemaking Old Medicine at the FDA?*, 3-6 (1997), in FOOD AND DRUG LAW: AN ELECTRONIC BOOK OF STUDENT PAPERS (Peter Barton Hutt, ed., 2011), available at [http://www.law.harvard.edu/faculty/hutt/book\\_index.html](http://www.law.harvard.edu/faculty/hutt/book_index.html).

<sup>19</sup> See generally, e.g., Rakoff, *supra* note 11; Seiguer and Smith, *supra* note 12.

guidance documents the FDA is bound to follow and (2) the degree to which courts should defer to FDA policies/textual interpretations expressed in guidance documents. I offer tentative answers to these doctrinal questions. Afterwards, I evaluate whether the FDA's increasing reliance on guidance has been beneficial for the agency, regulated entities, and regulatory beneficiaries. I conclude that, on the whole, the FDA's ever-growing use of guidance has benefited the FDA's stakeholders. I close the article with modest proposals for reform and identify areas for further research.

## *I. The History of Guidance at the FDA*

### *A. The Genesis of Guidance*

Although the FDA's overwhelming reliance on guidance is a relatively recent phenomenon,<sup>20</sup> the FDA and its predecessors<sup>21</sup> have been utilizing guidance documents to further their regulatory objectives for over a century.<sup>22</sup> Beginning in 1902, the Bureau of Chemistry, a prototype of the FDA that was housed within the United States Department of Agriculture ("USDA"), began issuing "Food Inspection Decisions" ("FIDs") in response to questions from regulated entities.<sup>23</sup> The Bureau was prompted to utilize informal guidance by the comparative informational disadvantages of setting regulatory policy *via* individual adjudications:

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<sup>20</sup> Rakoff, *supra* note 11, at 159-60.

<sup>21</sup> The FDA traces its lineage to the Agricultural Division of the Patent Office, which was transferred into the newly created USDA around 1862. The chemical laboratory morphed into the Division of Chemistry in 1890, and was rechristened the Bureau of Chemistry in 1901. The Bureau of Chemistry began the Food, Drug, and Insecticide Administration in 1927, which in 1930 officially became the FDA. The FDA operated under the auspices of the USDA until 1940, when it was transferred to the Federal Security Agency. The FDA was in turn transferred to the Department of Health, Education, and Welfare, which was renamed the Department of Health and Human Services in 1979. Peter Barton Hutt, *Symposium on the History of Fifty Years of Food Regulation Under the Federal Food, Drug, and Cosmetic Act: A Historical Introduction*, 45 FOOD DRUG COSM. L. J. 17, 18 (1990).

<sup>22</sup> Noah, *supra* note 11, at 115.

<sup>23</sup> United States Department of Agriculture, Bureau of Chemistry, FIDs 1-25, Introduction (1905). Individual FIDs will hereinafter be cited as "FID # (year of issuance)."

For the information of [regulated entities] and of the public it is advisable to publish more widely than would be possible by decisions given to individuals or firms the opinions of this Department rendered by the Secretary under the existing law relating to the [Bureau of Chemistry's regulatory policies].<sup>24</sup>

FIDs advised industry of the Bureau's current thinking on numerous diverse topics, including the maximum allowable quantity of sulfurous acids in wines,<sup>25</sup> the impermissibility of using fictitious firm names on product labels,<sup>26</sup> the coloring of butter and cheese,<sup>27</sup> and the illegality of the interstate shipment of the highly alcoholic beverage absinthe.<sup>28</sup> The agency issued FIDs, as well as other informal guidance documents, in printed publications called Service and Regulatory Announcements ("SRAs"), which were at first issued monthly but were later published on an irregular basis.<sup>29</sup> Interestingly, FIDs predate the Pure Food and Drug Act of 1906; FIDs 1-39 dealt only with imported foods and were therefore not distributed after the passage of the 1906 Act.<sup>30</sup> FIDs were always signed by the Secretary of Agriculture, and were occasionally also signed by the Secretary of the Treasury and the Secretary of Commerce; as a result, regulated entities gained useful insights into the plans and priorities of these agencies' leaders.<sup>31</sup> The Secretary of Agriculture took pains to emphasize that FIDs were informal guidance documents only, and that they did not carry the force of law:

From the tenor of many inquiries received in this Department it appears that many persons suppose that the answers to inquiries addressed to this Department, either in letters or in published decisions, have the force and

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<sup>24</sup> United States Department of Agriculture, Bureau of Chemistry, FIDs 1-25, Introduction (1905).

<sup>25</sup> FID 28 (1905).

<sup>26</sup> FID 46 (1906).

<sup>27</sup> FID 51 (1907).

<sup>28</sup> FID 147 (1912).

<sup>29</sup> Researching FDA with Published Primary Sources,

<http://www.fda.gov/AboutFDA/WhatWeDo/History/ResearchTools/ResearchingFDAwithPublishedPrimarySources/default.htm> (last visited Jun. 30, 2011) [hereinafter *Primary Sources*].

<sup>30</sup> FID 125 (1910).

<sup>31</sup> *Primary Sources*, *supra* note 29.

effect of the rules and regulations for the enforcement of the food and drugs act of June 30, 1906 . . . It seems highly desirable that an erroneous opinion of this kind should be corrected. The opinions or decisions of this Department do not add anything to the rules and regulations nor take anything away from them. They therefore are not to be considered in the light of rules and regulations. On the other hand, the decisions and opinions referred to express the attitude of this Department in relation to the interpretation of the law and the rules and regulations, and they are published for the information of the officials of the Department who may be charged with the execution of the law and especially to acquaint manufacturers, jobbers, and dealers with the attitude of this Department in these matters. They are therefore issued more in an advisory than in a mandatory spirit.<sup>32</sup>

The Bureau of Chemistry's stated purposes for utilizing informal guidance were to conserve resources and prevent offenses:

[I]t is evident that an overwhelming majority of the manufacturers, jobbers, and dealers of this country are determined to do their utmost to conform to the provisions of the act, to support it in every particular, and to accede to the opinions of this Department respecting its construction. It is hoped, therefore, that the publication of the opinions and decisions of the Department will lead to the avoidance of litigation which might arise due to decisions which may be reached by this Department indicating violations of the act, violations which would not have occurred had the opinions and decisions of the Department been brought to the attention of the offender.<sup>33</sup>

The Department of Agriculture continued issuing FIDs until shortly after 1938; by that time, both industry and agency employees had access to 212 documents and were able to conduct their operations accordingly.<sup>34</sup>

### *B. The Dawn of the FDA*

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<sup>32</sup> FID 44 (1906).

<sup>33</sup> FID 44 (1906).

<sup>34</sup> *Primary Sources, supra* note 29.

In 1938, Congress enacted the FDA's organic statute: the Federal Food, Drug, and Cosmetic Act ("FD&C").<sup>35</sup> Congress delegated substantial authority to the FDA to use whatever policymaking tools it deemed best to effectuate the FD&C's statutory mandate:

Congress obviously knew in 1938 that it could not foresee future developments, and that it must proceed primarily by establishing general principles, permitting implementation within broad parameters, if regulation in this important area was to be effective . . . In this respect, the Act must be regarded as a constitution. It establishes a set of fundamental objectives — safe, effective, wholesome, and truthfully-labeled products — without attempting to specify every detail of regulation. The mission of the Food and Drug Administration is to implement these objectives through the most effective and efficient controls that can be devised.<sup>36</sup>

From its inception until the early 1970s, the FDA primarily utilized case-by-case adjudication to enforce the FD&C's provisions.<sup>37</sup> However, even "[f]rom its earliest beginnings, the FDA found it desirable to issue guidance on which regulated firms could rely."<sup>38</sup> Starting in the late 1930s, the FDA issued advisory opinions in the form of trade correspondences ("TCs") "to advise regulated firms on how to comply with statutory requirements."<sup>39</sup> Like the FIDs, TCs were "excerpts from day-to-day replies to inquiries concerning the application of the statute to specific problems."<sup>40</sup> Likewise, TCs only purported to "represent the attitude of the Administration in the light of the facts submitted and other available information;" the advice within was "subject to modification by the Administration as additional facts [became] available and controlling

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<sup>35</sup> 21 U.S.C. § 301 *et seq.* (1938).

<sup>36</sup> Peter Barton Hutt, *Philosophy of Regulation Under the Federal Food, Drug, and Cosmetic Act*, 50 FOOD & DRUG L.J. 101, 102 (1995 (Historical Article, originally published in 1973)).

<sup>37</sup> Carey, *supra* note 18, at 3.

<sup>38</sup> Noah, *supra* note 11, at 114.

<sup>39</sup> *Id.* at 115-16 (1997); William Van Brunt, *Advisory Opinions*, 32 FOOD DRUG COSM. L. J. 304, 305 (1977).

<sup>40</sup> VINCENT A. KLEINFELD AND CHARLES WESLEY DUNN, FEDERAL FOOD, DRUG, AND COSMETIC ACT 1938-1949 561 (1949) [hereinafter *1938-49*].

decisions [were] rendered by the Federal courts."<sup>41</sup> Nevertheless, TCs "provided needed clarification and certainty to persons attempting to comply with statutory and regulatory requirements, and they also benefited the Agency by assuring consistency in actions taken by its employees."<sup>42</sup>

From 1939 to 1946, the FDA issued a total of 439 TCs regarding numerous and diverse products.<sup>43</sup> The FDA issued an average of 49 TCs per year, although this figure is skewed heavily by the whopping 336 TCs issued in 1940.<sup>44</sup> However, TCs were not compiled and published until 1949; rather, they "were mimeographed and distributed to the [agency's] staff to maintain uniformity in policy throughout the country."<sup>45</sup> To obtain insight into the inner workings of the FDA, manufacturers and retailers had to either rely on the correspondence they personally received from the FDA or travel to FDA headquarters or field offices to inspect the TCs.<sup>46</sup> In this respect, TCs were more informal and less public than FIDs. Some TCs addressed crucial concerns (*e.g.*, statement on label that a nonofficial drug contains nux vomica "does not relieve the manufacturer of the necessity of declaring the quantity or proportion of strychnine," a pesticide that can cause muscular convulsions and eventual death,<sup>47</sup> which is "one of the constituents of nux vomica"),<sup>48</sup> while others addressed more mundane issues ("Antipasto, an appetizer consisting of mixed vegetable and fish products, may be accepted as the common name

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<sup>41</sup> *Id.*

<sup>42</sup> Noah, *supra* note 11, at 114.

<sup>43</sup> After issuing 431 TCs under its first series, the FDA created a new "A" series in November 1945. However, the FDA only issued eight A-series TCs before ceasing the TC program altogether. A collection of every TC issued by the FDA may be found in *1938-1949, supra* note 40, at 561-753. TCs will hereinafter be cited as "TC-# (date of issuance)."

<sup>44</sup> *See* Appendix A, Figure 2, *infra*.

<sup>45</sup> *Primary Sources, supra* note 29.

<sup>46</sup> *Id.*

<sup>47</sup> Strychnine - Wikipedia, the Free Encyclopedia, <http://en.wikipedia.org/wiki/Strychnine> (last visited July 1, 2011).

<sup>48</sup> TC-270 (Aug. 20, 1940). *See also* TC-419 (Aug. 18, 1944) ("The labeling of a tonic containing strychnine should clearly indicate that it is a strychnine tonic.").

of the product").<sup>49</sup> Some afforded invaluable advice to a wide variety of regulated entities (e.g., a detailed and extensive "[m]emorandum listing a number of drug preparations with indications concerning the nature of warning statements which are not subject to adverse criticism" from the FDA);<sup>50</sup> others were ultra-specific and arguably humorous ("The unqualified expression 'telephone' to indicate sieve size of canned peas constitutes misbranding;"<sup>51</sup> "The designation 'Breakfast Prunes in Syrup' is inappropriate if dried prunes are used;"<sup>52</sup> "Rubber nipples are not regarded as subject to the Act, but labeling claims could render them subject"<sup>53</sup>). Some policies established by TCs have stood the test of time ("Sample packages distributed to physicians are not exempt from the mandatory labeling requirements of the Act"),<sup>54</sup> while others have fallen to the wayside ("No tolerance has been announced for caffeine in soft drinks, but its addition to such drinks has been discouraged.").<sup>55</sup> All in all, the FDA used informal guidance as an indispensable tool in its policymaking agenda.

### *C. The Administrative Procedure Act and the Nadir of Guidance*

1946 marked a watershed development in administrative law: the enactment of the Administrative Procedure Act ("APA").<sup>56</sup> Drafted in response to trenchant criticisms

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<sup>49</sup> TC-32 (Feb. 9, 1940).

<sup>50</sup> TC-14 (Nov. 1, 1940).

<sup>51</sup> TC-291 (May 7, 1940). While your author is aware that "Tall Telephone" is a variety of garden pea, he nonetheless finds the mental image of a person picking up a can of peas and saying "Hello?" endlessly amusing. Your author further enjoys imagining our prospective pea purchaser slowly adopting a disappointed facial expression, announcing "I'm calling the FDA to report this!" and then holding a different can of peas to his ear.

<sup>52</sup> TC-229 (Apr. 11, 1940).

<sup>53</sup> TC-114 (Feb. 29, 1940).

<sup>54</sup> Compare TC-86 (Feb. 21, 1940) with 21 CFR § 203.38 (2011) (labeling of drug sample units).

<sup>55</sup> TC-144 (Mar. 7, 1940). A large number of TCs that were in place for many years were likewise subsequently revoked. O'REILLY, *supra* note 11, at § 4:25 4-94 (citing 40 Fed. Reg. 22962 (May 27, 1975); 34 Fed. Reg. 7922 (May 20, 1969)).

<sup>56</sup> 5 U.S.C. 500 *et seq.* (1946).

that administrative agencies were subject to insufficient procedural limitations,<sup>57</sup> the APA was enacted "to foster clarity, uniformity and public participation in the administrative state."<sup>58</sup> In relevant part, the APA established specific procedural requirements for rulemaking and adjudication, as well as standards for judicial review of agency action.<sup>59</sup> Although the APA's procedural safeguards were weak enough to "provide[] agencies with broad freedom" and thereby "permit[] the growth of the modern regulatory state,"<sup>60</sup> the APA nonetheless subjected administrative agencies to greater scrutiny by "introduc[ing] more formal procedures into regulatory decisionmaking, impos[ing] a kind of judicialization on the administrative process, . . . and increas[ing] the supervisory powers of the courts over the administrative agencies."<sup>61</sup>

In response to the APA's renewed emphasis on procedural rigor, the FDA "concluded that opinions which would otherwise have emanated as trade correspondence should thereafter be issued more formally" to comply with the strictures of the APA.<sup>62</sup> As a result, no TCs were issued after 1946. Rather, the FDA published guidance documents in the Federal Register and the Code of Federal Regulations as "Statements of General

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<sup>57</sup> For example, "[i]n a widely publicized report published in 1938, Roscoe Pound, chairman of the special committee of the ABA on administrative law, excoriated the regulatory system for 'administrative absolutism' and catalogued the suspect 'tendencies' of administrative agencies, among them: (1) to decide without a hearing, (2) to decide on the basis of matters not before the tribunal, (3) to decide on the basis of preformed opinions, (4) to disregard jurisdictional limits, (5) to do what will get by, (6) to mix up rulemaking, investigation, and prosecution, as well as the functions of advocate, judge, and enforcement authority." Robert L. Rabin, *Federal Regulation in Historical Perspective*, 38 STAN. L. REV. 1189, 1264-66 (1986) (citing *Report of the Special Committee on Administrative Law*, 63 A.B.A. REP. 331, 346-51 (1938)).

<sup>58</sup> Hunnicutt, *supra* note 2, at 153-54.

<sup>59</sup> 5 U.S.C. §§ 551-59, 701-06 (1946).

<sup>60</sup> George B. Shepherd, *Fierce Compromise: The Administrative Procedure Act Emerges from New Deal Politics*, 90 NW. U. L. REV. 1557, 1559 (1996).

<sup>61</sup> Wolf Heydebrand, *Government Litigation and National Policymaking: From Roosevelt to Reagan*, 24 LAW & SOC'Y REV. 477, 488-89 (1990).

<sup>62</sup> 1938-49, *supra* note 40, 561.

Policy or Interpretation" (hereinafter "Statements").<sup>63</sup> Statements were therefore more public and more formal than both the TCs and the FIDs that preceded them. Because greater proceduralization increases the economic cost of agency policymaking,<sup>64</sup> the enactment of the APA, "together with the passage of time since the enactment of the Federal Food, Drug, and Cosmetic Act," reduced the number of opinions and guidance documents issued during this period.<sup>65</sup> Whereas, during the heyday of the TCs, the FDA issued an average of 49 guidance documents a year, the FDA only issued about 5 Statements annually between 1947 and 1956.<sup>66</sup>

Despite this increase in procedural formality, however, Statements still fell within the category of informal guidance because the FDA did not utilize the newly-minted notice-and-comment rulemaking procedures established by the APA to promulgate them. Even though they were published in the Code of Federal Regulations, Statements only needed to comply with the "Public Information" sections of the APA.<sup>67</sup> Statements therefore did not require costly and time-consuming procedures to promulgate.

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<sup>63</sup> *Id.*

<sup>64</sup> *E.g.*, Rakoff, *supra* note 11, at 164-65.

<sup>65</sup> 1938-49, *supra* note 40, 561.

<sup>66</sup> Compare Appendix A, Figure 2, *infra*, with Appendix A, Figure 3, *infra*. I should note, however, that the average annual number of TCs is skewed heavily by the massive number of TCs issued in 1940. Furthermore, I have not performed a quantitative analysis to determine whether this divergence is statistically significant, so my conclusion is necessarily impressionistic. Finally, correlation is not causation; a more rigorous examination, controlling for more variables, would be necessary to confirm that the enactment of the APA in fact resulted in fewer guidance documents. Given the massive overhaul of administrative procedure that the APA effected, however, this inference is extremely plausible.

<sup>67</sup> See, e.g., 21 C.F.R. § 3.1 (historical version, 1947) (citing § 3, 60 Stat. 237 (1946)). Had the FDA been required to utilize notice-and-comment procedures, the regulations would also have cited the rulemaking requirements of the APA, codified in § 4 of 60 Stat. 237. See also Eve H. Bachrach, *Federal Regulation of Soap Products*, in THE COSMETIC INDUSTRY: SCIENTIFIC AND REGULATORY FOUNDATIONS, 61, 64 (Norman F. Estrin, ed. 1984); VINCENT A. KLEINFELD AND CHARLES WESLEY DUNN, FEDERAL FOOD, DRUG, AND COSMETIC ACT 1953-1957 xiii (1957) (distinguishing between Statements of General Policy or Interpretation and regulations promulgated with "the force and effect of law") [hereinafter 1953-57]; 5 U.S.C. § 553(b)(A) (2011) ("interpretative rules" and "general statements of policy" exempt from the required rulemaking procedures established by the APA); 22 Fed. Reg. 7393 (1957) (stating that FDA Statement issued in conformity with APA's public information procedures but not its rulemaking requirements).

Like the TCs, the Statements only purported to be "day-by-day informal announcements and answers by the Administration on current problems . . . the opinions expressed in them necessarily change from time to time as more experience and data are gathered and interpretations of the statutory provisions are made by the courts."<sup>68</sup> Also like their predecessors, Statements provided crucial guidance to regulated entities regarding numerous interesting issues of public concern. (*e.g.*, "The Federal Security Agency no longer regards all salt substitutes as new drugs;"<sup>69</sup> "Labeling of Antibiotic Drugs for Veterinary Use;"<sup>70</sup> "The use of antibiotic drugs as food preservatives constitutes a public health hazard . . . [and] may be deemed an adulteration."<sup>71</sup>) Issuing these policies as guidance documents afforded the FDA great flexibility; from time to time, the FDA, *via* announcements and orders in the Federal Register, revoked previous Statements as they became obsolete or were superseded by statutory developments.<sup>72</sup>

#### *D. The Continuum of Formality*

In late 1957, the FDA announced "[a] new advisory information service" for industry that "provide[d] for the publication in the Federal Register from time to time of informal statements on subjects of trade interest."<sup>73</sup> The FDA thereby divided its Statements of General Policy or Interpretation into two general categories: Subpart A, denominated "Formal Statements of Policy or Interpretation," and the new Subpart B,

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<sup>68</sup> 1938-49, *supra* note 40, xvii.

<sup>69</sup> Statement of General Policy or Interpretation 3.20 (Feb. 14, 1951), in VINCENT A. KLEINFELD AND CHARLES WESLEY DUNN, FEDERAL FOOD, DRUG, AND COSMETIC ACT 1951-1952 385 (1953) [hereinafter 1951-52].

<sup>70</sup> Statement of General Policy or Interpretation 3.25 (Aug. 15, 1951), in 1951-52, *supra* note 69, 388.

<sup>71</sup> Statement of General Policy or Interpretation 3.29 (Feb. 18, 1953), in 1953-57, *supra* note 67, 310.

<sup>72</sup> *See, e.g.*, VINCENT A. KLEINFELD AND ALAN H. KAPLAN, FEDERAL FOOD, DRUG, AND COSMETIC ACT 1958-60 223, n.\* (1961) [hereinafter 1958-60].

<sup>73</sup> 1953-57, *supra* note 67, 808.

"Informal Statements of General Policy or Interpretation," which were "excerpted from letters written by responsible officials of the Food and Drug Administration to representatives of the affected industries and other persons," in response to inquiries "on subjects of general interest," as well as from other sources.<sup>74</sup> This new informal category was intended to "serve[] somewhat the same purpose as the former [TC] information series which was discontinued in early 1946," but unlike the TCs, these Informal Statements of General Policy or Interpretation were published in the Federal Register for ease of examination, and were therefore slightly more formal despite their name.<sup>75</sup> Thus, by 1957, the FDA had utilized a wide continuum of policymaking tools, from the very informal to the very formal: informal communications between industry representatives and low-level FDA officials, press releases, TCs, Informal Statements, Formal Statements, adjudications, notice-and-comment rulemaking, and formal rulemaking.

Formal Statements addressed issues of great political salience and public interest. For instance, after a number of women were severely injured after vaginally self-administering crystals or tablets of potassium permanganate under the erroneous impression that doing so would induce abortion,<sup>76</sup> the FDA issued a Formal Statement that potassium permanganate would be regarded as misbranded unless it either (1) bore a label limiting the chemical for prescription use only or (2) was greatly diluted in an

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<sup>74</sup> *Id.*; 1958-60, *supra* note 72, 223.

<sup>75</sup> 1953-57, *supra* note 67, 808.

<sup>76</sup> "Though all cases experienced fairly immediate per vagina bleeding post self-induced treatment, none terminated her pregnancy; instead, the caustic agents burned the vaginal fornix severely; in fact, the vast majority of cases delivered liveborn, normal fetuses after attempted abortion." BB Obeng, *The Lay Use of Potassium Permanganate as an Abortifacient.*, 22 BR. J. CLIN. PRACT. 465 (1968), *abstract available at* <http://www.ncbi.nlm.nih.gov/pubmed/5696512>.

aqueous solution and labeled for external use only.<sup>77</sup> Other Formal Statements aimed to reduce misuse of amphetamine and methamphetamine,<sup>78</sup> banned investigational use of LSD and other hallucinogenic drugs,<sup>79</sup> and addressed antibiotic use in food-producing animals,<sup>80</sup> among other things. It cannot be said, however, that Informal Statements were necessarily of lesser significance than Formal Statements. Indeed, Informal Statements touched on issues of great importance to many people's lives (*e.g.*, "The term 'kosher' should be used only on food products that meet certain religious dietary requirements"),<sup>81</sup> and occasionally Informal Statements were far more complex, detailed, and lengthy than Formal Statements.<sup>82</sup>

The FDA issued several Statements yearly until 1968, at which point Statements were discontinued.<sup>83</sup> Between 1957 and 1968, the FDA issued 85 total Statements, at an average of seven per year.<sup>84</sup>

### *E. Guidance Reborn*

The late 1960s and early 1970s marked a sea change at the FDA. The enlarged scope and increased complexity of regulatory legislation passed during this period led

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<sup>77</sup> Formal Statement of General Policy or Interpretation 3.7 (Aug. 23, 1960), in *1958-60*, *supra* note 72, 225-26. This Statement was amended on February 3, 1962. VINCENT A. KLEINFELD AND ALAN H. KAPLAN, FEDERAL FOOD, DRUG, AND COSMETIC ACT 1961-64 262-63 (1965) [hereinafter *1961-64*].

<sup>78</sup> Formal Statement of General Policy or Interpretation 3.8 (Feb. 10, 1965), in VINCENT A. KLEINFELD AND ALAN H. KAPLAN, FEDERAL FOOD, DRUG, AND COSMETIC ACT 1965-68 483 (1973) [hereinafter *1965-68*].

<sup>79</sup> Formal Statement of General Policy or Interpretation 3.47 (July 14, 1966), in *1965-68*, *supra* note 78, 495-96.

<sup>80</sup> Formal Statement of General Policy or Interpretation 3.25 (Apr. 11, 1968), in *1965-68*, *supra* note 78, 486.

<sup>81</sup> Informal Statement of General Policy or Interpretation 3.202 (Nov. 30, 1957), in *1953-57*, *supra* note 67, 809.

<sup>82</sup> Compare Informal Statement of General Policy or Interpretation 3.208 (Nov. 28, 1959), in *1958-60*, *supra* note 72, 237-43 with Formal Statement of General Policy or Interpretation 3.5 (Sept. 5, 1958), in *1958-60*, *supra* note 72, 224.

<sup>83</sup> Compare *1965-68*, *supra* note 78, 483-512 with VINCENT A. KLEINFELD, ALAN H. KAPLAN, & STEPHEN A. WEITZMAN, FEDERAL FOOD, DRUG, AND COSMETIC ACT 1969-1974 (1976).

<sup>84</sup> Appendix A, Figure 4, *infra*.

both the FDA and administrative agencies generally to disfavor administrative adjudication and adopt notice-and-comment rulemaking as their primary engine of policymaking.<sup>85</sup> The reasons for this shift were manifold: developing policy on a case-by-case basis became increasingly costly; agency-made law established through adjudication "often proved to be vague or contradictory;" achieving increasingly ambitious regulatory goals required "generally applicable standards with precise contours," which are difficult to establish in case-specific adjudications; Congress mandated the use of rulemaking in certain contexts under newly enacted regulatory statutes; and the Supreme Court clarified that resource-intensive trial-type procedures were typically unnecessary for most rulemaking proceedings.<sup>86</sup>

More importantly for our discussion, informal guidance also enjoyed a resurgence at the FDA during this time. In 1968, the FDA established the Compliance Policy Guides Manual system ("CPGs") "to establish an orderly method for assembling and maintaining statements of policy."<sup>87</sup> Like the TCs and Statements, CPGs were culled from correspondence with industry and internal policy memoranda, but they also included information from precedential judicial decisions, intra-agency multicenter jurisdictional agreements, preambles to proposed/final regulations/other documents intended for publication in the Federal Register, as well as FDA adjudications.<sup>88</sup> Like their predecessors, CPGs represented only the FDA's position of the moment; they were "not intended to create or confer any rights, privileges, or benefits on or for any private

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<sup>85</sup> Carey, *supra* note 18, at 2-4.

<sup>86</sup> Rakoff, *supra* note 11, at 163.

<sup>87</sup> Compliance Policy Guides > Introduction, <http://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm116791.htm> (last visited Jul. 7, 2011) [hereinafter *CPG Introduction*].

<sup>88</sup> *Id.*

person, but [were] intended for internal guidance."<sup>89</sup> Also like their predecessors, CPGs issued during this period covered a wide variety of interesting topics (*e.g.*, labeling requirements for allergenic extracts containing glycerin;<sup>90</sup> policies concerning "the interstate shipment of biological products for use in medical emergencies;"<sup>91</sup> "Filth from Insects, Rodents, and Other Pests in Foods"<sup>92</sup>). CPGs were made available to interested parties from the Public Records and Documents Center.<sup>93</sup> The FDA still utilizes CPGs today, and now makes them available on the FDA website.<sup>94</sup>

The FDA also issued guidance "in other documents designated as 'advisory opinions,' and in preambles to Federal Register documents."<sup>95</sup> Advisory opinions represented the FDA's official but informally issued opinion on more specific factual matters than those generally addressed by other guidance documents.<sup>96</sup> However, advisory opinions, broadly defined, are difficult to differentiate from other guidance documents at the margins; as will be explained in the following sections, this difficulty has since caused great ambiguities that plague the agency to this day.<sup>97</sup>

#### *F. 1977: Guidance Becomes Binding*

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<sup>89</sup> *Id.*

<sup>90</sup> CPG § 270.100 Final Container Labels - Allergenic Extracts Containing Glycerin; Reporting Changes (originally issued Jul. 1976), *available as revised at*

<http://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm122803.htm>.

<sup>91</sup> CPG § 220.100 - IS Shipment Biologicals for Medical Emergency (originally issued Dec. 1977), *available as revised at*

<http://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm073860.htm>.

<sup>92</sup> CPG § 555.600 Filth from Insects, Rodents, and Other Pests in Foods (originally issued Jan. 1973), *available as revised at*

<http://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm074559.htm>.

<sup>93</sup> 40 Fed. Reg. 40682, 40694 (1975).

<sup>94</sup> Manual of Compliance Policy Guides,

<http://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/default.htm>.

[hereinafter *Manual of CPGs*]

<sup>95</sup> 40 Fed. Reg. 40682, 40694 (1975).

<sup>96</sup> O'REILLY, *supra* note 11, § 4:25 4-93.

<sup>97</sup> *See infra* Section I.H.3.

By 1975, the FDA perceived a need to conduct its operations more systematically, publicly, and cohesively.<sup>98</sup> As the FDA became increasingly reliant on guidance documents to fulfill its regulatory mandate, it became acutely aware of the increased importance of "their [that is, guidance documents'] methods of development, their availability, notice of any changes, and an opportunity to participate in their development and modification."<sup>99</sup> On September 3rd of that year, the FDA published the following statement in a Notice of Proposed Rulemaking in the Federal Register:

The present administrative practices and procedures of the Food and Drug Administration are largely uncodified and, to the extent that they are included in existing regulations, are spread throughout numerous sections in the Code of Federal Regulations and in agency manuals. Many of these practices and procedures have been developed over the years on an ad hoc basis, to meet immediate needs, without systematically integrating them into the agency's overall practices and procedures. Many of the agency's practices and procedures have not been written down in any manual or regulation. Accordingly, the Commissioner of Food and Drugs has concluded that a thorough review of agency practices and procedures should be undertaken, and that comprehensive regulations should be adopted to codify existing requirements, establish new requirements where none currently exist, and conform present regulations so that practices and procedures will be applied consistently throughout the agency.<sup>100</sup>

As part of its sweeping reform project, "the FDA promulgated a regulation providing that any officially issued advisory opinion or guideline would be binding on the agency."<sup>101</sup> In other words, the FDA obligated itself to follow the opinions expressed

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<sup>98</sup> See generally Peter Barton Hutt, *FDA Court Actions & Recent Legal Developments*, 39 ASS'N OF FOOD & DRUG OFFICIALS Q. BULL. 11 (1975); Peter Barton Hutt, *Public Information and Public Participation in the Food and Drug Administration*, 36 ASS'N OF FOOD & DRUG OFFICIALS Q. BULL. 212 (1972) [hereinafter Hutt, *Public Info*].

<sup>99</sup> 40 Fed. Reg. 40682, 40695 (1975).

<sup>100</sup> 40 Fed. Reg. 40682, 40682-83 (1975).

<sup>101</sup> Noah, *supra* note 11, at 114 (citing 42 Fed. Reg. 4680, 4708-10 (1977) (codified as amended at 21 C.F.R. §§ 10.85, 10.90 (1997)). The FDA originally tried to finalize these and other procedural reforms without public comment, but were rebuffed by the District Court of the District of Columbia, which concluded that even though the proposed regulations "were completely procedural in nature, they were so comprehensive" that they required notice-and-comment rulemaking to promulgate. Letter from Peter Barton Hutt, Senior Counsel, Covington & Burling LLP and Lecturer on Law, Harvard Law School, to author (July 27, 2011) (on file with author) [hereinafter *Letter*]; 40 Fed. Reg. 22950, 22950-51 (1975);

in its own guidance until amended or revoked, unless those opinions arose from informal communications with lower-level employees, or if emergency situations required deviation from established guidelines.<sup>102</sup> However, official guidance only bound the FDA, not regulated entities or courts. In other words, guidance documents established safe harbors within which regulated actors could conduct their operations with reasonable certainty that they would be adjudged compliant with applicable rules and regulations (subject, of course, to the possibility that the FDA could later modify its policy), but did not create substantive rules that entities were required to follow.<sup>103</sup> Binding effect was not restricted to guidance documents subsequent to its new regulation; the FDA explicitly noted that the opinions it previously published in Statements of Policy or Interpretation in the Federal Register or issued in TCS, CPGs, and other comparable documents would also bind the FDA "unless subsequently repudiated by the agency or overruled by a court."<sup>104</sup> The FDA offered the following rationale for this sweeping reform:

Prior Food and Drug Administration policy has not distinguished between formal advisory opinions and informal oral advice and correspondence; as a result, confusion and uncertainty has been engendered both within the agency and outside as to whether opinions expressed in correspondence or orally carry the weight of the agency or only of the individual agency employee involved. Absent specific regulations to the contrary, the

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Gregory M. Fischer, *Third Class of Drugs - A Current View*, 46 FOOD DRUG COSM. L.J. 583, 614 (1991); *Am. Coll. of Neuropsychopharmacology v. Weinberger*, Civ. No. 75-1187 (D.D.C. 1975).

<sup>102</sup> 42 Fed. Reg. 4680, 4708-10 (1977) (codified as amended at 21 C.F.R. §§ 10.85, 10.90 (2011)).

<sup>103</sup> 42 Fed. Reg. 4680, 4709 (1977) (codified as amended at 21 C.F.R. §§ 10.85, 10.90 (2011)) ("An advisory opinion may be used in administrative or court proceedings to illustrate acceptable and unacceptable procedures or standards, but not as a legal requirement . . . A person may rely upon a guideline with assurance that it is acceptable to the Food and Drug Administration, or may follow different procedures or standards. Where a person chooses to use different procedures or standards, he may, but is in no instance required to, discuss the matter in advance with the Food and Drug Administration to prevent the expenditure of money and effort on activity that may later be determined to be unacceptable."). *See also* Noah, *supra* note 11, at 116-18 ("The regulation does nothing more than bind the FDA in the sense that it agrees to issue reliable advice about how it interprets the requirements imposed by the statute and regulations. Formal advisory opinions and guidelines would not, for instance, give third parties the right to object to Agency decisions accepting submissions by a regulated firm that are allegedly inconsistent with those opinions or guidelines.").

<sup>104</sup> 42 Fed. Reg. 4680, 4709 (1977) (codified as amended at 21 C.F.R. §§ 10.85, 10.90 (2011)).

statements of a government employee do not bind the government . . . Accordingly, because of the lack of any agency regulations on this matter, none of the correspondence or oral advice previously issued by the agency has had any binding legal effect. In many instances, important agency correspondence relating to the legal status of ingredients and products has not been compiled or reviewed in any comprehensive or systematic way, with the result that few in the agency have known about the existence of such correspondence[;] nor has [the public understood] that such correspondence has no legal status . . . For this reason, on recent occasions the agency has been forced to issue regulations formally withdrawing prior opinion letters relating to the food additive and new drug status of Products . . . The Commissioner would resolve the present uncertainty by the proposal of regulations that would clearly and explicitly recognize the difference between the informal opinion of an individual in the agency, which represents his best information and advice, and the formal opinion of the agency, which represents a position of the Food and Drug Administration that is binding and commits the agency to the views expressed until they are formally modified or revoked.<sup>105</sup>

The new regulations attempted to precisely define a category of guidance documents called "guidelines," as differentiated from advisory opinions, that "establish[ed] principles or practices of general applicability [that] d[id] not include decisions or advice limited to particular situations," and established procedures for their amendment, revocation, and issuance.<sup>106</sup> The FDA also established a formal mechanism by which "[a]ny person could request an advisory opinion from the Commissioner with respect to any matter of general applicability,"<sup>107</sup> required guidance documents to be

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<sup>105</sup> 40 Fed. Reg. 40682, 40694 (1975).

<sup>106</sup> 21 C.F.R. § 10.90(b) (historical version, 1978).

<sup>107</sup> 42 Fed. Reg. 4680, 4708 (1977) (codified as amended at 21 C.F.R. §§ 10.85, 10.90 (2011)).

"included in the public file of guidelines established by the Hearing Clerk,"<sup>108</sup> and allowed interested parties to submit comments on advisory opinions.<sup>109</sup>

These changes was revolutionary. Previously, guidance represented no more than the FDA's current thinking at the moment, subject to change with little to no warning.<sup>110</sup> Henceforth, regulated entities could reasonably place unprecedented reliance on the FDA's informal advice, as long as it came in the form of a written document that originated with high-level FDA officials.<sup>111</sup> The new system also afforded greater opportunities for public participation in the policymaking process. Although the FDA refused requests to subject all of its guidance documents to the costly and labor-intensive notice-and-comment rulemaking procedures,<sup>112</sup> it gave regulated entities both an unprecedented opportunity to submit their views regarding advisory opinions and a designated process for requesting guidance on any topic of general interest to industry.<sup>113</sup> Importantly, proclaiming informal guidance binding did not unduly hinder the FDA's flexibility. The process for revoking or amending prior guidance documents and notifying

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<sup>108</sup> 42 Fed. Reg. 4680, 4709 (1977) (codified as amended at 21 C.F.R. §§ 10.85, 10.90 (2011)). However, due to resource constraints, the FDA rejected requests to require the publication of all advisory opinions in the Federal Register. 42 Fed. Reg. 4680, 4693-94 (1977); 40 Fed. Reg. 40682, 40695 (1975). The FDA concluded that its guidance would nevertheless be sufficiently public: "Such advisory opinions may be compiled as part of the agency's Compliance Policy Guides manual, or in a separate compilation of advisory opinions. The substance of these advisory opinions would undoubtedly be disseminated widely by the agency trade associations, and the trade press." 40 Fed. Reg. 40682, 40695 (1975).

<sup>109</sup> 42 Fed. Reg. 4680, 4709 (1977) (codified as amended at 21 C.F.R. §§ 10.85, 10.90 (2011)).

<sup>110</sup> See *supra* Sections I.B-C; I.E.

<sup>111</sup> See Noah, *supra* note 11, at 114, 116-18.

<sup>112</sup> 42 Fed. Reg. 4680, 4694 (1977).

<sup>113</sup> 42 Fed. Reg. 4680, 4708-09 (1977) (codified as amended at 21 C.F.R. §§ 10.85, 10.90 (2011)). It should be noted, however, that not all commentators view the guidance request process as particularly beneficial for industry. "It is axiomatic that the person requesting the agency's advice must be prepared to live with any answer received, even an unfavorable one, and that some particularly uncertain areas are best left unexplored." O'REILLY, *supra* note 11, § 4:25 4-95 (citing Kleinfeld, *Approach to FDA: Tactics and Strategy*, in FEDERAL REGULATION OF THE DRUG INDUSTRY (V. Kleinfeld ed. 1972)). Some attorneys' views on the process are therefore well summed up by the following pithy quote: "*When to write the Agency*: Practically never." *Id.*

interested parties of modifications of agency policy was not particularly onerous.<sup>114</sup>

These changes therefore not only benefited industry to a large extent, they also "exemplified the sort of agency self-discipline that courts and commentators" had long endorsed for the ever-growing administrative state, and did so without unduly constraining the FDA's authority.<sup>115</sup>

### G. Chevron

1984 marked a massive victory for administrative agencies in the United States: *Chevron, U.S.A., Inc. v. National Resources Defense Council, Inc.*<sup>116</sup> *Chevron* established a two-step test for determining whether an agency's interpretation of an ambiguous provision in its organic statute could withstand judicial challenge:

When a court reviews an agency's construction of the statute which it administers, it is confronted with two questions. First, always, is the question whether Congress has directly spoken to the precise question at issue. If the intent of Congress is clear, that is the end of the matter; for the court, as well as the agency, must give effect to the unambiguously expressed intent of Congress.<sup>117</sup> If, however, the court determines Congress has not directly addressed the precise question at issue, the court does not simply impose its own construction on the statute, as would be necessary in the absence of an administrative interpretation. Rather, if the statute is silent or ambiguous with respect to the specific issue, the question for the court is whether the agency's answer is based on a permissible construction of the statute.<sup>118</sup>

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<sup>114</sup> 42 Fed. Reg. 4680, 4709-10 (1977) (codified as amended at 21 C.F.R. §§ 10.85, 10.90 (2011)) ("A guideline may be amended or revoked upon approval of the amended guideline or revocation of the guideline by the relevant bureau director and publication by the Commissioner in the Federal Register of a notice of such amendment or revocation. The notice shall state (i) the title of the guideline, (ii) the subject matter it covers, and (iii) the office or individual responsible for maintaining the guideline."). *See also* Noah, *supra* note 11, at 114.

<sup>115</sup> Noah, *supra* note 11, at 114.

<sup>116</sup> 467 U.S. 837 (1984).

<sup>117</sup> To determine whether the statutory text unambiguously addresses the question at issue, courts utilize the "traditional tools of statutory construction." *Id.* at 843 n.9.

<sup>118</sup> *Id.* at 842-43.

*Chevron* was revolutionary: "the decision has become . . . the undisputed starting point for any assessment of the allocation of authority between federal courts and administrative agencies,"<sup>119</sup> because *Chevron* arguably greatly increased the amount of deference courts give to agencies' interpretations of their organic statutes.<sup>120</sup> Judicial deference is a crucial factor in any agency's ability to fulfill its regulatory objectives, and the FDA is no exception:

One can loosely define deference as the willingness of a court to accept an agency's interpretations of a statute or policy over competing interpretations offered by regulated persons or public interest groups. Once the agency decides the issue, a rigorous "hard look" by a federal court might overrule the agency's interpretation of the statute, but a deferential review will likely accept the agency's interpretation--and with it, the agency's decision regarding issuing the license or rule. Thus, the key to any agency's successful defense of its decisions is the willingness of federal judges to give deference to its expertise. Indeed, agencies fervently seek deference to ensure the enforceability of their policy decisions. If an agency does not receive consistent deference from the courts, regulated entities will likely deem the agency less potent; in turn, those entities will be less likely to respect agency decisions. As with any administrative agency, deference is a cornerstone of the FDA's effectiveness. If it were not accorded deference, the many hours spent formulating and promulgating rules [and policies] would amount to a waste.<sup>121</sup>

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<sup>119</sup> Sunstein, *supra* note 2, at 188. *But see Christensen v. Harris County*, 529 U.S. 576, 596 (2000) (Breyer, J., dissenting) (arguing that *Chevron* was an outgrowth of prior caselaw, rather than a massive change to it).

<sup>120</sup> Jeffrey A. Pojanowski, *Reason and Reasonableness in Review of Agency Decisions*, 104 NW. U. L. REV. 799, 804 (2010) (citing Peter H. Schuck & E. Donald Elliott, *To the Chevron Station: An Empirical Study of Administrative Law*, 1990 DUKE L.J. 984, 1029-43); Elizabeth Garrett, *Legislating Chevron*, 101 MICH. L. REV. 2637, 2645 n.35 (2003). *But see* Connor N. Raso & William N. Eskridge, Jr., *Chevron as a Canon, Not a Precedent: An Empirical Study of What Motivates Justices in Agency Deference Cases*, 110 COLUM. L. REV. 1727, 1739-40 (2010) (summarizing empirical studies suggesting ambiguity regarding whether *Chevron* actually increased judicial deference to agency interpretations). Interestingly, there is reason to believe this marked change in administrative law doctrine was unintentional. "One surprise is the absence of any evidence in the written record indicating that the Justices realized the full implications of their landmark administrative law decision in . . . *Chevron*. There is no comment in the written exchanges among the Justices that reflects any appreciation of the major change in administrative law the decision effected." Robert Percival, *Environmental Law in the Supreme Court: Highlights from the Marshall Papers*, 23 ENVTL. L. REP. 10606, 10613 (1993).

<sup>121</sup> James T. O'Reilly, *Losing Deference in the FDA's Second Century: Judicial Review, Politics, and a Diminished Legacy of Expertise*, 93 CORNELL L. REV. 939, 941-42 (2008) (internal citations omitted).

Because rulemaking, adjudication, and guidance regularly require interpretation of ambiguous statutory provisions,<sup>122</sup> agency policies survived judicial review at greater rates after *Chevron*.<sup>123</sup> *Chevron* deference therefore became a sought-after commodity for administrative agencies seeking to ensure that their policies would be upheld in court.<sup>124</sup>

After 1984, the FDA successfully defended several policies issued in informal guidance documents from judicial challenge by invoking *Chevron* deference. For instance, in *Young v. Community Nutrition Institute*,<sup>125</sup> the Supreme Court afforded *Chevron* deference to a policy expressed in an "action level," which the FDA initially published as a guidance document in the Federal Register without formal procedures.<sup>126</sup> In other words, even though the policy was established in a document that neither bound regulated entities nor was promulgated with the "force of law," the Supreme Court still deferred to the FDA's judgment and gave the agency's policy the Court's imprimatur.<sup>127</sup> *Chevron* therefore made informal guidance a powerful weapon for the FDA.

*Chevron* led to victories for the FDA in the lower courts as well. For example, the United States District Court of the District of Columbia afforded *Chevron* deference to an FDA policy statement relating to rDNA-engineered foods that interpreted the Generally Recognized As Safe ("GRAS") provision of the FD&C Act.<sup>128</sup> Again, this policy statement was given deference even though it was not the product of notice-and-comment

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<sup>122</sup> Jonathan R. Siegel, *Guardians of the Background Principles*, 2009 MICH. ST. L. REV. 123, 130.

<sup>123</sup> Pojanowski, *supra* note 120, at 804 (citing Schuck & Elliott, *supra* note 120, at 1029-43). *But see* Raso & Eskridge, *supra* note 120, at 1739-40.

<sup>124</sup> O'Reilly, *supra* note 121, at 941-42.

<sup>125</sup> 476 U.S. 974 (1986).

<sup>126</sup> *Id.* at 976-78 (quoting 46 Fed. Reg. 7448 (1981)) ("On some occasions, the FDA has instead set 'action levels' through a less formal process. In setting an action level, the FDA essentially assures food producers that it ordinarily will not enforce the general adulteration provisions of the Act against them if the quantity of the harmful added substance in their food is less than the quantity specified by the action level.").

<sup>127</sup> *See* Sunstein, *supra* note 2, at 208-10.

<sup>128</sup> *Alliance for Bio-Integrity v. Shalala*, 116 F.Supp.2d 166, 176-179 (D.D.C. 2000).

rulemaking.<sup>129</sup> While there was some disagreement among courts and commentators during this time regarding whether informal documents warranted *Chevron* deference as a general matter,<sup>130</sup> a number of other cases also afforded *Chevron* deference to FDA guidance documents.<sup>131</sup>

Cases like *Chevron* and *Young* at first seemed to suggest that courts would defer to almost any reasonable and authoritative interpretation of an ambiguous provision of a statute the FDA administers, regardless of the procedures used to formulate the policy expressed in that interpretation.<sup>132</sup> Indeed, *Chevron* "ma[de] no mention of and d[id] not appear to have been concerned with whether an interpretation of an administrative agency was adopted as part of a formal rulemaking process or not."<sup>133</sup> Such an approach would have rendered guidance a tremendously powerful weapon in the FDA's arsenal; the FDA could flexibly and inexpensively set new policies in response to changing circumstances

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<sup>129</sup> *Id.* at 172-73.

<sup>130</sup> Kevin J. Miller, *Welfare and the Minimum Wage: Are Workfare Participants "Employees" Under the Fair Labor Standards Act?*, 66 U. CHI. L. REV. 183, 191 n.44 (1999).

<sup>131</sup> See *National Pharmaceutical Alliance v. Henney*, 47 F.Supp.2d 37 (D.D.C. 1999); *Berlex Laboratories, Inc. v. FDA*, 942 F.Supp. 19 (D.D.C. 1996). See generally Patricia G. Chapman, *Has the Chevron Doctrine Ran Out of Gas? Senza Ripieni Use of Chevron Deference or the Rule of Lenity*, 19 MISS. C. L. REV. 115, 137 (1998).

<sup>132</sup> Sunstein, *supra* note 2, at 208-10. "Without pausing to explore the [question of whether *Chevron* deference is warranted for interpretations formulated without formal procedures,] the Court [in *Young*] deferred to the agency and upheld its interpretation." *Id.* at 208. *Young* therefore seemed to suggest that the *Chevron* doctrine operates as follows: "Whenever an agency makes an authoritative interpretation of a statute that it administers, that interpretation falls under the *Chevron* framework, unless the agency's self-interest is so conspicuously at stake that it is implausible to infer a congressional delegation of law-interpreting power. On this approach, it is necessary only to know whether purported interpreters authoritatively speak for the agency itself. If they do, the *Chevron* framework applies." *Id.* at 210. As explained in greater detail *infra* Section I.I., however, this interpretation of *Chevron* was not borne out in subsequent cases. See also *United States v. Mead Corp.*, 533 U.S. 218, 239-261 (2001) (Scalia, J., dissenting) ("Whereas previously a reasonable agency application of an ambiguous statutory provision had to be sustained so long as it represented the agency's authoritative interpretation, henceforth such an application can be set aside unless 'it appears that Congress delegated authority to the agency generally to make rules carrying the force of law,' as by giving an agency 'power to engage in adjudication or notice-and-comment rulemaking, or ... some other [procedure] indicati[ng] comparable congressional intent,' and 'the agency interpretation claiming deference was promulgated in the exercise of that authority.'" (citations omitted)).

<sup>133</sup> John P.C. Duncan, *The Course of Federal Preemption of State Banking Law*, 18 ANN. REV. BANKING L. 221, 266 (1999).

that would regularly receive deference in judicial proceedings, even though those policies did not technically bind regulated entities.

That, however, was not to be. As will be described in Section I.I. *infra*, subsequent caselaw greatly reduced the scope of agency interpretations entitled to *Chevron* deference. While this development may have partially assuaged concerns that the FDA and other agencies were inappropriately treating non-binding guidance documents as if they had binding effect,<sup>134</sup> this relief has come at a high price; it is now extremely uncertain which statutory interpretations by administrative agencies receive judicial deference and, if so, how much. Before diving into that murky quagmire, however, I first turn to a chronologically antecedent but equally confusing set of developments.

#### *H. Muddying the Waters*

In the 1990s, the FDA made a number of decisions that once again radically changed its informal guidance regime. As the procedural requirements associated with notice-and-comment rulemaking became increasingly stringent over the years,<sup>135</sup> the FDA simultaneously radically decreased the number of regulations it adopted annually while greatly increasing "the number of FDA-issued documents intended to give guidance to the regulated industry but not adopted through public procedures."<sup>136</sup> For the first time, informal guidance became the FDA's primary method of policymaking.<sup>137</sup>

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<sup>134</sup> See *supra* note 11.

<sup>135</sup> See generally Carey, *supra* note 18, For an excellent yet succinct historical summary of the ossification of notice-and-comment rulemaking, see Rakoff, *supra* note 11, at 164-65. But see O'Connell, *supra* note 5, at 932-36 (arguing "that the procedural costs to rulemaking (from the agency's perspective) are not so high as to prohibit considerable rulemaking activity by agencies").

<sup>136</sup> Rakoff, *supra* note 11, at 168.

<sup>137</sup> *Id.* See generally Seiguer and Smith, *supra* note 12.

Around the same time, the FDA rescinded its prior decision to make guidance documents binding upon the agency, and promulgated a regulation establishing Good Guidance Practices the agency was required to follow when formulating and issuing informal guidance. However, in doing so, the FDA created vexing ambiguities that persist to this day.

### *I. Guidance Becomes Non-Binding... Again*

By 1992, the FDA became increasingly trepidatious about its 1977 decision to render its official guidance documents binding on the agency. Citing a perceived need "to ensure that its advisory opinion and guideline regulations are consistent with principles of estoppel and with sound public policy," the FDA proposed a rule in the Federal Register that, when finalized, would render both its past and future guidance documents non-binding.<sup>138</sup> The FDA insisted, however, "that advisory opinions, while not legally binding FDA to a particular course of action, would still represent the agency's best advice on the matter at issue at the time they are rendered," and that "guidelines would continue to provide to persons dealing with the agency useful information about procedures or practices that the agency believes are generally desirable."<sup>139</sup> Previously issued guidance documents would remain in effect, but would not bind the agency.<sup>140</sup>

The FDA stated that one of the reasons for its decision to reverse course on this issue was the D.C. Circuit's then-recent decision in *Community Nutrition Institute v. Young*,<sup>141</sup> which "held that the FDA could not cabin its prosecutorial discretion by

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<sup>138</sup> 57 Fed. Reg. 47314, 47314 (1992).

<sup>139</sup> *Id.*

<sup>140</sup> *Id.* at 47315.

<sup>141</sup> 818 F.2d 943 (D.C. Cir. 1987); 57 Fed. Reg. 47314, 47315 (1992).

promising not to enforce [certain provisions] of the FD&C Act in certain circumstances, unless it had issued an appropriate regulation after notice-and-comment rulemaking."<sup>142</sup> The FDA concluded from this that it was unlawful for the agency to tie its hands by issuing binding guidance documents that could preclude it from fully enforcing the Act.<sup>143</sup> The FDA likewise feared that its regulations to that effect were "inconsistent with the intent of the notice and comment provisions of the APA."<sup>144</sup> After the FDA released its proposed rule, some scholars questioned whether these conclusions were doctrinally correct, and accused the FDA of "undermin[ing] a sensible a legally permissible system" "for no good reason."<sup>145</sup> A number of people also submitted comments on the FDA's proposed change during the notice-and-comment process, requesting that the FDA keep guidance binding.<sup>146</sup> The FDA nevertheless maintained that precedent and good policy mandated that guidance once again be rendered non-binding, and stated that most participants who submitted comments during the rulemaking process "agreed that guidance documents should not be binding."<sup>147</sup> As a result, the change went into effect.<sup>148</sup> The FDA accordingly deleted the entire regulatory provision relating to guidelines, a type of informal guidance that purportedly "establish[es] principles or practices of general applicability and do[es] not include decisions or advice on particular situations," to make room for the developments described below.<sup>149</sup>

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<sup>142</sup> Noah, *supra* note 11, at 137 (citing *CNI*, 818 F.2d at 948-49).

<sup>143</sup> 57 Fed. Reg. 47314, 47315 (1992).

<sup>144</sup> *Id.*

<sup>145</sup> *See generally* Noah, *supra* note 11.

<sup>146</sup> 62 Fed. Reg. 8961, 8962-63 (1997).

<sup>147</sup> *Id.*

<sup>148</sup> *Id.* (codified as amended at 21 C.F.R. § 10.115 (2011)).

<sup>149</sup> *Compare* 21 C.F.R. § 10.90(b) (Historical Version, 2000) *with* 21 C.F.R. § 10.90(b) (Historical Version, 2001).

## 2. Good Guidance Practices

Around the same time, the FDA further increased the formality of guidance in other respects by promulgating regulations codifying its "policies and procedures for developing, issuing, and using guidance documents" in a document entitled Good Guidance Practices ("GGPs").<sup>150</sup> This development was spurred by a petition issued by the Indiana Medical Devices Manufacturers Council, who "requested that FDA control the initiation, development, and issuance of guidance documents by written procedures that assure the appropriate level of meaningful public participation,"<sup>151</sup> as well as by concerns from courts and other industry players that the guidance process was being "subverted."<sup>152</sup> Agreeing "that public participation generally benefits the guidance document development process," and emphasizing "the importance of communicating more clearly to its employees and to the public the [newly] nonbinding nature of guidance documents," the FDA initiated a notice-and-comment rulemaking proceeding and solicited recommendations for improving its guidance procedures.<sup>153</sup> In doing so, the FDA hoped to

(1) Provide assistance to the regulated industry by clarifying requirements that have been imposed by Congress or issued in regulations by FDA and by explaining how industry may comply with those statutory and regulatory requirements and (2) provide specific review and enforcement approaches to help ensure that FDA's employees implement the agency's mandate in an effective, fair, and consistent manner.<sup>154</sup>

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<sup>150</sup> 21 C.F.R. § 10.115 (2011).

<sup>151</sup> 62 Fed. Reg. 8961, 8961 (1997).

<sup>152</sup> Rakoff, *supra* note 11, at 168.

<sup>153</sup> 61 Fed. Reg. 9181, 9181 (1996).

<sup>154</sup> 62 Fed. Reg. 8961, 8967 (1997).

The FDA's proposal received the imprimatur of Congress, and was codified in the Food and Drug Administration Modernization Act of 1997 ("FDAMA").<sup>155</sup> The GGP's officially went into effect shortly after the turn of the millennium, and created mandatory guidance procedures that remain in place today.<sup>156</sup>

As codified in 21 C.F.R. § 10.115, the GGPs establish two tiers of guidance. The first category, dubbed "Level 1 guidance documents," "include guidance documents 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>157</sup> Any guidance documents that do not fall within this category, including "guidance documents that set forth existing practices or minor changes in interpretation or policy," are designated as "Level 2 guidance documents."<sup>158</sup> The procedures for issuing a Level 1 guidance document are similar to, but less rigorous than, the requirements for informal rulemaking established in the Administrative Procedure Act:<sup>159</sup> the FDA must publish a notice in the Federal Register after a draft guidance is available, make its draft guidance available on the Internet and in hard copy, and invite and review comments on the proposed

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<sup>155</sup> Pub. L. No. 105-115, §405, 111 Stat. 2296, 2368-69 (codified at 21 U.S.C. § 371(h) (1997)). "Following the FDA's publication of its original GGP, Congress then mandated by law certain aspects of the 1997 GGP document in the Food and Drug Administration Modernization Act of 1997 (FDAMA). In FDAMA, Congress detailed basic elements of good guidance practices and required the FDA to issue new GGP as regulations. In the legislative history of FDAMA, Congress expressed particular concern about public knowledge of, and access to, FDA guidance documents; the lack of a systematic process for adopting guidance documents and for allowing public input; and inconsistency in the use of guidance documents." Paul R. Noe & John D. Graham, *Due Process and Management for Guidance Documents: Good Governance Long Overdue*, 25 YALE J. ON REG. 103, 107 (2008) (citations omitted).

<sup>156</sup> 21 C.F.R. § 10.115 (historical version, 2001); 21 C.F.R. § 10.115 (2011).

<sup>157</sup> 21 C.F.R. § 10.115(c)(1) (2011).

<sup>158</sup> *Id.* § 10.115(c)(2).

<sup>159</sup> See 5 U.S.C. § 553 (2011); Hunnicutt, *supra* note 2, at 180; Michael Jon Andersen, *Bound Guidance: FDA Rulemaking for Off-Label Pharmaceutical Drug Marketing*, 60 CASE W. RES. L. REV. 531, 536-37 (2010). See also 65 Fed. Reg. 56468, 56473 (2000) (differentiating informal guidance from notice-and-comment rulemaking).

guidance.<sup>160</sup> Unlike rules promulgated through notice-and-comment, however, Level 1 guidance does not require the agency to respond to significant comments it receives,<sup>161</sup> the FDA need only "review" submitted comments.<sup>162</sup> This frees the FDA from one of the major procedural burdens associated with notice-and-comment rulemaking.<sup>163</sup>

Level 2 guidance documents also require procedures that resemble notice-and-comment,<sup>164</sup> but in turn are less rigorous than the procedures for Level 1 documents. Unlike Level 1 documents, the FDA need not publish notice in the Federal Register for Level 2 documents; it only need make the document available on the internet and in hard copy.<sup>165</sup> More importantly, whereas the FDA may not begin implementation of a Level 1 document until interested parties have had an opportunity for comment, the FDA may implement Level 2 documents the instant they are issued, as long as the agency is receptive to any comments it may subsequently receive.<sup>166</sup>

Interested parties may, at any time, submit comments requesting that specific guidances be revised or withdrawn.<sup>167</sup> Interested parties may likewise suggest topics for new guidance documents<sup>168</sup> and "submit drafts of proposed guidance documents for FDA

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<sup>160</sup> 21 C.F.R. § 10.115(g)(1)-(3) (2011).

<sup>161</sup> Mendelson, *supra* note 10, at 425-26. *See also* United States v. Nova Scotia Food Prods. Corp., 568 F.2d 240, 252-253 (1977). Some have viewed this aspect of the GGPs quite negatively. Seiguer and Smith, *supra* note 12, at 30 (noting that some industry representatives believe that "even though FDA accepts comments from the public, . . . it is very unusual for FDA to actually change its position or incorporate any of the feedback into the guidance").

<sup>162</sup> 21 C.F.R. § 10.115(g)(1)(iv)(A) (2011).

<sup>163</sup> *See Nova Scotia*, 568 F.2d at 252-253 (holding a regulation invalid for failing to respond to significant comments, *inter alia*).

<sup>164</sup> 21 C.F.R. § 10.115(g)(4) (2011).

<sup>165</sup> *Compare id.* § 10.115(g)(4)(i) *with id.* § 10.115(g)(1).

<sup>166</sup> *Compare id.* § 10.115(g)(4)(i) *with id.* § 10.115(g)(1). *See also* Andersen, *supra* note 159, at 537.

<sup>167</sup> 21 C.F.R. §§ 10.115(g)(5), (f)(4) (2011).

<sup>168</sup> *Id.* § 10.115(f)(2).

to consider."<sup>169</sup> Finally, guidance documents must be "approved by appropriate senior FDA officials" to be validly issued.<sup>170</sup>

The GGPs explicitly state that guidance documents "do not legally bind the public or FDA."<sup>171</sup> To that end, guidance documents must not include mandatory language, including words like "shall," "must," "required," or "requirement," unless those words are used "to describe a statutory or regulatory requirement."<sup>172</sup> Even though guidance documents technically no longer "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."<sup>173</sup> Failure to obtain such approval amounts to a regulatory violation. Moreover, even though the FDA is not rigidly bound by the substance of its guidance documents, it is bound by the procedural requirements of the GGPs because they are enshrined in duly-promulgated regulations and statutory law.<sup>174</sup> Thus, "[t]he 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."<sup>175</sup> To that end, 21 C.F.R. § 10.115 also establishes procedures to ensure that FDA employees and officials are complying with GGP requirements.<sup>176</sup>

The GGPs also aimed to increase regulatory clarity by mandating that all guidance documents "[i]dentify the activity to which and the people to whom the

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<sup>169</sup> *Id.* § 10.115(f)(3).

<sup>170</sup> *Id.* § 10.115(j).

<sup>171</sup> *Id.* § 10.115(d)(1).

<sup>172</sup> *Id.* § 10.115(i)(2).

<sup>173</sup> *Id.* § 10.115(d)(3). *But see* Hunnicutt, *supra* note 2, at 182-83 (criticizing this provision's lack of clarity).

<sup>174</sup> *Supra* notes 155-156.

<sup>175</sup> 21 C.F.R. § 10.115(e) (2011).

<sup>176</sup> *Id.* §§ 10.115(l), (o).

document applies,"<sup>177</sup> and also identify on the face of the document that the policy constitutes non-binding guidance.<sup>178</sup>

Thus, the FDA's activity leading up to the turn of the millennium may best be described as taking two steps forward and one step back in terms of proceduralization: guidance was no longer binding on the agency, but the agency exhibited much greater self-discipline in the guidance issuance process. The GGPs provided for unprecedented public participation in the process of making, revising, and withdrawing informal guidance documents, to the benefit of industry.

### *3. Confusion Confounded*

The FDA's aim in these reforms appears to have been to render all forms of informal guidance, including "formal advisory opinions and guidelines," non-binding upon the agency, while allowing for greater public participation and clarity in the policymaking process.<sup>179</sup> However, it is not altogether clear that the FDA fully achieved all of these goals. At the close of rulemaking, two separate and arguably conflicting provisions regarding guidance existed in the Code of Federal Regulations. The new GGPs explicitly provided that a large subset of informal guidance would no longer be considered binding,<sup>180</sup> and the FDA removed its former provision on "guidelines" to the contrary from the Code of Federal Regulations.<sup>181</sup> However, the FDA left a different regulation that dealt with a subset of guidance documents labeled "advisory opinions" largely unmodified from the 1977 regulations that rendered those documents binding in

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<sup>177</sup> *Id.* § 10.115(i)(iii).

<sup>178</sup> *Id.* §§ 10.115(i)(i), (i)(iv).

<sup>179</sup> Noah, *supra* note 11, at 114; 57 Fed. Reg. 47314, 47314 (1992); 61 Fed. Reg. 9181, 9181 (1996).

<sup>180</sup> 21 C.F.R. § 10.115 (historical version, 2001).

<sup>181</sup> *Compare* 21 C.F.R. § 10.90(b) (historical version, 1978) *with* 21 C.F.R. § 10.90(b) (2011).

the first place.<sup>182</sup> Under these regulations, "advisory opinions" are defined as a broad category including not only "documents specifically identified as advisory opinions," but also TCs, CPGs, and "[a]ny portion of a Federal Register notice other than the text of a proposed or final regulation."<sup>183</sup> (I shall hereinafter use the umbrella term "advisory opinions" to refer to this entire category, rather than the very small subset of FDA documents explicitly identified as advisory opinions *per se*.)<sup>184</sup> Thus, "the agency has not implemented aspects of its 1992 proposal that would have eliminated the binding effect of its prior advisory opinions."<sup>185</sup> As a result, a validly promulgated regulation that binds the FDA to its advisory opinions remains on the books. Oddly, the FDA drafted and published a proposed amendment that would have rendered advisory opinions non-binding, but did not finalize it in the Code of Federal Regulations, for reasons that are not readily apparent.<sup>186</sup> This is bizarre, given the FDA's previously stated intention "that

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<sup>182</sup> Compare 42 Fed. Reg. 4680, 4708-09 (1977) with 21 C.F.R. § 10.85 (historical version, 2001) ("An advisory opinion represents the formal position of FDA on a matter and except as provided in paragraph (f) of this section, obligates the agency to follow it until it is amended or revoked. The Commissioner may not recommend legal action against a person or product with respect to an action taken in conformity with an advisory opinion which has not been amended or revoked.")

<sup>183</sup> 21 C.F.R. § 10.85(d) (2011).

<sup>184</sup> "FDA issues virtually no advisory opinions of the type described in [21 C.F.R. § 10.85(a)] . . . Most documents that have the same status as an advisory opinion . . . fall within the preambles to proposed or final regulations, the compliance policy guides, and the other items identified in that subsection. Considering the number of Federal Register preambles, that is undoubtedly by far the greatest, and most important, source of statements that have the status of an advisory opinion." *Letter, supra* note 101.

<sup>185</sup> Barbara J. Evans & Eric M. Meslin, *Encouraging Translational Research Through Harmonization of FDA and Common Rule Informed Consent Requirements for Research with Banked Specimens*, 27 J. LEGAL MED. 119, 157 n.118 (2006).

<sup>186</sup> 57 Fed. Reg. 47314, 47317 (1992) ("An advisory opinion represents the best advice of FDA on a matter at the time of its issuance. However, *an advisory opinion does not bind the agency*, and it does not create or confer any rights, privileges, or benefits for or on any person." (emphasis added)). The FDA mentioned the proposed provision several years later, but did not give much useful information for resolving the paradox at issue: "In the Federal Register of October 15, 1992 . . . FDA proposed to amend §§10.85 and 10.90, which address advisory opinions and guidelines, to delete the provisions that obligate the agency to follow advisory opinions and guidelines until they are amended or revoked (except in unusual situations involving immediate and significant danger to health). As set forth in the proposed rule, those provisions appear to be inconsistent with the general principle that Federal agencies may not be estopped from enforcing the law. Although FDA has not yet issued a final rule, the agency plans to make final decisions on the 1992 proposal under that rulemaking." 61 Fed. Reg. 9181, 9183 n.1 (1996) (internal citations omitted). In a subsequent volume of the Federal Register, the FDA perfunctorily responded to a comment requesting an

guidelines have the same legal status as advisory opinions."<sup>187</sup> Nevertheless, at the close of rulemaking, there were, and still are,<sup>188</sup> two distinct categories of informal guidance on the books: "advisory opinions," which purport to bind the FDA, and "guidance documents," which do not.

This bipartite structure has resulted in ambiguity and uncertainty regarding which policies bind the FDA, if any.<sup>189</sup> Although advisory opinions and guidance documents may be differentiated in the abstract - advisory opinions typically cover more specific factual matters, whereas guidance usually creates broader, more general policies<sup>190</sup> -

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explanation of how the GGPs affected the status of advisory opinions: "We issue advisory opinions under § 10.85. We anticipate modifying § 10.85 and explaining the effect of § 10.115 on previously issued advisory opinions in a separate rulemaking effort. As such, the comment is outside the scope of this rulemaking." 65 Fed. Reg. 56468, 56474 (2000). This rulemaking never took place, and the proposed amendment was never unearthed. *See infra* note 200.

<sup>187</sup> 57 Fed. Reg. 47314, 47314 (1992).

<sup>188</sup> Compare 21 C.F.R. § 10.85 (historical version, 2001) with 21 C.F.R. § 10.85 (2011).

<sup>189</sup> Telephone Interview with Peter Barton Hutt, Senior Counsel, Covington & Burling LLP, Former Chief Counsel for the Food and Drug Administration (July 8, 2011) (on file with author) [hereinafter *Telephone Interview*]. For an example of this confusion in the academic literature, compare Rebecca M. Bratspies, *Glowing in the Dark: How America's First Transgenic Animal Escaped Regulation*, 6 MINN. J.L. SCI. & TECH. 457, 476 n.78 (2005) (arguing that a particular document was an advisory opinion that bound the FDA) with Lars Noah, *Managing Biotechnology's [R]evolution: Has Guarded Enthusiasm Become Benign Neglect?*, 11 VA. J.L. & TECH 4, 63 n.233 (2006) (arguing the opposite); see also Drew L. Kershen, *Health and Food Safety: The Benefits of BT-Corn*, 61 FOOD & DRUG L.J. 197, 212 n.98 (2006) (assuming the FDA's proposal regarding advisory opinions had been finalized); Margaret Gilhooley, *The Administrative Conference and the Progress of Food and Drug Reform*, 30 ARIZ. ST. L.J. 129, 144 (1998) (same); O'REILLY, *supra* note 11 § 4:24 4-88-92 (placing CPGs in the "FDA guidance documents" section rather than the "advisory opinions" section, despite their status as advisory opinions under 21 C.F.R. § 10.85). See also Hunnicutt, *supra* note 2, at 184-85 (arguing that the GGPs insufficiently specify which types of nonlegislative rules constitute non-binding "guidance documents").

<sup>190</sup> O'REILLY, *supra* note 11 § 4:25 4-93 ("Formal FDA pronouncements on specific sets of facts are advisory opinions . . . [they are] rarer and more weighty than a guideline, more specific, and more binding."); *Telephone Interview*, *supra* note 189. See also 21 C.F.R. § 10.115(b) (2011) ("What is a guidance document? (1) Guidance documents are documents prepared for FDA staff, applicants/sponsors, and the public that describe the agency's interpretation of or policy on a regulatory issue. (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. (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."); 21 C.F.R. § 10.85(d) (2011) (A statement of policy or interpretation made in the following documents, unless subsequently repudiated by the agency or overruled by a court, will constitute an advisory opinion: (1) Any portion of a Federal Register notice other than the text of a proposed or final

distinguishing the two in practice is not always simple, especially at the margins. For one, the applicable regulations do not specify where on the continuum of breadth of applicability advisory opinions end and guidance documents begin. In fact, 21 C.F.R. § 10.85(a)(2)(iv) suggests that advisory opinions should only be issued on "policy issue[s] of *broad applicability*," even though advisory opinions purport to be less broad than guidance documents.<sup>191</sup> To compound the confusion, some CPGs, which are categorized as advisory opinions under 21 C.F.R. § 10.85(d)<sup>192</sup> and therefore "obligate[] the agency to follow [them] until [they are] amended or revoked,"<sup>193</sup> nonetheless are often labeled by the FDA with disclaimers that suggest the policy is non-binding.<sup>194</sup> The FDA likewise

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regulation, e.g., a notice to manufacturers or a preamble to a proposed or final regulation. (2) Trade Correspondence (T.C. Nos. 1–431 and 1A–8A) issued by FDA between 1938 and 1946. (3) Compliance policy guides issued by FDA beginning in 1968 and codified in the Compliance Policy Guides manual. (4) Other documents specifically identified as advisory opinions, e.g., advisory opinions on the performance standard for diagnostic X-ray systems, issued before July 1, 1975, and filed in a permanent public file for prior advisory opinions maintained by the Division of Freedom of Information (ELEM–1029)."

<sup>191</sup> 21 C.F.R. § 10.85(a)(2)(iv) (2011) (emphasis added). *See also Telephone Interview, supra* note 189. *See also, e.g.*, 67 Fed. Reg. 77498, 77499 (2002) ("An advisory opinion represents the formal position of FDA on a matter of *general applicability*" (emphasis added)).

<sup>192</sup> "A statement of policy or interpretation made in the following documents, unless subsequently repudiated by the agency or overruled by a court, will constitute an advisory opinion: . . . (3) *Compliance policy guides issued by FDA beginning in 1968 and codified in the Compliance Policy Guides manual.*" 21 C.F.R. § 10.85(d) (2011) (emphasis added).

<sup>193</sup> *Id.* § 10.85(e) (2011).

<sup>194</sup> *See, e.g.*, CPG § 500.500 Guidance Levels for 3-MCPD(3-chloro-1,2-propanediol) in Acid-Hydrolyzed Protein and Asian-Style Sauces (Mar. 14, 2008), *available at* <http://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm074419.htm> ("This Compliance Policy Guide represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person *and does not operate to bind FDA* or the public." (emphasis added)); CPG § 280.100 - Stability Requirements - Licensed In Vitro Diagnostic Products (Aug. 14, 2000), *available at* <http://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm073881.htm> (same); CPG § 490.100 Process Validation Requirements for Drug Products and Active Pharmaceutical Ingredients Subject to Pre-Market Approval (revised Mar. 12, 2004), *available at* <http://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm074411.htm> (same); CPG § 110.100 Certification for Exports (revised Apr. 14, 2000), *available at* <http://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm073830.htm> (describing the document as both a "CPG" and a "guidance document"). Many similar documents may be found at *Manual of CPGs, supra* note 94. The Office of Management and Budget, in a document intended "to clarify what guidance is allowed to be issued by federal agencies under the Administrative Procedure Act," also categorized "compliance guides" as "guidance documents," which would presumably be non-binding. Ian J. Kellogg, *Prescription for a Cure: Does the FDA's Draft Guidance Adequately Manage Advisory Committee Members' Conflicts of Interest?*, 19 STAN. L. & POL'Y REV. 300, 315-16 (2008) (citing

mixes guidance documents and compliance guides together under the single heading "Guidance Documents" on its website.<sup>195</sup> More importantly, the GGPs mandate that

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 GGP's must be followed whenever regulatory expectations that are not readily apparent from the statute or regulations are first communicated to a broad public audience.<sup>196</sup>

If "advisory opinions" form a separate and distinct category from "guidance documents," as the Code of Federal Regulations suggests, then it appears that the FDA violates its own duly promulgated regulations when it uses advisory opinions, such as CPGs, to create broadly applicable policies. While many advisory opinions do not violate this provision because they address specific, individualized concerns, some advisory opinions do indeed "informally communicate new or different regulatory expectations to a broad public audience for the first time" and are therefore of questionable validity.<sup>197</sup>

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OMB Bulletin, Final Bulletin for Agency Good Guidance Practices, 72 Fed. Reg. 3432, 3434 (Jan 25, 2007)). This further exacerbates the confusion.

<sup>195</sup> See Guidance Documents,

<http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/default.htm> (last visited Jul. 18, 2011) [hereinafter *Guidance Documents*].

<sup>196</sup> 21 C.F.R. § 10.115(e) (2011).

<sup>197</sup> See CPG § 100.550 Status and Responsibilities of Contract Sterilizers Engaged in the Sterilization of Drugs and Devices (revised Oct. 3, 2006), *available at*

<http://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm073824.htm> (providing new or different regulatory expectations to all contract sterilizers of all drugs and devices). Note that although CPGs count as binding advisory opinions under 21 C.F.R. § 10.85, this CPG is preceded by a disclaimer that it "does not operate to bind FDA." *Id.* Also note that these revisions establishing new regulatory expectations occurred several years after October 19, 2000, the effective date for the GGPs, and are therefore subject to its restrictions against using policymaking tools other than guidance documents to informally communicate regulatory expectations. *See, e.g.*, 65 Fed. Reg. 56468, 56468 (2000). For similar examples, *see also* CPG § 100.700 GWQAP Pre-Award Evaluation - Inadequate Information to Evaluate Prospective Supplier (revised Apr. 25, 2005), *available at*

<http://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm073826.htm>; CPG § 110.300 Registration of Food Facilities Under the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (issued Dec. 2003), *available at*

<http://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm122876.htm>; CPG § 110.310 Prior Notice of Imported Food Under the Public Health Security and Bioterrorism Preparedness and Response Act of 2002: Compliance Policy Guide, Guidance for FDA and CBP Staff (May 2009), *available at*

This confusing state of affairs has not escaped the eye of industry. During the GGP rulemaking proceeding, one commenter requested that the FDA "clarify the status of advisory opinions and determine whether they are guidance documents."<sup>198</sup> The FDA's response was perfunctory: "We issue advisory opinions under § 10.85. We anticipate modifying § 10.85 and explaining the effect of § 10.115 on previously issued advisory opinions in a separate rulemaking effort. As such, the comment is outside the scope of this rulemaking."<sup>199</sup> However, it does not appear that this separate rulemaking effort ever occurred, and there is no sign that it will be conducted in the near future.<sup>200</sup>

Thus, it is uncertain whether advisory opinions that are labeled as non-binding "guidance" do, in fact, bind the FDA. I argue that they do, despite the FDA's repeated assertions to the contrary in the preambles to its CPGs. Consider the following hypothetical situation: a high-ranking FDA official departs from a policy established in one of the aforementioned CPGs that are defined as advisory opinions under FDA regulations, yet disclaim binding effect in its introductory text. The FDA has not amended or revoked this CPG, and there is no "immediate and significant danger to health" that demands noncompliance with the CPG; the CPG is therefore fully valid and effective.<sup>201</sup> This departure is likely unlawful. 21 C.F.R. § 10.85 (binding advisory opinions) and 21 C.F.R. § 10.115 (non-binding guidance documents) are both duly

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<http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/FoodDefenseandEmergencyResponse/ucm153055.htm>.

<sup>198</sup> 65 Fed. Reg. 56468, 56474 (2000).

<sup>199</sup> *Id.*

<sup>200</sup> § 10.85 has not changed since the FDA announced that the agency anticipated modifying it. *Compare* 21 C.F.R. § 10.85 (historical version, 2001) *with* 21 C.F.R. § 10.85 (2011). Furthermore, an examination of all Federal Register documents that cite 21 C.F.R. § 10.85 obtained using the "KeyCite Citing References" function on Westlaw on July 9, 2011 revealed no sign that the FDA has any current intention of undertaking this rulemaking process.

<sup>201</sup> *See* 21 C.F.R. § 10.85(f) (2011).

promulgated regulations that are actively in force. The FDA may not ignore them,<sup>202</sup> and a court would almost certainly interpret the regulatory scheme to give effect to both provisions.<sup>203</sup> Thus, if a regulated entity were to challenge the FDA's policy reversal in a judicial proceeding, the court could deem the FDA's departure from a binding policy to be "not in accordance with law" under the Administrative Procedure Act, and could therefore "hold unlawful and set aside" the FDA's decision.<sup>204</sup>

Although agencies' interpretations of ambiguous provisions in their own regulations are entitled to deference,<sup>205</sup> agencies are not permitted to amend or revoke their own regulations *via* informal guidance documents that have not passed through the notice-and-comment rulemaking process.<sup>206</sup> Advisory opinions that disclaim binding effect appear to do just that: they contradict the plain text of 21 C.F.R. § 10.85(e) that clearly indicates that the FDA is obligated to follow its own advisory opinions until they have been officially amended or revoked. Thus, the FDA should not operate under the assumption that all of its informal guidance documents are non-binding, or that it can

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<sup>202</sup> "An agency must follow its own regulations until they are validly amended or rescinded." PETER L. STRAUSS, TODD D. RAKOFF & CYNTHIA R. FARINA, GELLHORN AND BYSE'S ADMINISTRATIVE LAW: CASES AND COMMENTS 913-914 (Revised 10th ed. 2003) (citing *Accardi v. Shaughnessy*, 347 U.S. 260 (1954); *United States v. Nixon*, 418 U.S. 683 (1974); *INS v. Yang*, 519 U.S. 26 (1996)).

<sup>203</sup> *Cf.* *FDA v. Brown & Williamson Tobacco Corp.* 529 U.S. 120, 133 (2000) ("It is a 'fundamental canon of statutory construction that the words of a statute must be read in their context and with a view to their place in the overall statutory scheme.' A court must therefore interpret the statute 'as a symmetrical and coherent regulatory scheme,' and 'fit, if possible, all parts into an harmonious whole.'" (internal citations omitted)). There is no reason to believe this canon would not also be applicable to the construction of regulations.

<sup>204</sup> 5 U.S.C. § 706(2)(A) (2011).

<sup>205</sup> *E.g.*, *Bowles v. Seminole Rock & Sand Co.*, 325 U.S. 410, 413-14 (1945) ("Since this [case] involves an interpretation of an administrative regulation a court must necessarily look to the administrative construction of the regulation if the meaning of the words used is in doubt. The intention of Congress or the principles of the Constitution in some situations may be relevant in the first instance in choosing between various constructions. But the ultimate criterion is the administrative interpretation, which becomes of controlling weight unless it is plainly erroneous or inconsistent with the regulation.").

<sup>206</sup> If a guidance document "effectively amend[s]" or "contradict[s] the meaning of" a rule promulgated through notice-and-comment rulemaking, courts are likely to deem it a legislative rule that itself must pass through notice-and-comment rulemaking to have effect. *Raso*, *supra* note 5, at 788-90 (citing *Am. Mining Cong. v. MSHA*, 995 F.2d 1106 (D.C. Cir. 1993); *Hemp Indus. Ass'n v. DEA*, 333 F.3d 1082, 1087-91 (9th Cir. 2003); *Alaska Prof'l Hunters Ass'n v. FAA*, 177 F.3d 1030, 1034 (D.C. Cir. 1999)).

override its own duly enacted regulations simply by including disclaimers of binding effect in its advisory opinions.

Likewise, as mentioned previously, 21 C.F.R. § 10.115(e) prohibits using types of informal guidance that fall outside the definition of "guidance documents" to create broadly applicable policies. 21 C.F.R. § 10.115, like 21 C.F.R. § 10.85, is also a legally binding regulation, passed through the notice-and-comment rulemaking process. Therefore, if the FDA were to point to a policy established in an advisory opinion "to illustrate acceptable and unacceptable procedures or standards" in an administrative or court proceeding, as is contemplated by 21 C.F.R. § 10.85(j), a regulated party would likely be able to successfully challenge that policy if it is a broadly applicable policy formulated in derogation of 21 C.F.R. § 10.115(e). This would further hamper the FDA's enforcement power and exacerbate litigation costs.

Moreover, if an advisory opinion establishes a broadly applicable policy that "(i) Set[s] forth initial interpretations of statutory or regulatory requirements; (ii) Set[s] forth changes in interpretation or policy that are of more than a minor nature; (iii) Include[s] complex scientific issues; or (iv) Cover[s] highly controversial issues," then a regulated party could likely successfully challenge the policy in an enforcement proceeding as noncompliant with the mandatory procedures for Level 1 guidance documents.<sup>207</sup>

My conclusion that advisory opinions remain binding is very tentative, because an additional wrinkle remains: some aspects of the GGPs, including those that render guidance documents non-binding upon the agency, were enacted into the Food and Drug Administration Modernization Act of 1997.<sup>208</sup> Just as an informal guidance document

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<sup>207</sup> See 21 C.F.R. § 10.115(c)(1) (2011).

<sup>208</sup> 21 U.S.C. § 371(h)(1)(B) (2011) ("guidance documents shall not be binding on the Secretary").

cannot amend or revoke a regulation duly promulgated through notice-and-comment rulemaking, an administrative regulation cannot trump a congressional statute. Thus, whether binding advisory opinions survived the 1997 Act depends on the definition of "guidance documents" in the statute that renders those types of documents non-binding. If "guidance documents" refers to all forms of informal guidance, including advisory opinions, then advisory opinions will not bind the FDA. If, however, "guidance documents" is a term of art that refers to policies of broad applicability that do not include advisory opinions, then the advisory opinions would bind the FDA. I personally think the latter definition is more likely, for the following reasons: Congress took this section of the Act wholesale from the FDA's proposed GGP's, and thus arguably adopted the FDA's definitions of the terms within. Because the FDA promulgated regulations on "guidance documents" without modifying or deleting their regulatory provisions on "advisory opinions" or proclaiming them overruled, it is likely that those two terms are conceptually distinct, albeit perhaps overlapping at the margins. Moreover, the FDA considered, but did not ultimately promulgate, a regulation that would have made "guidance documents" a subcategory of advisory opinions;<sup>209</sup> if "guidance documents" was an umbrella term that included advisory opinions, this proposal would make no sense. This further indicates that the two categories are separate and distinct. It therefore appears that Congress only meant to render guidance documents, and not advisory opinions, non-binding on the FDA.

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<sup>209</sup> 65 Fed. Reg. 7321, 7328 (2000) ("In 21 CFR part 10, remove the words 'guideline' and 'guidelines' wherever they appear and add in their place the words 'guidance document' and 'guidance documents,' respectively, in the following places: . . . Section 10.85(d)(5)"). 21 C.F.R. § 10.85(d) is the subsection that lists various documents that count as advisory opinions, such as TCs and CPGs.

Then again, the opposite conclusion is also plausible. Thus, it is anyone's guess which informal guidance documents bind the FDA, if any. Put simply, the doctrine regarding whether and which informal guidance documents bind the FDA is a mess, and someone - whether it be the FDA, Congress, or the courts - should step in and clarify it.

That said, the practical effect of the difference between binding advisory opinions and non-binding guidance documents should not be overstated. "Binding" and "non-binding" are relative terms. The FDA is free to amend or revoke any of its informal guidance, regardless of whether or not those documents have binding effect, without having to go through particularly costly or time-consuming procedures.<sup>210</sup> In other words, the cost of departing from "binding" guidance is not much greater than that of departing from non-binding guidance. Moreover, the FDA is free to disregard a "binding" advisory opinion "[i]n unusual situations involving an immediate and significant danger to health" with the Commissioner's approval,<sup>211</sup> and FDA employees may depart from "non-binding" guidance documents "only with appropriate justification and supervisory concurrence."<sup>212</sup> Thus, to industry, there may be little practical difference between the two in most cases.

The consequences for the FDA could conceivably be massive, however. As explained previously, if and when a high-level FDA official departs from a policy set forth in a binding advisory opinion under the mistaken impression that the document is actually non-binding, without formally amending or revoking that advisory opinion, the FDA will probably be unable to successfully defend its policy reversal from judicial challenge. This could be costly for the agency and could make it difficult for the FDA to

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<sup>210</sup> See 21 C.F.R. §§ 10.85(g), 10.115(k) (2011).

<sup>211</sup> *Id.* § 10.85(f).

<sup>212</sup> *Id.* § 10.115(d)(3). *But see* Hunnicutt, *supra* note 2, at 182-83 (criticizing the provision's lack of clarity).

fulfill its regulatory objectives. Also, as stated earlier, the same would be true if and when the FDA improperly establishes broad policies in advisory opinions. Additionally, as will be described in greater detail *infra*, the confusion regarding the binding status of advisory opinions could affect the degree of deference the judiciary grants to the FDA's interpretations of ambiguous provisions of its organic statute.

Moreover, some commentators have argued that the FDA is increasingly in danger of losing its strong reputation as a scientifically expert, depoliticized agency.<sup>213</sup> If these criticisms are correct, the FDA cannot afford looking like an agency that refuses to play by its own rules, lest it risk losing even further support from the executive branch, Congress, the judiciary, industry, and the public. The FDA must clearly specify which guidance is binding on the agency and which is not, and it must follow those determinations accordingly.

*I. And Behold, a Pale Horse, and His Name That Sat on Him was Mead, and Barnhart  
Followed With Him*

Beginning in 2000, the Supreme Court decided three cases that severely threatened the FDA's ability to rely on guidance as its principal policymaking tool and introduced great uncertainty and confusion into the doctrine of judicial review of agency statutory interpretations: *Christensen*, *Mead*, and *Barnhart*. Although these cases involved the scope of the *Chevron* framework, they did not address how the two-step *Chevron* inquiry proceeds; rather, they dealt with the preliminary question of when, and

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<sup>213</sup> See generally O'Reilly, *supra* note 121; David C. Vladeck, *The FDA and Deference Lost: A Self-Inflicted Wound or the Product of a Wounded Agency? A Response to Professor O'Reilly*, 93 CORNELL L. REV. 981 (2008).

under what circumstances, the *Chevron* doctrine applies at all. These cases have thus been dubbed the *Chevron* Step Zero trilogy.<sup>214</sup>

The first decision, *Christensen v. Harris County*,<sup>215</sup> held that an opinion letter informally issued by the Department of Labor was not entitled to *Chevron* deference, but not because it failed *Chevron's* two-step inquiry. The Court broadly stated that "[i]nterpretations such as those in opinion letters -- like interpretations contained in policy statements, agency manuals, and enforcement guidelines, all of which lack the force of law -- do not warrant *Chevron*-style deference."<sup>216</sup> *Christensen* also emphasized the importance of agency procedures in producing agency interpretations: "[t]he Court distinguished opinion letters and their analogues from interpretations 'arrived at after, for example, a formal adjudication or notice-and-comment rulemaking.'"<sup>217</sup> Rather, opinion letters could at most receive judicial "respect" in accordance with the Court's pre-*Chevron* decision in *Skidmore v. Swift & Co.*,<sup>218</sup> a case many believed to be "an anachronism" that failed to survive *Chevron*.<sup>219</sup> Thus, judicial deference to these types of interpretations would henceforth "depend upon the thoroughness evident in its consideration, the validity of its reasoning, its consistency with earlier and later pronouncements, and all those factors which give it power to persuade, if lacking power to control."<sup>220</sup> This standard, known as *Skidmore* "respect," is notably less deferential than *Chevron* deference,<sup>221</sup> and arguably affords courts, rather than agencies, interpretive

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<sup>214</sup> See generally, e.g., Sunstein, *supra* note 2.

<sup>215</sup> 529 U.S. 576 (2000).

<sup>216</sup> *Id.* at 587 (emphasis added).

<sup>217</sup> Sunstein, *supra* note 2, at 212 (quoting *Christensen*, 529 U.S. at 587).

<sup>218</sup> 323 U.S. 134, 140 (1944).

<sup>219</sup> E.g., *Christensen*, 529 U.S. at 589 (Scalia, J., concurring in part and concurring in the judgment).

<sup>220</sup> *Skidmore*, 323 U.S. at 140.

<sup>221</sup> E.g., Johnson, *supra* note 13, at 741.

control over ambiguous provisions of regulatory statutes.<sup>222</sup> *Christensen* also clearly established that *Chevron* has a "Step Zero" in addition to its two-step inquiry - before determining whether the agency has permissibly interpreted an ambiguous provision in its organic statute, courts must first determine whether the *Chevron* doctrine is applicable at all; if not, the court must instead evaluate the agency's interpretation under the newly-reincarnated *Skidmore* framework.<sup>223</sup>

*Christensen's* overall tenor marked a turn away from the Court's approach in *Young* discussed *supra* Section I.G., in which the Court afforded *Chevron* deference to an action level that the FDA set through informal processes. *Christensen* suggested that procedural formality would henceforth be a necessary condition for judicial deference. The decision therefore marked a major defeat for agencies, like the FDA, that utilized guidance as their principal policymaking tool. The Court's increased emphasis on procedural rigor signaled that the FDA might subsequently receive judicial deference far less often, and would consequently find it far more difficult to fulfill its regulatory mandate.<sup>224</sup> However, *Christensen* left notable ambiguities in the doctrine:

By pointing first to the 'force of law,' and second to the processes that produce agency interpretations, the Court did not specify which of these two factors was critical to its ruling, nor did it explain the relationship between them. And the Court did not say whether interpretations that lack the force of law, or that do not emerge from relatively formal procedures, are always to be assessed under *Skidmore*.<sup>225</sup>

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<sup>222</sup> Lisa Schultz Bressman, *How Mead Has Muddled Judicial Review of Agency Action*, 58 VAND. L. REV. 1443, 1446-47 (2005); *but see* Nat'l Cable & Telecomms. Ass'n v. Brand X Internet Servs., 125 S.Ct. 2688, 2691 (2005) (holding that prior judicial interpretation of ambiguous statutory provision does not preclude *Chevron* deference to subsequent agency interpretation).

<sup>223</sup> Sunstein, *supra* note 2, at 212.

<sup>224</sup> *See* O'Reilly, *supra* note 121, at 941-42.

<sup>225</sup> Sunstein, *supra* note 2, at 212.

Thus, administrative agencies would have to await further word from the Court to fully understand the impact of this doctrinal change on their ability to use guidance to achieve their regulatory objectives.

Unfortunately, subsequent cases only further confused the doctrine. The next episode in the trilogy occurred one year later, in *United States v. Mead Corporation*.<sup>226</sup> In *Mead*, the Supreme Court held that an informal and non-precedential tariff classification ruling by the United States Customs Service was not entitled to *Chevron* deference, and remanded to determine whether the ruling was nonetheless entitled to *Skidmore* respect.<sup>227</sup> The Court's rationale for its decision was opaque. The opinion suggests that *Chevron* applies "when it appears that Congress delegated authority to the agency generally to make rules carrying the force of law, and that the agency interpretation claiming deference was promulgated in the exercise of that authority."<sup>228</sup> While a "very good indicator of delegation" is congressional authorization to "use relatively formal procedures" to "produce[] regulations or rulings for which deference is claimed," coupled with the actual exercise of those procedures, "*Chevron* deference might also be appropriate 'even when no such administrative formality was required and none was afforded.'"<sup>229</sup> Thus, *Mead* supported *Christensen*'s holding that procedural formality is an important factor under *Chevron* Step Zero, but rejected its apparent suggestion that procedural formality is a necessary condition for *Chevron* deference.<sup>230</sup>

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<sup>226</sup> 533 U.S. 218 (2001).

<sup>227</sup> *Id.* at 221-239.

<sup>228</sup> *Id.* at 226-27.

<sup>229</sup> Sunstein, *supra* note 2, at 214 (quoting *Mead*, 533 U.S. at 229-31).

<sup>230</sup> *Id.* at 214-15.

The Court stated that the Customs rulings were not entitled to *Chevron* deference because of their procedural informality and their "sheer volume,"<sup>231</sup> but the Court gave very little guidance regarding which types of agency interpretations *are* entitled to *Chevron* deference. "*Mead* suggests that Congress might, under unidentified circumstances, be best read to call for deference even when an agency is not using formal procedures and that agency's actions lack the force of law,"<sup>232</sup> but *Mead* does not offer many useful clues for divining what those unidentified circumstances entail.

The possibility that deference could be warranted in the absence of procedural formality and force of law was realized one year later in *Barnhart v. Walton*,<sup>233</sup> the final step in the *Chevron* Step Zero trilogy. Although the agency at issue in *Barnhart* had "initially reached its interpretation" of an ambiguous provision of its organic statute "through less formal means, . . . the Court said that the use of those means did not preclude *Chevron* deference."<sup>234</sup> *Barnhart* listed a slew of previously unarticulated factors that bear on whether an agency interpretation warrants *Chevron* deference:

[T]he interstitial nature of the legal question, the related expertise of the Agency, the importance of the question to the administration of the statute, the complexity of that administration, and the careful consideration the Agency has given the question over a long period of time all indicate that *Chevron* provides the appropriate legal lens through which to view the legality of the Agency interpretation here at issue.<sup>235</sup>

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<sup>231</sup> "Any suggestion that rulings intended to have the force of law are being churned out at a rate of 10,000 a year at an agency's 46 scattered offices is simply self-refuting." *Mead*, 533 U.S. at 233; Sunstein, *supra* note 2, at 215.

<sup>232</sup> Sunstein, *supra* note 2, at 216.

<sup>233</sup> 535 U.S. 212 (2002).

<sup>234</sup> Sunstein, *supra* note 2, at 217 (citing *Barnhart*, 535 U.S. at 221). Although the interpretation at issue in *Barnhart* had, subsequent to its issuance, been promulgated as a regulation through the notice-and-comment rulemaking process, the Court "consider[ed] the agency's interpretation as if it had never been issued through notice-and-comment rulemaking" and nonetheless concluded that *Chevron* deference was warranted. Bressman, *supra* note 222, at 1456 (citing *Barnhart*, 535 U.S. at 219-221).

<sup>235</sup> *Barnhart*, 535 U.S. at 222.

The Court therefore "read *Mead* to say that *Chevron* deference would depend on 'the interpretive method used and the nature of the question at issue.'"<sup>236</sup> Thus, after *Barnhart*, "[t]he grant of authority to act with the force of law" is no longer a necessary condition to receive *Chevron* deference; it is merely one of many important factors in an increasingly complicated and indeterminate balancing test.<sup>237</sup>

The upshot of the Step Zero trilogy is that agencies now find it more difficult to receive *Chevron* deference and thereby defend policies expressed through informal means from judicial challenge.<sup>238</sup> Empirical data tentatively suggests that agencies have accordingly begun to shy away from guidance in favor of more costly notice-and-comment rulemaking to receive greater deference and thereby effect their statutory mandates, although further research is necessary to confirm this.<sup>239</sup> Commentators therefore fear that *Mead* has contributed to the ossification of the administrative state and reduced agencies' flexibility to respond to changing circumstances.<sup>240</sup>

To say that *Mead* and its brethren has been neither well-received nor well-understood by the legal community is an understatement.<sup>241</sup> One scholar has labeled these

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<sup>236</sup> Sunstein, *supra* note 2, at 217 (citing *Barnhart*, 535 U.S. at 222).

<sup>237</sup> *Id.* at 218. *See also id.* at 216 (describing the *Chevron* Step Zero inquiry as a "complex, . . . rule-free inquiry").

<sup>238</sup> Eric R. Womack, *Into the Third Era of Administrative Law: An Empirical Study of the Supreme Court's Retreat from Chevron Principles in United States v. Mead*, 107 DICK. L. REV. 289, 327-28, 341 (2002); Peter A. Appel, *Wilderness and the Courts*, 29 STAN. ENVTL. L.J. 62, 114 (2010); Amy J. Wildermuth, *Solving the Puzzle of Mead and Christensen: What Would Justice Stevens Do?*, 74 FORDHAM L. REV. 1877, 1899 (2006). *But see* Kristin E. Hickman & Matthew D. Krueger, *In Search of the Modern Skidmore Standard*, 107 COLUM. L. REV. 1235 (2007) (suggesting that *Skidmore* respect, while less deferential than *Chevron* deference, is still a relatively deferential standard).

<sup>239</sup> O'Connell, *supra* note 5, at 932-33. However, some argue that "*Mead* has had no impact whatever on FDA with respect to the choice between informal guidance and notice-and-comment rulemaking" because the advantages of guidance, particularly "the ease with which guidance can be issued," still outweigh the potential loss of judicial deference. *Letter, supra* note 101.

<sup>240</sup> Bressman, *supra* note 222, at 1446-47; *Mead*, 533 U.S. 218, 246-250 (2001) (Scalia, J., dissenting).

<sup>241</sup> *See generally, e.g.*, Sunstein, *supra* note 2 ("the extraordinary complexity introduced by the emerging law of Step Zero serves no useful purpose"); Bressman, *supra* note 222; *Mead*, 533 U.S. at 239-261 (Scalia, J., dissenting).

decisions "confusing, . . . confused, . . ." and "downright perverse."<sup>242</sup> A federal appellate judge, emphasizing the uncertainty generated by *Mead*, had this to say: "After *Mead*, we are certain of only two things about the continuum of deference owed to agency decisions: *Chevron* provides an example of when *Chevron* deference applies, and *Mead* provides an example of when it does not."<sup>243</sup> Professor Bressman, in an extensively researched and thoughtful article on the aftermath of the *Mead* trilogy, observes that "*Mead* and *Barnhart* suggest disparate tests for *Chevron* deference, leaving individual panels (even individual judges) simply to select between them."<sup>244</sup> As a result,

[S]ome courts concentrate on whether an interpretation binds more than the parties at hand; some broaden this analysis to ask whether, in addition to binding effect, the interpretation reflects public participation; some limit their focus to whether an agency interpretation reflects careful consideration; and some expand this focus, weighing careful consideration along with agency expertise and statutory complexity.<sup>245</sup>

Consequently, many courts use different tests to reach wildly divergent results in seemingly similar circumstances.<sup>246</sup> Other courts, faced with this palpable uncertainty, simply duck the question,<sup>247</sup> and others arguably misunderstand *Mead* so severely that they utilize the decision in completely unrelated contexts.<sup>248</sup> Thus, it is now largely unknown whether and how much deference any given agency interpretation will receive.<sup>249</sup>

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<sup>242</sup> Seidenfeld, *supra* note 2, at 279-80.

<sup>243</sup> *Wilderness Soc'y v. United States Fish & Wildlife Serv.*, 316 F.3d 913, 921 (9th Cir. 2003) (Graber, J.), *rev'd en banc*, 353 F.3d 1051 (9th Cir. 2003).

<sup>244</sup> Bressman, *supra* note 222, at 1461.

<sup>245</sup> *Id.* at 1459.

<sup>246</sup> *See generally id.* at 1458-64.

<sup>247</sup> *See generally id.* at 1464-69.

<sup>248</sup> *See generally id.* at 1469-74.

<sup>249</sup> Although somewhat outside the scope of this article, it is not even clear that regulations promulgated through notice-and-comment rulemaking that carry the force of law are automatically entitled to *Chevron* deference after *Mead*. *Id.* at 1448 (citing *Nat'l Cable & Telecomms. Ass'n v. Brand X Internet Servs.*, 125 S.Ct. 2688, 2712 (Breyer, J., concurring)).

How have these doctrinal developments affected the level of judicial deference that FDA guidance receives? The FDA has, in at least one case, conceded that one of its advisory opinions was entitled to only *Skidmore* deference,<sup>250</sup> but it is uncertain whether this concession was necessary as a doctrinal matter. Although it is impossible to truly know until greater doctrinal coherence emerges, I tentatively conclude that FDA guidance is entitled to *Chevron* deference, even though a significant number of courts that have addressed the issue have concluded otherwise. The following is intended to be a positive, doctrinal analysis; I shall address whether or not the FDA's informal guidance documents *should* receive *Chevron* deference as a normative matter *infra*.

I first note that FDA guidance documents that interpret FDA regulations, rather than congressional statutes, are likely unaffected by the *Mead* trilogy. "Guidance that clearly interprets an existing legislative rule, and not a statute, may fall outside the *Chevron* regime and instead receive *Seminole Rock* deference," under which an agency's interpretation of its own rules is given "controlling weight unless it is plainly erroneous or inconsistent with the regulation;" a generous standard akin to *Chevron* deference.<sup>251</sup> Because a substantial number of FDA guidance documents interpret the FDA's own rules rather than statutory provisions,<sup>252</sup> a large number of FDA policies will still likely receive substantial judicial deference.

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<sup>250</sup> See *Kellogg v. Wyeth*, 612 F.Supp.2d 421, 433 n.6 (D.Vt. 2008).

<sup>251</sup> *Raso*, *supra* note 5, at 794-95 (citing *Bowles v. Seminole Rock & Sand Co.*, 325 U.S. 410, 414 (1945)).

<sup>252</sup> See, e.g., CPG § 110.310 Prior Notice of Imported Food Under the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (May 2009), available at <http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/FoodDefenseandEmergencyResponse/ucm153055.htm> (interpreting 21 CFR §§ 1.276-1.285); Guidance for Industry: Bottled Water: Arsenic; Small Entity Compliance Guide (Apr. 2009), available at <http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/ChemicalContaminantsandPesticides/ucm151384.htm> (interpreting various FDA regulations). See generally *Guidance Documents*, *supra* note 195.

To determine the status of the remaining interpretations, I will first examine federal cases that have directly addressed the issue. Afterwards, I shall engage in my own independent analysis based on the numerous factors the Supreme Court has articulated in the Step Zero trilogy.

### *I. Mead and FDA Guidance in the Federal Courts*

The Supreme Court has offered little further guidance regarding the level of deference that informal FDA documents warrant. The few subsequent Supreme Court cases that have addressed both FDA policies and *Mead* offer little clarification.<sup>253</sup> For example, although *Wyeth v. Levine* held that a policy expressed in the preamble to a legislative rule, which counts as an advisory opinion under FDA regulations and therefore qualifies as an informal guidance document,<sup>254</sup> was not entitled to *Chevron* deference,<sup>255</sup> courts have noted that *Wyeth's* rationale was likely more influenced by "a defect in the thoroughness of the FDA's views,"<sup>256</sup> as well as the general presumption against preemption of state law,<sup>257</sup> than by the policy's informal status. Thus, we must look to the lower federal courts for further direction.

Unfortunately, very few lower court cases are directly on point either.<sup>258</sup> A search of all federal cases involving both the FDA and the *Christensen/Mead/Barnhart* trilogy

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<sup>253</sup> See *Wyeth v. Levine*, 129 S.Ct. 1187, 1201-02 (2009) (policy expressed in legislative rule did not merit deference due to major change in longstanding position without warning or opportunity to comment); *Riegel v. Medtronic, Inc.*, 552 U.S. 312, 326-27 (2008) (finding statutory language unambiguous and thus discussing *Mead* only hypothetically).

<sup>254</sup> 21 C.F.R. § 10.85(d)(1) (2011). *But see* Section I.H.3. *supra*.

<sup>255</sup> *Wyeth*, 129 S.Ct. at 1201-02 (2009).

<sup>256</sup> *Farina v. Nokia, Inc.*, 625 F.3d 97, 127 n.27 (3d Cir. 2010) (describing *Wyeth's* rationale).

<sup>257</sup> See *infra* note 260.

<sup>258</sup> Several cases concerned policies expressed in legal briefs, informal adjudications, or letters to individual parties on case-specific matters, none of which can be classified as guidance documents for a general audience. See, e.g., *Mylan Labs., Inc. v. Thompson*, 389 F.3d 1272, 1278-84 (D.C. Cir. 2004); *Apotex, Inc.*

revealed only two circuit court cases that directly addressed the degree of deference owed to FDA guidance documents. Both are from the Third Circuit, and they point in opposite directions. In *Holk v. Snapple Beverage Corporation*, the Third Circuit declined to give deference to FDA policy statements published in the Federal Register that purported to preempt state law claims, emphasizing that the policies were not formulated through formal procedures like notice-and-comment rulemaking.<sup>259</sup> However, this stress on procedural formality may have been more attributable to the strong presumption against preemption than any doctrinal changes *Mead* effected; many courts hold that *Chevron* deference is inappropriate when any agency opines on the degree to which its regulations and adjudications preempt state law.<sup>260</sup> Indeed, the Third Circuit previously upheld a FDA policy expressed in a CPG in *Wedgewood Village Pharmacy, Incorporated v. United States*, "even though the CPG was not the product of notice and comment

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v. FDA, 226 Fed.Appx. 4 at \*1 (D.C. Cir. 2007); *Sottera, Inc. v. FDA*, 627 F.3d 891, 903-04 (D.C. 2010); *Horn v. Thoratec Corp.*, 376 F.3d 163, 177-79 (3d Cir. 2004); *Doe v. Rumsfeld*, 297 F.Supp.2d 119, 131-32 (D.D.C. 2003); *Collagenex Pharm., Inc. v. Thompson*, 2005 WL 256561 (D.D.C. 2005); *Allergan, Inc. v. Crawford*, 398 F.Supp.2d 13 (D.D.C. 2005). Although letters to individual parties may be technically categorized as guidance documents, they rarely set wide-ranging, general policies due to their individualized, case-specific nature. I have also excluded from this discussion any circuit or district court cases that were subsequently reversed or vacated.

<sup>259</sup> 575 F.3d 329, 340-42 (3d Cir. 2009).

<sup>260</sup> *Id.* at 340 (emphasizing that only federal law, such as statutes and regulations, and not mere federal policy, may preempt state law) (quoting *Fellner v. Tri-Union Seafoods, LLC*, 539 F.3d 237, 243 (3d Cir. 2008)). Note that the opinion at no point mentions *Chevron* or *Skidmore*, which further indicates the court's decision was more likely based on the presumption against preemption than on any specific doctrine of deference to agency interpretations. For other cases refusing to grant deference to informal FDA statements claiming preemption of state law, *see also, e.g., Fellner*, 539 F.3d 237; *In re Zyprexa Prods. Liab. Litig.*, 489 F.Supp.2d 230, 272-74 (E.D.N.Y. 2007); *Perry v. Novartis Pharm. Corp.*, 456 F.Supp.2d 678, 682-84 (E.D.Pa. 2006) ("Thus, to the degree that the FDA seeks to address ambiguities in the FDCA or in its own regulations, we will give that opinion great weight. Where, however, the agency attempts to 'supply, on Congress's behalf, the clear legislative statement of intent required to overcome the presumption against preemption,' no deference is warranted." (internal citations omitted)); *Tucker v. SmithKline Beecham Corp.*, 596 F.Supp.2d 1225, 1230-33 (S.D.Ind. 2008). For cases illustrating the strong presumption against federal preemption of state law, *see generally Rice v. Santa Fe Elevator Corp.*, 331 U.S. 218 (1947); *Cipollone v. Liggett Group, Inc.*, 505 U.S. 504 (1992). As a doctrinal matter, it is currently uncertain how the presumption against preemption interacts with the *Chevron* doctrine. *Compare Massachusetts v. DOT*, 93 F.3d 890 (D.C. Cir. 1996) *with Brannan v. United Student Aid Funds, Inc.*, 94 F.3d 1260 (9th Cir. 1996).

rulemaking."<sup>261</sup> Although the court declined to "determine the precise level of deference, if any, owed the CPG because the FDA need[ed] only show that the factors outlined in the CPG . . . [were] a reasonable basis upon which to initiate an inspection under the FDCA," the court, quoting *Barnhart*, emphasized that the FDA's policies "reflect[ed] the FDA's 'careful consideration ... over a long period of time.'"<sup>262</sup>

While most district court cases that address the issue withhold *Chevron* deference from informal guidance documents issued by the FDA, they do so for starkly different reasons. Some decisions emphasize the need for notice-and-comment procedures, and evaluate documents passed without formal procedures under the *Skidmore* framework.<sup>263</sup> Others emphasize the consistency (or lack thereof) of the FDA's position, and withhold *Chevron* deference when the FDA has markedly reversed course.<sup>264</sup> Still others emphasize that the FDA's informal guidance does not bind the public and therefore lacks the force of law, and withhold deference accordingly.<sup>265</sup> Finally, some cases twist *Mead*

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<sup>261</sup> 421 F.3d 263, 272-73 (3d Cir. 2005).

<sup>262</sup> *Id.* (quoting *Barnhart v. Walton*, 535 U.S. 212, 222 (2002)).

<sup>263</sup> *Bartlett v. Mut. Pharm. Co.*, 659 F.Supp.2d 279, 302-04 (2009) (refusing to grant *Chevron* deference to footnote in proposed FDA regulation that "was not incorporated into the final version of the rule and therefore was not subjected to the notice-and-comment procedure"); *Barnhill v. Teva Pharm. USA, Inc.*, Slip Copy, 2007 WL 6947996 at \*4-6 (S.D.Ala. 2007) ("An agency's advisory opinion is entitled to deference only to the extent it has the power to persuade."); *Weiss v. Fujisawa Pharm. Co.*, 464 F.Supp.2d 666, 673-76 (E.D.Ky. 2006) ("Even though it represents FDA's formal position on a matter and obligates the agency to follow it until amended or revoked, an advisory opinion is also entitled only to limited deference because it is not subject to notice and comment procedures." (internal citations omitted)); *Von Koenig v. Snapple Beverage Corp.*, 713 F.Supp.2d 1066, 1076 (E.D.Cal. 2010); *In re Vioxx Prods. Liab. Litig.*, 501 F.Supp.2d 776, 786-87 (E.D. La. 2007).

<sup>264</sup> *Weiss*, 464 F.Supp.2d at 673-76 ("FDA's position has not been consistent and is therefore entitled only to *Skidmore* deference."); *Kellogg v. Wyeth*, 612 F.Supp.2d 421, 432-35 (D.Vt. 2008); *Vioxx*, 501 F.Supp.2d at 786-87. *But see* Thomas L. Casey, III, *Towards Function and Fair Notice: Two Models for Effecting Executive Policy Through Changing Agency Interpretations of Ambiguous Statutes and Rules*, 2008 MICH. ST. L. REV. 725, 735 n.64 (arguing that "the 'consistency' of an agency's interpretation has generally not been a deciding factor in lower court cases applying *Skidmore* subsequent to *Mead*") (citing *Hickman & Krueger*, *supra* note 238, at 1286).

<sup>265</sup> *Perry*, 456 F.Supp.2d at 682-84.

in interesting fashions to deny deference.<sup>266</sup> Thus, while the relevant district court cases suggest deference is unwarranted to FDA guidance, there is no consensus regarding why this is so. Furthermore, the overwhelming majority of post-*Mead* district court cases address the FDA's reversal of its longstanding policy on preemption; thus, for the reasons discussed previously, courts' reasons for denying deference may relate more to the strong presumption against preemption than the informal status of the FDA's guidance documents and regulatory preambles.<sup>267</sup> Thus, it is worth performing an independent analysis of the *Christensen/Mead/Barnhart* factors to determine how much, if any, deference FDA guidance should receive as a doctrinal matter.

## 2. *The Christensen/Mead/Barnhart Factors*

I conclude that FDA guidance documents, or at least those promulgated in accordance with the GGPs, are entitled to *Chevron* deference because the bulk of the factors mentioned in *Christensen*, *Mead*, and *Barnhart* indicate that *Chevron*, not *Skidmore* or *de novo*, is the correct standard to apply. This conclusion is obviously tentative; the courts have not clarified how these factors should be weighed, if they are even to be weighed at all.<sup>268</sup> I further acknowledge that a number of commentators have

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<sup>266</sup> In *Sandoz, Inc. v. Leavitt*, 427 F.Supp.2d 29 (D.D.C. 2006), the court cited *Mead* for the proposition that an agency could not contradict or ease the plain terms of the statute it administers. *Id.* at 37 n.9. This, however, seems more like a *Chevron* Step One issue than a Step Zero issue that would necessitate resort to the *Mead* doctrine. *Chevron, U.S.A., Inc. v. National Resources Defense Council, Inc.*, 467 U.S. 837, 842-43 (1984) ("First, always, is the question whether Congress has directly spoken to the precise question at issue. If the intent of Congress is clear, that is the end of the matter; for the court, as well as the agency, must give effect to the unambiguously expressed intent of Congress.").

<sup>267</sup> See *supra* note 260. For further discussion regarding how the FDA's changed policy in preemption has led to lost deference, see O'Reilly, *supra* note 121, at 967-72.

<sup>268</sup> See Bressman, *supra* note 222, at 1445-46. But see Hickman & Krueger, *supra* note 238 (suggesting that most appellate courts use a "sliding scale" approach that balances a variety of factors).

disagreed with my conclusion.<sup>269</sup> I nonetheless hope that this analysis can assist courts, academicians, regulated entities, and the FDA, and help resolve the confusion surrounding the Step Zero triumvirate.

*a. Careful Consideration and Expertise*

Many courts, following language from *Barnhart*, emphasize the importance of an agency's careful consideration and agency expertise when determining the amount of deference an agency should receive when interpreting a complex statutory scheme.<sup>270</sup> Although some commentators fear that the recent politicization of the FDA has eroded its reputation for scientific expertise, the FDA is undoubtedly an expert agency in a unique position to make informed judgments regarding the regulation of food, drugs, and cosmetics.<sup>271</sup> Courts continue to defer to the FDA on these grounds in similar contexts.<sup>272</sup> This factor therefore strongly counsels in favor of *Chevron* deference for FDA guidance documents. In fact, some courts have already deferred to interpretations expressed in FDA guidance on this basis.<sup>273</sup>

*b. Binding Effect and the Force of Law*

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<sup>269</sup> See, e.g., David M. Dudzinski, *Reflections on Historical, Scientific, and Legal Issues Relevant to Designing Approval Pathways for Generic Versions of Recombinant Protein-Based Therapeutics and Monoclonal Antibodies*, 60 FOOD & DRUG L.J. 143, 212-13 (2005).

<sup>270</sup> Bressman, *supra* note 222, at 1459-60.

<sup>271</sup> See generally O'Reilly, *supra* note 121.

<sup>272</sup> "There is no denying the complexity of the statutory regime under which the FDA operates, the FDA's expertise or the careful craft of the scheme it devised to reconcile the various statutory provisions." Mylan Labs., Inc. v. Thompson, 389 F.3d 1272, 1280 (D.C. Cir. 2004). *Accord* Collagenex Pharm., Inc. v. Thompson, 2005 WL 256561 at \*8 (D.D.C. 2005); Allergan, Inc. v. Crawford, 398 F.Supp.2d 13, 21-22 (D.D.C. 2005).

<sup>273</sup> Wedgewood Village Pharmacy, Inc. v. United States, 421 F.3d 263, 272-73 (3d Cir. 2005).

Other courts, citing *Mead*, emphasize the binding effect, or lack thereof, of the challenged interpretation.<sup>274</sup> Although it is uncertain whether guidance documents bind the FDA,<sup>275</sup> no guidance documents bind regulated parties;<sup>276</sup> thus, this factor probably weighs against *Chevron* deference for FDA guidance documents, although that would not necessarily preclude lower-level *Skidmore* respect.

There are countervailing considerations, however. First, advisory opinions and guidance documents purport to have general applicability even if they lack the force of law. Unlike the case-specific ruling letters unworthy of *Chevron* deference in *Mead*,<sup>277</sup> the FDA's interpretations embodied in guidance documents "appl[y] 'equally to all claimants,'" which may weigh in favor of higher-level deference.<sup>278</sup> Finally, as previously explained in (arguably excruciating) detail, it is uncertain which, if any, guidance documents/advisory opinions bind the FDA, and to what degree.<sup>279</sup> Advisory opinions that bind the FDA would have greater claim to judicial deference than guidance documents that do not. This provides an additional incentive for the FDA to clarify how the GGP's have affected the binding status of advisory opinions.

In sum, while the force of law/binding effect factor weighs against deference, it may not do so particularly strongly. Because *Barnhart* indicates that the force of law is not necessary to receive *Chevron* deference, this factor may be outweighed by other considerations.<sup>280</sup>

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<sup>274</sup> Bressman, *supra* note 222, at 1463.

<sup>275</sup> See *supra* Section I.H.3.

<sup>276</sup> See *supra* Sections I.F; I.H.1.

<sup>277</sup> 533 U.S. 218, 232 (2001).

<sup>278</sup> Cf. Bressman, *supra* note 222, at 1462-63 (citing *Wilderness Soc'y v. United States Fish & Wildlife Serv.*, 353 F.3d 1051 (9th Cir. 2003); *Schneider v. Feinberg*, 345 F.3d 135, 143 (2d Cir. 2003)).

<sup>279</sup> See *supra* Section I.H.3.

<sup>280</sup> Sunstein, *supra* note 2, at 216.

*c. Formality of Procedures and Public Participation*

Many courts, when evaluating an agency interpretation issued through procedures less formal than notice-and-comment rulemaking or formal adjudication, focus on whether the agency arrived at its interpretation using a method that facilitated deliberation and public participation.<sup>281</sup> Notwithstanding the Supreme Court's suggestion in *Christensen* that "interpretations contained in policy statements, agency manuals, and enforcement guidelines" are relegated to, at most, *Skidmore* respect,<sup>282</sup> *Mead* emphatically clarifies that formal procedures are not a necessary condition for *Chevron* deference.<sup>283</sup> 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.<sup>284</sup> This strongly suggests that FDA guidance, or at least Level 1 guidance documents, should receive *Chevron* deference.

*d. Other Considerations*

Other relevant factors also counsel in favor of *Chevron* deference to FDA guidance. First, unlike the tariff classifications deemed unworthy of *Chevron* deference in *Mead*, guidance documents that comply with the strictures of the GGPs are not "being churned out at a rate of 10,000 a year;"<sup>285</sup> the FDA issues CPGs and guidance documents

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<sup>281</sup> Bressman, *supra* note 222, at 1458-60.

<sup>282</sup> 529 U.S. 576, 587 (2000).

<sup>283</sup> Sunstein, *supra* note 2, at 214-15 ("[T]he Court in *Mead* squarely rejected a possible reading of *Christensen*: that agency interpretations lacking the force of law, or not preceded by formal procedures, would always be evaluated under *Skidmore*.").

<sup>284</sup> See *supra* Section I.H.2.

<sup>285</sup> 533 U.S. 218, 233 (2001).

intended for a wide audience far more judiciously.<sup>286</sup> This further strengthens the case for judicial deference to such documents.<sup>287</sup>

Secondly, *Barnhart* expressly states that interpretations that attempt to resolve questions of an "interstitial nature" are more likely to receive *Chevron* deference.<sup>288</sup> Many of the FDA's guidance documents are intended to fill in the gaps of the FD&C Act.<sup>289</sup> This further increases the likelihood that FDA guidance is entitled to *Chevron* deference.

Finally, by enshrining the GGPs in the FDAMA,<sup>290</sup> Congress has signaled that it expects and desires the FDA to make policy through guidance, provided that the FDA follows specified procedures. Insofar as *Chevron* and *Mead* derive from the theory that deference is warranted when Congress has delegated interpretive authority to the agency and the agency has utilized the authority granted to it by Congress,<sup>291</sup> one could reasonably argue that the FDA should receive deference when it produces policies through a system that has received Congress's imprimatur.

#### *e. Conclusion*

Because all of the above factors, with the single exception of binding effect/force of law, counsel in favor of *Chevron* deference, I conclude that *Chevron* is the appropriate framework to apply for FDA guidance documents. I concede that many district courts that have addressed the issue have concluded otherwise, but submit that these district

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<sup>286</sup> See Appendix A, Figure 5, *infra*. Accord Seiguer and Smith, *supra* note 12, 26 (Exhibit 5) (demonstrating that the FDA issues a total of approximately 100 guidance documents a year).

<sup>287</sup> Letters to individual firms from lower-level FDA employees may not be entitled to a high level of deference on this ground, however.

<sup>288</sup> 535 U.S. 212, 222 (2002); Sunstein, *supra* note 2, at 231-32.

<sup>289</sup> See *supra* Introduction.

<sup>290</sup> See *supra* Section I.H.2.

<sup>291</sup> See *United States v. Mead Corp.*, 533 U.S. 218, 226-27 (2001).

court decisions were influenced more by the presumption against preemption than an in-depth analysis of the applicable standard. Time will tell whose interpretation will prevail.

### *J. The Present Day*

Notwithstanding the doctrinal confusion described above, guidance is still alive and well at the FDA. *Mead* has not significantly deterred the FDA from using guidance as its primary method of policymaking.<sup>292</sup> The FDA currently produces roughly twice as many guidance documents per year as legislative rules,<sup>293</sup> and statistics suggest its annual output of guidance has increased regularly since the formulation of the GGPs.<sup>294</sup> The FDA continues to supply valuable guidance on a great variety of fascinating topics, many of which are at the forefront of scientific discovery (*e.g.*, "Source Animal, Product, Preclinical, and Clinical Issues Concerning the Use of Xenotransplantation Products in Humans;"<sup>295</sup> "ANDAs: Pharmaceutical Solid Polymorphism: Chemistry, Manufacturing, and Controls Information;"<sup>296</sup> "Current Good Manufacturing Practice in Manufacturing, Packaging, Labeling, or Holding Operations for Dietary Supplements"<sup>297</sup>).

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<sup>292</sup> *Letter, supra* note 101 ("It is my observation . . . that *Mead* has had no impact whatever on FDA with respect to the choice between informal guidance and notice-and-comment rulemaking. FDA has overwhelmingly chosen informal guidance for extremely practical reasons -- namely, the ease with which guidance can be issued."). *Accord* Appendix A, Figure 5, *infra*.

<sup>293</sup> Seiguer and Smith, *supra* note 12, at 25-26.

<sup>294</sup> *See* Appendix A, Figure 5, *infra*.

<sup>295</sup> Guidance for Industry: Source Animal, Product, Preclinical, and Clinical Issues Concerning the Use of Xenotransplantation Products in Humans (Apr. 2003), *available at* <http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Xenotransplantation/ucm074354.htm>.

<sup>296</sup> Guidance for Industry: ANDAs: Pharmaceutical Solid Polymorphism: Chemistry, Manufacturing, and Controls Information (Jul. 2007), *available at* <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm072866.pdf>.

<sup>297</sup> Guidance for Industry: Current Good Manufacturing Practice in Manufacturing, Packaging, Labeling, or Holding Operations for Dietary Supplements; Small Entity Compliance Guide (Dec. 2010), *available at* <http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/SmallBusinessesSmallEntityComplianceGuides/ucm238182.htm>.

From yesterday's FIDs to today's guidance documents on incredibly sophisticated topics, the FDA's various forms of guidance have always helped businesses avoid costly prosecution, and have facilitated the fulfillment of the FDA's regulatory mission. Ambiguities about binding effect and *Chevron* deference aside, it appears that the FDA will continue to use guidance as its primary policymaking method to effectuate its statutory mandate in the future.

## *II. Advantages and Disadvantages of Guidance for Stakeholders*

The foregoing has been a largely descriptive and historical account of the growth of guidance at the FDA. I now switch gears to evaluate whether, on the whole, these historical developments have been advantageous for the FDA's major stakeholders: regulated entities, regulatory beneficiaries (*i.e.*, the general public), and the agency itself. I conclude that although some entities have realized greater benefits from guidance than others, the growth of guidance at the FDA has been beneficial overall. I nonetheless recommend modest reforms that could allow stakeholders to fully realize all the benefits of guidance while minimizing its shortcomings.

### *A. Effect on the FDA*

The FDA has clearly benefited overall from its increased use of guidance. First and foremost, the FDA's implementation of informal guidance has conserved crucial administrative resources. Because the FDA operates under severe resource constraints that make it difficult to shoulder the massive regulatory burden Congress has assigned to

it,<sup>298</sup> guidance is a crucial weapon in the FDA's arsenal. Policymaking *via* informal guidance is far less costly and time-consuming than rulemaking.<sup>299</sup> As one FDA official has remarked, "To do a rule, it's a huge ordeal . . . there are economic analyses of the impact [of the proposed regulation], notice and comment, involvement of [the Office of Management and Budget], etc."<sup>300</sup> Many FDA officials have therefore agreed that using guidance instead confers massive cost advantages to the agency.<sup>301</sup> In the same vein, just as no statute can specify solutions in advance to every conceivable regulatory issue that could arise,<sup>302</sup> no regulation promulgated through notice-and-comment rulemaking could "realistically define and set forth every nuance of" the agency's approach.<sup>303</sup> Agencies must fill in the gaps. Guidance documents therefore allow agencies to inexpensively and quickly clarify and supplement legislative rules.<sup>304</sup> After all, "[i]t would be highly cumbersome to require rulemaking every time a detail is explained or amplified."<sup>305</sup>

Moreover, although it is difficult to empirically verify, evidence suggests that guidance facilitates voluntary industry compliance with FDA regulations and thereby conserves agency resources that would otherwise be consumed by adjudication and

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<sup>298</sup> Vladeck, *supra* note 213, at 983, 989-90, 998-99.

<sup>299</sup> *E.g.*, Raso, *supra* note 5, at 804-05; Jessica Mantel, *Procedural Safeguards for Agency Guidance: A Source of Legitimacy for the Administrative State*, 61 ADMIN. L. REV. 343, 351 (2009); Seiguer and Smith, *supra* note 12, at 24. This proposition is also borne out by empirical analysis. O'Connell, *supra* note 5, at 936 (data "suggests that notice-and-comment rulemaking has significant costs that agencies want to avoid").

<sup>300</sup> Seiguer and Smith, *supra* note 12, at 24.

<sup>301</sup> *Id.*

<sup>302</sup> John F. Manning, *Textualism as a Nondelegation Doctrine*, 97 COLUM. L. REV. 673, 699 (1997) (quoting *Mistretta v. United States*, 488 U.S. 361, 415 (1989) (Scalia, J., dissenting)). *See also* Hutt, *supra* note 36, at 102.

<sup>303</sup> Mendelson, *supra* note 10, at 410.

<sup>304</sup> *Id.*

<sup>305</sup> *Id.* It should be noted, however, that the agency would not necessarily need to use informal guidance documents to interpret ambiguous provisions in its regulations; courts permit agencies to use a variety of tools to fill in gaps in their regulations. *E.g.*, *Auer v. Robbins*, 519 U.S. 452, 461-62 (1997) ("Because the salary-basis test is a creature of the Secretary's own regulations, his interpretation of it is, under our jurisprudence, controlling unless 'plainly erroneous or inconsistent with the regulation.' . . . Petitioners complain that the Secretary's interpretation comes to us *in the form of a legal brief; but that does not, in the circumstances of this case, make it unworthy of deference.*" (emphasis added; internal citations omitted)).

enforcement proceedings.<sup>306</sup> Many representatives from the food, drug, and cosmetic industries have explained that "industry treats guidances no differently than rules . . . . Most business people don't know the difference between a reg[ulation promulgated through notice-and-comment rulemaking] and a guidance, so by and large the business field" is likely to follow guidance documents as if they were binding rules to avoid the risk of costly enforcement proceedings.<sup>307</sup> The likelihood that guidance averts costly litigation is increased by the fact that, unlike some agencies that may only threaten fines or inspections for noncompliance, the FDA "hold[s] gatekeeping power over private parties," especially in the context of new drugs and medical devices - FDA approval (or the lack thereof) can make or break a company.<sup>308</sup> "This power gives regulated entities a strong incentive to cooperate with the" FDA.<sup>309</sup>

Also, because litigants often face difficulties obtaining judicial review of guidance documents,<sup>310</sup> the FDA may be able to "forestall expensive litigation over [a given] policy's validity and avoid the possibility of an adverse judicial ruling" by utilizing guidance instead of rulemaking or adjudication.<sup>311</sup>

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<sup>306</sup> It is of course difficult to reliably estimate how many infractions would occur in the absence of guidance. However, anecdotal evidence collected from interviews conducted with industry representatives indicates that guidance does indeed prevent regulatory violations. Seiguer and Smith, *supra* note 12, at 27-31. *See also, c.f.*, FID 44 (Dec. 1, 1906) ("[I]t is evident that an overwhelming majority of the manufacturers, jobbers, and dealers of this country are determined to do their utmost to conform to the provisions of the act . . . . It is hoped, therefore, that the publication of the opinions and decisions of the Department will lead to the avoidance of litigation which might arise."); Peter A. Joy, *Making Ethics Opinions Meaningful: Toward More Effective Regulation of Lawyers' Conduct*, 15 GEO. J. LEGAL ETHICS 313, 367-68 (2002) ("agency officials presumably believe that the costs [of guidance] are offset by better voluntary compliance and a reduced need for enforcement"); Mendelson, *supra* note 10, at 412-13; Hunnicutt, *supra* note 2, at 172 (citing Anthony, *supra* note 11, at 1328-30) ("[P]eople tend to acquiesce to that which the government informs them constitutes the law.").

<sup>307</sup> Seiguer and Smith, *supra* note 12, at 29-30.

<sup>308</sup> Raso, *supra* note 5, at 803-04 (citing 21 U.S.C. § 360e).

<sup>309</sup> *Id.* at 803.

<sup>310</sup> Courts have often declined to deem policies expressed in guidance document final agency actions ripe for review. Mendelson, *supra* note 10, at 411-12; Raso, *supra* note 5, at 795.

<sup>311</sup> Mendelson, *supra* note 10, at 408.

Secondly, guidance facilitates regulatory flexibility.<sup>312</sup> Some FDA policies are subject to "such frequent change as to make their publication for [notice-and-comment rulemaking] virtually impossible."<sup>313</sup> Rulemaking, unlike guidance, "is ill-adapted to many technological and scientific problems," and may result in "rules that, by the time they are final, already have outlived their usefulness because technological or scientific advances have superseded them."<sup>314</sup> Guidance therefore allows the FDA to quickly respond to unforeseen emergencies and the rapid pace of scientific discovery and technological innovation.<sup>315</sup> For instance, only a few days after "a major break in a 120-inch diameter MWRA pipe that transports water to communities east of Weston, Massachusetts," the FDA was able to formulate and release a guidance document advising food manufacturers of proper water-use procedures in areas affected by a boil-water advisory.<sup>316</sup> Likewise, the FDA has been able to quickly issue guidance regarding evolving issues such as bioterrorism<sup>317</sup> and biotechnology.<sup>318</sup> Not only can guidance be issued relatively quickly in response to changing circumstances, it can also be "revoked relatively easily by publishing notice of revocation in the Federal Register."<sup>319</sup> Guidance

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<sup>312</sup> Johnson, *supra* note 13, at 701.

<sup>313</sup> 40 Fed. Reg. 40682, 40695 (1975).

<sup>314</sup> Bressman, *supra* note 222, at 1483 (quoting Lisa Schultz Bressman, *Beyond Accountability: Arbitrariness and Legitimacy in the Administrative State*, 78 N.Y.U. L. REV. 461, 545-46 (2003)).

<sup>315</sup> Seiguer and Smith, *supra* note 12, at 23.

<sup>316</sup> Guidance for Industry: Use of Water by Food Manufacturers in Areas Subject to a Boil-Water Advisory (May 2010), *available at* <http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/FoodDefenseandEmergencyResponse/ucm211373.htm>.

<sup>317</sup> CPG § 110.300, Registration of Food Facilities Under the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (originally issued Dec. 2003), *available at* <http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/FoodDefenseandEmergencyResponse/ucm121288.htm>.

<sup>318</sup> Guidance for Industry: Recommendations for the Early Food Safety Evaluation of New Non-Pesticidal Proteins Produced by New Plant Varieties Intended for Food Use (Jun. 2006), *available at* <http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/Biotechnology/ucm096156.htm>.

<sup>319</sup> Andersen, *supra* note 159, at 545. Mr. Andersen notes, however, that because "the FDA uses the more extensive notice-and-comment[-style] procedure for its guidance documents," as mandated by the GGPs,

has also afforded the FDA the ability to experiment with new policies before assuming the risk and cost of the rulemaking process.<sup>320</sup> Along similar lines, guidance permits the FDA to establish and publicize policies for which notice-and-comment rulemaking would be inappropriate: some policies constitute only minor suggestions to manufacturers and retailers that would not justify the expense of rulemaking, while other policies are so "voluminous and complex" that subjecting them to public comment would produce an administrative nightmare.<sup>321</sup> Thus, many FDA officials have remarked that guidance is the best way to provide detailed scientific information to the FDA's constituencies.<sup>322</sup> Guidance therefore provides a procedural apparatus through which the FDA can formulate systematic, agency-wide policies that might not otherwise exist.

Third, guidance allows the FDA to inexpensively regularize the conduct of low-level employees throughout the agency, "without risking an outside suit based on later noncompliance with [a policy that would otherwise be promulgated as a] legislative rule."<sup>323</sup> Guidance can ensure that FDA employees all over the United States will treat like situations alike, without necessitating resort to the notice-and-comment process.

For these reasons and more, many FDA representatives perceive that the agency's ever-increasing use of guidance has been beneficial.<sup>324</sup> Downsides do exist, however.

While guidance is often more cost-effective than rulemaking, that is not always the case.

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"that might impose a greater burden on the subsequent administration" to revoke prior guidance. *Id.* at 545 (citing Jack M. Beermann, *Presidential Power in Transitions*, 83 B.U. L. REV. 947, 994 (2003)).

<sup>320</sup> 40 Fed. Reg. 40682, 40695 (1975) ("The Commissioner recognizes that such guidelines, which do not have the legal status of regulations, are increasingly important in providing assistance both to the regulated industry and to agency employees who are charged with consistent and fair administration of the law. In many instances, such guidelines would be available on an informal basis before comparable regulations could be promulgated.").

<sup>321</sup> 40 Fed. Reg. 40682, 40695 (1975).

<sup>322</sup> Seiguer and Smith, *supra* note 12, at 23-24.

<sup>323</sup> Mendelson, *supra* note 10, at 409; *see also* Johnson, *supra* note 13, at 702.

<sup>324</sup> *See generally* Seiguer and Smith, *supra* note 12.

"There is a sense [among some FDA officials] that the development of guidances has come to resemble rulemaking in terms of the extent of clearance and time required to develop and implement them" because of the increased proceduralization established by the notice-and-comment-like requirements of the GGPs, as well as other layers of oversight.<sup>325</sup> Indeed, some guidance documents "take as long as rules to develop" and can trigger significant paperwork burdens.<sup>326</sup> Thus, some of the benefits of guidance may have been diminished somewhat.

Another disadvantage of guidance relates to the FDA's perceived credibility. The FDA's ability to achieve its regulatory objectives depends largely on the judicial branch's willingness to uphold FDA policies.<sup>327</sup> Judges' willingness to do so in turn depends in part on the FDA's reputation as a scientifically expert, depoliticized agency; courts are more likely to defer to decisions that appear the product of impartial, considered decisionmaking than those that appear to result from political posturing.<sup>328</sup> In recent years, however, the FDA has begun to be viewed by some commentators, rightly or wrongly, as a pawn of the executive branch, for reasons largely outside the scope of this article.<sup>329</sup> Guidance threatens to exacerbate this problem. Many commentators have accused administrative agencies generally of misusing guidance documents to circumvent procedures that "protect citizens from arbitrary decisions and enable citizens to

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<sup>325</sup> *Id.* at 24, 27.

<sup>326</sup> *Id.* at 24.

<sup>327</sup> O'Reilly, *supra* note 121, at 941-48.

<sup>328</sup> *See generally id.*

<sup>329</sup> *See generally id.* (alleging that the FDA has made ill-considered policy reversals to benefit Republican interests during President George W. Bush's administration); Vladeck, *supra* note 213 (blaming the FDA's lost credibility on a confluence of needlessly politicized decisions, crippling resource constraints, and a crisis in leadership).

effectively participate in the process."<sup>330</sup> Specifically, industry representatives have accused the FDA of inappropriately treating guidance documents as binding rules.<sup>331</sup> Thus, heavy reliance on guidance may create the impression that the FDA is setting policy opportunistically and capriciously. This impression may be inconsistent with reality; political scientist and recent law school graduate Connor Raso suggests in a deft empirical analysis of guidance documents at numerous agencies, including the FDA, that, contrary to widespread belief, "concern over agency abuse of guidance is" generally "overwrought."<sup>332</sup> However, if the perception that agencies abuse guidance nevertheless persists, the FDA may find it increasingly difficult to inexpensively create policies that will receive the judicial branch's imprimatur.

Finally, the *Mead* trilogy threatens to severely decrease the amount of deference afforded to FDA guidance documents. Therefore, to the extent the FDA relies on guidance as its primary mode of policymaking, it may find it increasingly difficult to win victories in court.

All in all, however, it appears that the added advantages of convenience, flexibility, cost savings, and intra-agency discipline outweigh the disadvantages of guidance. Thus, I conclude that the FDA has benefited greatly from its increasing reliance on guidance.

### *B. Effect on Regulated Entities*

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<sup>330</sup> H.R. REP. NO. 106-1009, at 1 (2000). *See generally, e.g.*, Hunnicutt, *supra* note 2; Andersen, *supra* note 159.

<sup>331</sup> Seiguer and Smith, *supra* note 12, at 29-30.

<sup>332</sup> *See generally* Raso, *supra* note 5. While Raso's study has some limitations that he readily acknowledges, he painstakingly analyzes numerous metrics, all of which support his hypothesis, and his Note has consequently been lauded by leading textbook authors. Peter Shane, *Might the Motivation for Agency Guidance Be the Public's Need for Guidance?*, JOTWELL, Mar. 22, 2010, <http://adlaw.jotwell.com/might-the-motivation-for-agency-guidance-be-the-publics-need-for-guidance/>.

The effect of guidance on regulated entities is more dichotomous. As Professor Michael Asimow notes, guidance is beneficial to industry insofar as it reduces uncertainty and mitigates business risk:

Members of the public who live and do business in the shadow of regulation need to learn what the agency thinks the law means and how discretion may be exercised. Increasing the level of people's understanding about what the law requires of them is a good thing for society; it reduces the number of unintentional law violations, and it reduces the transaction costs incurred in planning private transactions.<sup>333</sup>

As a result, many representatives of the food, drug, and cosmetic industries have applauded the certainty that FDA guidance provides.<sup>334</sup> Industry players particularly dislike uncertainty in the form of long waiting periods; thus, even though there have been instances where the guidance-making process has been plagued by delays, guidance has greatly benefited industry by enabling the FDA to broadcast its positions on pressing issues sooner than would generally occur through rulemaking.<sup>335</sup> Guidance also provides certainty in the form of consistency by ensuring that lower-level agency employees will treat similar situations alike.<sup>336</sup> This provides a level playing field for industry, which industry representatives consider a "paramount concern."<sup>337</sup>

The GGPs have provided further benefit to regulated entities. Publishing guidance in the Federal Register and requiring guidance documents to clearly state to what activities and entities the policy applies has "enhance[d] understanding among the public

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<sup>333</sup> Michael Asimow, *California Underground Regulations*, 44 ADMIN. L. REV. 43, 43 (1992) (citing MICHAEL ASIMOW, *ADVICE TO THE PUBLIC FROM FEDERAL ADMINISTRATIVE AGENCIES* 11-15 (1973)).

<sup>334</sup> Seiguer and Smith, *supra* note 12, at 29-31.

<sup>335</sup> *Id.* at 31.

<sup>336</sup> See Mendelson, *supra* note 10, at 409 (citing Peter L. Strauss, *Publication Rules in the Rulemaking Spectrum: Assuring Proper Respect for an Essential Element*, 53 ADMIN. L. REV. 803, 842-43 (2001)) ("Agencies rely on [guidance documents] to ensure that lower-level employees complete forms correctly and make consistent (and thus more predictable) decisions.").

<sup>337</sup> Seiguer and Smith, *supra* note 12, at 30.

and the Agency" and "contribute[d] to better awareness of the FDA's rules."<sup>338</sup> Moreover, as scientific advancement becomes increasingly complicated, the opportunities for public participation established by the GGPs are "essential" to ensure sensible regulatory policy "in areas where the expertise needed to develop a particular guidance . . . resides outside of the agency."<sup>339</sup>

However, even though the GGPs allow for greater public participation, guidance remains less formal than the notice-and-comment rulemaking process; as a result, industry representatives still have a diminished ability to provide input on the policies that will ultimately control their operations. The fact that the GGPs approximate notice-and-comment procedures alleviates this concern, but these procedures do not require the FDA to strongly consider and respond to all industry-submitted comments.<sup>340</sup> As a result, some industry representatives have stated that "even though FDA accepts comments from the public, . . . it is very unusual for the FDA to actually change its position or incorporate any of the feedback into the guidance or final rule."<sup>341</sup> Not all industry representatives share this pessimistic view, however.<sup>342</sup>

Likewise, obtaining judicial review of policies expressed in guidance documents is quite difficult due to the finality and ripeness doctrines, unlike regulations promulgated through notice-and-comment rulemaking.<sup>343</sup> Thus, a firm that disagrees with an FDA policy expressed in a guidance document or believes the policy is not issued in

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<sup>338</sup> Hunnicutt, *supra* note 2, at 180.

<sup>339</sup> Seiguer and Smith, *supra* note 12, at 30-31. For instance, "[t]he recent development process for the guidance on pharmacogenomics data submission was cited as a good example of creating more transparency." *Id.*

<sup>340</sup> *See supra* Section I.H.2.

<sup>341</sup> Seiguer and Smith, *supra* note 12, at 30.

<sup>342</sup> *Id.*

<sup>343</sup> Raso, *supra* note 5, at 795; Johnson, *supra* note 13, at 712-13.

accordance with law has little recourse if the FDA refuses to acknowledge its dissenting comments; it must either abide by the policy or roll the dice and risk penalties.<sup>344</sup>

Thus, the industry's views are divided on guidance: some businesses appreciate guidance for clearly delineating the legal boundaries of their activities in advance, while others decry its lack of procedural formality.<sup>345</sup> Of course, some grumbling from industry is always to be expected; nobody enjoys being regulated by the government, and businesses will naturally criticize any regime that restricts their action. That said, some of the industry's criticisms are valid and warranted; perhaps the FDA should pay greater attention to the comments it receives, although requiring the agency to respond to each and every important comment, as it is required to in notice-and-comment rulemaking, would unwisely eliminate many of the cost savings that guidance confers on the FDA and obliterate the distinction between guidance documents and rules.

The growth of guidance has thus conferred benefits and disadvantages upon industry. Because guidance shows no signs of flagging, industry must adapt accordingly.

### *C. Effect on Regulatory Beneficiaries*

Some of the features of guidance that benefit the FDA also benefit regulatory beneficiaries. For instance, the FDA is better able to protect the consuming public if it can create or modify policy quickly and inexpensively through guidance documents in response to changing circumstances. Given the aforementioned severe resource constraints at the FDA, guidance is therefore vital to protect the public.<sup>346</sup> Although the GGPs impose some additional procedural costs on the guidance-making process, to the

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<sup>344</sup> Johnson, *supra* note 13, at 712; Mendelson, *supra* note 10, at 412-13.

<sup>345</sup> Seiguer and Smith, *supra* note 12, at 27-31.

<sup>346</sup> Vladeck, *supra* note 213, at 983-84, 989-90, 998-99.

detriment of both the agency and the public, those costs are partially offset by the increased opportunities for public comment, which helps guard against the dreaded phenomenon of agency capture.<sup>347</sup> However, regulatory beneficiaries are less likely to get involved in guidance development than regulated businesses because the marginal benefit to any one individual from any given change in regulatory policy is unlikely to outweigh the costs of organizing.<sup>348</sup> Thus, while the GGPs may be beneficial to stakeholders overall, their benefit to regulatory beneficiaries is attenuated. Indeed, even though the GGPs create far more opportunities for public participation than the guidance-making procedures of other agencies,<sup>349</sup> some have criticized the GGPs for not going far enough to facilitate participation from regulatory beneficiaries.<sup>350</sup>

Likewise, if judicial review of FDA guidance is difficult to obtain for regulated entities, it is almost impossible to obtain for regulatory beneficiaries because of the doctrines of standing, finality, and ripeness.<sup>351</sup> In particular, when the FDA issues a guidance document promising not to bring enforcement actions against businesses that

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<sup>347</sup> Johnson, *supra* note 13, at 703.

<sup>348</sup> "[C]ertain characteristics of regulatory beneficiaries may lead them to be less involved in policy development. First, learning about the existence of guidances before they are finalized can be difficult and expensive unless the agency chooses to give public notice or else initiates contact. Regulatory beneficiary groups may have fewer resources to devote to this sort of information gathering. Second, if regulatory beneficiary groups are diffuse or poorly organized, they may face significant obstacles to organizing in a way that fully represents their interests . . . The intended beneficiaries of these statutes represent extraordinarily large and diffuse groups, including not only those who currently benefit from these laws but also many who cannot yet self-identify (such as . . . fetuses, in the case of toxics and food safety regulation) . . . Third, regulatory beneficiaries may lack the political clout that might otherwise motivate an agency to seek their approval . . . Finally, regulated entities may have more to lose and more to spend than regulatory beneficiaries, giving them both a greater incentive and a greater ability to participate in the process." Mendelson, *supra* note 10, at 430-31.

<sup>349</sup> See generally *id.* (arguing that most agencies' guidance-making processes provide insufficient protections for regulatory beneficiaries, and that procedural reform of informal guidance is warranted).

<sup>350</sup> *Id.* at 428-29 (arguing that the GGPs "create[] asymmetrical public participation").

<sup>351</sup> *Id.* at 420-24.

comply with enumerated requirements, regulatory beneficiaries will likely never be able to challenge that policy due to the rule against judicial review of agency inaction.<sup>352</sup>

While it is difficult to weigh these largely incommensurate costs and benefits to regulatory beneficiaries, I conclude that the FDA's guidance regime, subjected to the rigors of the GGPs, is on balance good for the general public. If the FDA did not have guidance at its disposal, it would have to create policy through ossified and costly means, namely rulemaking and adjudication. Given the FDA's budget constraints, I argue that the public is better served by partially sacrificing public participation and judicial review for bureaucratic efficiency. Although the general public has largely lost its faith in the view that agencies are completely depoliticized entities that make decisions solely based on science, accumulated wisdom, and expertise, the FDA remains an expert agency that is generally in a better position than the public to set regulatory policy. 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.<sup>353</sup> The current guidance regime may have its lumps, but on the whole it appears to effectively balance both political accountability and cost-effectiveness.

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<sup>352</sup> *Id.* at 421-22 (citing *Heckler v. Chaney*, 470 U.S. 821, 831-32 (1985)).

<sup>353</sup> For instance, while it is undoubtedly important for the FDA to monitor and investigate levels of pathogens in dairy products, it is unlikely that the average consumer will dispute the FDA's decision to set a tolerance level for *Bacillus cereus* in milk at 10<sup>4</sup> cfu/g, rather than, say, 10<sup>3</sup> cfu/g. *See* Compliance Policy Guide § 527.300, Dairy Products - Microbial Contaminants and Alkaline Phosphatase Activity (Dec. 2010), available at <http://www.fda.gov/downloads/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/UCM238465.pdf>. While the general public's presumed inability to understand and meaningfully comment upon very complex FDA policies certainly does not justify totally excluding the public from the deliberative process, *c.f.* Hutt, *supra* note 98, at 220, the benefits of administrative ease likely outweigh the cost of decreased public participation in such cases.

#### *D. Suggested Reforms*

Thus, it seems that the pros of the FDA's current guidance regime outweigh its cons. As Professor Rakoff argues,

[i]n the process of regulating the economy through administrative action, processes which are partially formal, and partially informal, are to be preferred over either very formal processes or very informal processes. In other words, the general run of economic regulation -- which does not greatly implicate civil liberties -- will be best carried out by a process lying somewhere in the middle of the scale.<sup>354</sup>

The GGPs therefore create a guidance system that establishes an arguably ideal intermediate level of (in)formality by largely avoiding both crippling ossification and unchecked bureaucratic discretion. I therefore suggest no major procedural reforms for the FDA's guidance regime, save perhaps for the minor suggestion that the FDA do more to assure regulated entities that they seriously consider the comments submitted by industry. Rather, my reform proposals relate to the two major sources of ambiguity that I discussed earlier: the confusion regarding whether and which guidance documents bind the FDA, and the question of the degree of judicial deference owed to FDA guidance documents.

##### *1. The FDA Should Clarify, via Notice-and-Comment Rulemaking, that Advisory Opinions Are Non-Binding*

The FDA should finish the job it started in 1992 and promulgate its previously proposed regulation deeming all guidance documents non-binding, be they advisory opinions, CPGs, etc. The FDA already acts as if many of these documents are non-

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<sup>354</sup> Rakoff, *supra* note 11, at 171-72.

binding, especially the CPGs;<sup>355</sup> the notice-and-comment rulemaking would thus be a simple housecleaning measure that would not significantly affect the way the FDA currently engages in policymaking, but would eliminate the risk that the FDA could be held to a policy it erroneously considered non-binding. Moreover, the proposed regulation would probably not encounter much opposition; of the people who submitted comments when the FDA did away with binding effect for guidance documents, more were in favor of the FDA's reversal in policy than against it.<sup>356</sup>

This solution is preferable to the other options. I do not recommend that the FDA instead promulgate a regulation attempting to differentiate between binding advisory opinions and non-binding guidance documents; the two are too difficult to distinguish at the margins, and the regulation would therefore engender even more confusion.<sup>357</sup> Nor is it presently a viable option for the FDA to return to its 1977 regime where all guidance documents bind the agency; that possibility was foreclosed by the FDAMA's codification of the GGP's.<sup>358</sup>

## 2. *Congress or the Supreme Court Must Clarify Mead*

The Supreme Court's decisions in *Mead* and its progeny have rendered judicial review of all guidance documents a catastrophic mess that will continue to consume precious litigation resources until the confusion is resolved.<sup>359</sup> *Mead* likewise threatens to further ossify agency policymaking by driving agencies to costly and inflexible notice-

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<sup>355</sup> See *supra* Section I.H.3.

<sup>356</sup> 62 Fed. Reg. 8961, 8962-63 (1997).

<sup>357</sup> Telephone Interview, *supra* note 189.

<sup>358</sup> Pub. L. No. 105-115, §405, 111 Stat. 2296, 2368-69 (codified at 21 U.S.C. § 371(h) (1997)).

<sup>359</sup> See *supra* Section I.H.

and-comment rulemaking to achieve *Chevron* deference.<sup>360</sup> Many agree that either Congress<sup>361</sup> or the Supreme Court should replace *Mead* with an alternate approach; what scholars disagree about is what that alternate approach should be.

I first argue that *Mead* should be replaced with an across-the-board rule of some sort, rather than the indeterminate multi-factor standard that currently exists. As Professor Sunstein persuasively argues,

[t]he Court seems to have opted for a complex standard over a simple rule in precisely the circumstances in which a complex standard makes the least sense: numerous decisions in which little is gained by particularized judgments. These are the settings in which a standard imposes high decisional burdens while also offering little or no gain in terms of increased accuracy. Because the scope of judicial review of agency interpretations comes up so often--indeed, because that issue is the opening question in a vast array of administrative law cases--the Step Zero trilogy forces courts to undertake complex inquiries when it is far from clear that anything at all is gained by the ultimate conclusion that *Skidmore*, rather than *Chevron*, provides the governing standard.<sup>362</sup>

There are numerous across-the-board rules that could conceivably replace *Mead*: (1) all authoritative agency interpretations of ambiguous provisions of their organic statutes could receive *Chevron* deference;<sup>363</sup> (2) only policies formulated through formal adjudication and notice-and-comment rulemaking are eligible for *Chevron* deference, while all other informal interpretations could receive, at most, *Skidmore* respect;<sup>364</sup> (3) informal guidance could be reviewed *de novo*; (4) etc. While it is beyond the scope of this article to opine on what standard should apply for all agencies, I conclude that, at least as far as the FDA is concerned, Congress should mandate *Chevron* deference for

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<sup>360</sup> See *supra* Section I.H.

<sup>361</sup> Many scholars agree that Congress may permissibly modify the *Chevron* framework. Cf., e.g., Thomas W. Merrill, *Judicial Deference to Executive Precedent*, 101 YALE L.J. 969, 1031 (1992).

<sup>362</sup> Sunstein, *supra* note 2, at 228-29. See generally Louis Kaplow, *Rules Versus Standards: An Economic Analysis*, 42 DUKE L.J. 557 (1992).

<sup>363</sup> See, e.g., *United States v. Mead Corp.*, 533 U.S. 218, 241 (2001) (Scalia, J., dissenting).

<sup>364</sup> See, e.g., Johnson, *supra* note 13 740-41.

guidance documents issued in accordance with the GGPs, or at least for Level 1 Guidance Documents. I generally agree with Professor Bressman that "we should restrict *Chevron* deference to procedures or interpretations that reflect transparency, rationality, and consistency,"<sup>365</sup> and I argue that FDA guidance documents promulgated in accordance with the GGPs largely fulfill those important values. They are transparent insofar as they subject proposed FDA policies to a probing review process that approximates the rigor of notice-and-comment rulemaking and provides opportunities for public participation. They are rational insofar as they originate from an expert agency applying its accumulated wisdom to a complex statutory scheme. While I acknowledge that the non-binding nature of guidance may threaten the value of consistency,<sup>366</sup> there are other strong mechanisms for ensuring administrative consistency; namely, the APA's prohibition against arbitrary and capricious changes in policy.<sup>367</sup> Indeed, the *Chevron* case itself granted deference to an interpretation the agency had not held consistently over time; consistency is therefore decidedly not a necessary condition for *Chevron* deference, even if it is relevant.<sup>368</sup> Furthermore, as described *supra* in Section I.I.2, guidance documents promulgated in accordance with the GGPs fulfill many of the *Christensen/Mead/Barnhart* factors, and therefore encourage the values those decisions

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<sup>365</sup> Bressman, *supra* note 222, at 1492.

<sup>366</sup> Of course, if advisory opinions and CPGs do indeed bind the FDA, the case for *Chevron* deference to those documents would be much stronger. See *supra* Section I.H.3.

<sup>367</sup> 5 U.S.C. § 706(2)(A) (2011). As the Supreme Court has held, "[a]gency inconsistency is not a basis for declining to analyze the agency's interpretation under the *Chevron* framework. Unexplained inconsistency is, at most, a reason for holding an interpretation to be an arbitrary and capricious change from agency practice under the Administrative Procedure Act." *Nat'l Cable & Telecomms. Ass'n v. Brand X Internet Servs.*, 545 U.S. 967, 981 (2005) (citing *Motor Vehicle Mfrs. Ass'n of United States, Inc. v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 46–57 (1983)).

<sup>368</sup> "The fact that the agency has from time to time changed its interpretation of the term 'source' does not, as respondents argue, lead us to conclude that no deference should be accorded the agency's interpretation of the statute. An initial agency interpretation is not instantly carved in stone. On the contrary, the agency, to engage in informed rulemaking, must consider varying interpretations and the wisdom of its policy on a continuing basis." 467 U.S. 837, 863-64 (1984).

aimed to secure. Finally, *Chevron* deference is desirable as a normative matter because it would help the FDA, an underfunded and overworked agency charged with the massive and vitally important task of ensuring the safety of the American people,<sup>369</sup> fulfill its regulatory objectives inexpensively without hampering its flexibility. Because empirical research suggests that, despite popular belief, agencies do not strategically abuse guidance to avoid the rulemaking process for inappropriate or improper reasons,<sup>370</sup> I argue that critics of guidance need not be so averse to applying *Chevron* deference to FDA guidance documents. Indeed, "*Chevron* is no blank check to agencies;" the *Chevron* two-step framework ensures "that agencies will lose if Congress has clearly forbidden them from acting as they have chosen," and the decision "operates as a safeguard against insufficiently justified interpretations."<sup>371</sup> Additionally, "judicial review always remains available for lack of substantial evidence or arbitrariness, and unreasonable agency decisions will be struck down even if there is no problem under either step of *Chevron*."<sup>372</sup>

Thus, guidance documents should receive *Chevron* deference as both a doctrinal and a normative matter. Congress could effect this change by amending the section of the FDAMA that codified the GGPs to explicitly state that *Chevron* is the proper framework to apply to guidance documents, or alternatively by amending the APA to clarify the circumstances in which *Chevron* deference is applicable for all agencies.

### *III. Possible Directions for Future Research*

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<sup>369</sup> See Vladeck, *supra* note 213, at 983, 989-90, 998-99.

<sup>370</sup> See generally Raso, *supra* note 5.

<sup>371</sup> Sunstein, *supra* note 2, at 227-28 (citations omitted).

<sup>372</sup> *Id.* at 228 (citations omitted).

Other possible directions for further research abound. While I have collected some data regarding the FDA's average annual output of guidance documents during various key periods of administrative law,<sup>373</sup> I have not undertaken a rigorous quantitative analysis to test for statistical significance and control for lurking variables; nor have I compiled matching data of the FDA's average annual output of regulations promulgated through formal and informal rulemaking for comparison purposes. I strongly urge one whose undergraduate statistics textbook is far less dusty than mine to investigate and compare these variables over time. It would be particularly useful to empirically analyze whether *Mead* has affected the frequency with which the FDA issues guidance documents; although it appears that the *Mead* trilogy has not significantly deterred the FDA from utilizing guidance,<sup>374</sup> statistical investigation would nonetheless be worthwhile.

Similar historical and normative analyses of policymaking at other administrative agencies could be performed as well. Not only would such studies be of value to persons primarily interested in those agencies, they would also permit a comparison of various agencies' behavior over time in response to changing circumstances. From this, one could extrapolate the ideal means of policymaking for a number of agencies, in order that agencies may conduct their operations in a manner that maximizes stakeholder welfare. To be sure, there is no "one-size-fits-all" policymaking approach for administrative agencies - all agencies are very different - but such scholarship could shed light on which methods are most effective for agencies with certain characteristics.

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<sup>373</sup> See *infra* Appendix A.

<sup>374</sup> See Section I.J. *supra*.

Also, as an anecdotal matter, it would be fascinating to investigate why the FDA abandoned its original regulation that would have rendered advisory opinions non-binding.

### *Conclusion*

The story of guidance at the FDA is full of twists and turns. After a century of experimentation, the FDA has stumbled upon a formula that reasonably accommodates the conflicting interests of stakeholders. If slight tweaks are made to resolve vexing doctrinal ambiguities, the FDA will be in an excellent position to protect consumers of food, drugs, devices, and cosmetics for the centuries to come.

*Appendix A: FDA Guidance by Year*

Figure 1. Food Inspection Decisions (FIDs) Issued by the Bureau of Chemistry Between 1902-1927 (Approximate)<sup>375</sup>

<b>Year</b>	<b># of FIDs*</b>
1902	1
1903	1
1904	6
1905	24
1906	16
1907	35
1908	19
1909	8
1910	19
1911	9
1912	11
1913	3
1914	5
1915	5
1916	4
1917	5
1918	7
1919	3
1920	3
1921	3
1922	3
1923	3
1924	2
1925	2
1926	8
1927	7
<b>Total</b>	<b>212</b>
<b>Avg.</b>	<b>8</b>

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<sup>375</sup> Figures for years 1914-1927 are approximate but the total of 212 is accurate.

Figure 2. Trade Correspondences Issued Between 1938-46<sup>376</sup>

<b>Year</b>	<b># of Trade Correspondences</b>
1938	6
1939	7
1940	336
1941	29
1942	18
1943	14
1944	14
1945	12
1946	3
<b>Total</b>	<b>439</b>
<b>Avg./Year</b>	<b>49</b>

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<sup>376</sup> 1938-49, *supra* note 40, 561-753.

Figure 3. Statements of General Policy or Interpretation Issued Between 1947-56  
(Includes Amendments)<sup>377</sup>

<b>Year</b>	<b># of Statements</b>
1947	2
1948	5
1949	6
1950	7
1951	6
1952	2
1953	5
1954	6
1955	4
1956	3
<b>Total</b>	<b>46</b>
<b>Avg./Year</b>	<b>5</b>

<sup>377</sup> 1938-49, *supra* note 40, 755-62; VINCENT A. KLEINFELD AND CHARLES WESLEY DUNN, FEDERAL FOOD, DRUG, AND COSMETIC ACT 1949-1950 283-90 (1951); 1951-52, *supra* note 69, 385-89; 1953-57, *supra* note 67, 309-22.

Figure 4. Formal and Informal Statements of General Policy or Interpretation Issued Between 1957-1968 (Includes Amendments)<sup>378</sup>

<b>Year</b>	<b># Formal Statements</b>	<b># Informal Statements</b>	<b>Total # of Statements</b>
1957	3	13	16
1958	3	8	11
1959	5	3	8
1960	3	0	3
1961	2	2	4
1962	2	1	3
1963	2	1	3
1964	4	0	4
1965	7	0	7
1966	7	0	7
1967	6	1	7
1968	12	0	12
<b>Total</b>	<b>56</b>	<b>29</b>	<b>85</b>
<b>Avg./Year</b>	<b>5</b>	<b>2</b>	<b>7</b>

<sup>378</sup> 1953-57, *supra* note 67, 807-10; 1958-60, *supra* note 72, 223-248; 1961-64, *supra* note 77, 261-72; 1965-68, *supra* note 78, 483-512.

Figure 5. Guidance Issued by FDA in Accordance with GGP, 1975-2009, by Center (Approximate)<sup>379</sup>

<b>Year</b>	<b>CBER</b>	<b>CDER</b>	<b>CDRH</b>	<b>CFSCAN</b>	<b>CVM</b>	<b>Comm.</b>	<b>Total</b>
<b>1975</b>	0	0	3	0	1	0	4
<b>1976</b>	0	0	11	0	1	0	12
<b>1977</b>	0	5	6	0	0	0	11
<b>1978</b>	0	2	3	0	0	0	5
<b>1979</b>	0	0	1	0	0	0	1
<b>1980</b>	1	0	4	0	0	0	5
<b>1981</b>	0	0	3	0	0	0	3
<b>1982</b>	0	0	1	1	0	0	2
<b>1983</b>	0	0	2	1	1	0	4
<b>1984</b>	0	1	1	0	2	0	4
<b>1985</b>	1	1	6	2	2	0	12
<b>1986</b>	0	0	3	0	0	0	3
<b>1987</b>	2	9	10	0	0	0	21
<b>1988</b>	0	1	6	1	0	1	9
<b>1989</b>	2	6	12	0	0	0	20
<b>1990</b>	0	2	11	0	1	0	14
<b>1991</b>	1	0	12	1	0	0	14
<b>1992</b>	3	5	16	1	1	0	26
<b>1993</b>	1	6	27	4	2	1	41
<b>1994</b>	2	10	28	1	4	0	45
<b>1995</b>	5	11	36	4	1	0	57
<b>1996</b>	2	12	40	2	1	0	57
<b>1997</b>	5	20	29	5	0	3	62

<sup>379</sup> These statistics have been collected from the comprehensive list of FDA guidance documents available at 75 Fed. Reg. 48180, 48180-48233 (2010). (Key: CBER = Center for Biologics Evaluation and Research; CDER = Center for Drug Evaluation and Research; CDRH = Center for Devices and Radiological Health; CFSCAN = Center for Food Safety and Applied Nutrition; CVM = Center for Veterinary Medicine; Comm. = Office of the Commissioner.) Figures include both draft and final guidance, including guidance that is no longer effective. These figures are approximate because the list is both over- and under-inclusive. The figures only represent documents labeled by the FDA as "guidance" simpliciter; they do not include CPGs, TCs, informal letters to individual parties, or preambles to federal regulations. The figures also do not include revisions to existing guidance or guidance documents listed without an issuance date on the comprehensive list. Some figures may therefore be deflated. On the other hand, because some centers include some guidance documents under more than one category, some figures may be inflated. The statistics nonetheless paint a reasonably accurate picture of the FDA's ever-increasing use of guidance.

<b>1998</b>	16	61	55	5	5	18	160
<b>1999</b>	19	25	20	11	5	2	82
<b>2000</b>	16	26	37	5	3	1	88
<b>2001</b>	26	31	27	16	12	5	117
<b>2002</b>	12	23	24	11	10	4	84
<b>2003</b>	24	29	30	27	7	5	122
<b>2004</b>	21	37	27	17	3	9	114
<b>2005</b>	19	36	28	9	4	10	106
<b>2006</b>	32	39	32	13	16	16	148
<b>2007</b>	28	20	39	13	10	5	115
<b>2008</b>	26	30	40	15	6	7	124
<b>2009</b>	30	59	29	25	16	10	169
<b>Total</b>	294	507	659	190	114	97	1861
<b>Avg.</b>	8	14	19	5	3	3	53