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DRUG REGULATION AND THE CONSTITUTION AFTER WESTERN STATES

Margaret Gilhooley *

I. INTRODUCTION

For the first time, the Supreme Court of the United States has invalidated a provision of the federal laws governing food and drugs1 based on the constitutional protections for commercial speech. In Thompson v. Western States Medical Center,2 the Court found that the First Amendment barred Congress from precluding advertising about “drug compounding” when other restrictions, such as a warning about the lack of Food and Drug Administration (“FDA”) testing, provided adequate alternatives to protect the public.3 Drug compounding is the practice in which a pharmacist produces unapproved variations of approved drugs to meet individual needs in accordance with a physician’s prescrip-

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2. 122 S. Ct. 1497 (2002).
3. Id. at 1506, 1508. The effect of the litigation has been to invalidate the entire provision that exempted pharmacy compounding from the usual drug approval requirements since no party appealed the lower court’s finding that the advertising restriction was non-severable. The legality of compounding activity will turn on whether the specific practice violates general provisions of the law, such as those relating to interstate commerce and an intent to distribute a new drug. See 21 U.S.C. §§ 321(g), 331(a), 331(k), 352(f), 355 (2001). The FDAMA provision resembles a "safe harbor" rather than a specific prohibition. In Washington Legal Foundation v. Henney, a legislative provision that was merely a safe harbor was found not to present a facial challenge to speech, making preenforcement review inappropriate. 202 F.3d 331 (D.C. Cir. 2000). See Margaret Gilhooley, Constitutionalizing Food and Drug Law: When Avoidance Is Right, 38 HOU. L. REV. 1383 (2002).
tion. Congress barred advertisements about compounding for specific drugs because, according to the FDA, the ads are “fair proxy for actual or intended large-scale manufacturing” of untested drugs. This article examines the dispute among the Justices regarding the rigor with which the commercial speech test announced in Central Hudson Gas & Electric Corp. v. Public Service Commission of New York is applied, and the tensions involved in reconciling stricter commercial speech protections with the deference accorded Congress in the regulation of commercial products. The article then turns to Western States’s wider relevance to food and drug regulation, and the extent to which a disclaimer about the lack of FDA testing or approval might be considered a constitutionally permitted alternative to meeting statutory requirements for FDA drug approval. Attention is given to whether any changes in the FDA’s approach to the direct-to-consumer (“DTC”) advertising of prescription drugs are needed on constitutional grounds, or alternatively on a statutory or policy basis. The paper also explores the difficulties in developing non-misleading disclosures for drugs that are promoted for off-label unapproved uses, and the likely resistance to fully adequate disclosures.

II. COMMERCIAL SPEECH ANALYSIS

A. Central Hudson as Applied: The Dispute About Its Meaning

The evolving tests and growing reach of commercial speech protections have already received extensive analysis. In Western States...
States, the Court applied the framework set forth in *Central Hudson*, although Justice O'Connor acknowledged the dissatisfaction various Justices have expressed with the test. What deserves comment here is that while the Justices use the same test, they differ on its meaning in practice. The majority emphasized the need for an express showing by the government about the lack of alternative, less restrictive means of accomplishing the interest served by the regulation. Justice Breyer's dissent was more willing to read the government's regulatory rationale broadly in ways that serve the underlying safety aim of the statute. The majority opinion criticized the dissent as providing "hypothesized justifications" for the scheme, an inappropriate approach in dealing with speech protections. Exploring these differences involves an examination of drug compounding and the intricacies of the multi-pronged *Central Hudson* test.

B. The Majority Identifies the Government's Basis

The government did not argue that ads for drug compounding concerned an unlawful activity or that they were inherently misleading, which, if established, would have justified regulation. Instead, the government sought to show that the remaining three prongs of the *Central Hudson* test were met: that the restriction served a substantial governmental interest, that it directly advanced the interest, and that it was "not more extensive than necessary" to serve the interest.

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9. 447 U.S. at 566.
10. W. States, 122 S. Ct. at 1504. Neither party contended that any other test should be applied. *Id.* Justice Thomas concurred in the application of the test but reiterated his preference for a different test. *Id.* at 1509 (Thomas, J., concurring).
11. *Id.* at 1506.
12. *Id.* at 1510, 1515 (Breyer, J., dissenting).
13. *Id.* at 1507.
14. *Id.* at 1504.
15. *Id.* at 1504–06.
The government identified an interest in preserving the integrity of the new drug approval process, since systematic testing protects the public from safety risks and ineffective drugs that doctors cannot discover from observation in the practice of medicine. The government also identified an interest in allowing pharmacies to compound variations of drugs when a physician prescribes the compound for patients who have allergies, require special dosages, or have other individualized needs. The FDA recognized that requiring FDA pre-market approval of all drug compounding would, as a practical matter, eliminate the activity because of the costs involved in conducting drug testing and obtaining agency approval. The government believed there was a separate substantial interest in balancing the availability of drug compounding to meet individualized needs with preventing the practice from being a guise for unregulated drug manufacturing on a large scale. To draw this line, Congress exempted drug compounding from new drug approval requirements, subject to restrictions such as limits on the amount of compounding done in advance of a physician prescription, limits on shipments out-of-state, and most importantly, a prohibition on advertisement of the availability of compounding for specific drugs. According to the government, the advertising restriction directly advanced this balancing interest because ads were neither needed nor useful for services to meet customized individual needs, but were associated with the production of drugs for a large market. Thus, the government contended that advertising is “a fair proxy for actual or intended large-scale manufacturing,” for which drug approval is required.

16. Id. at 1504.
17. Id. at 1504–05.
18. Id. at 1505. “Pharmacists do not make enough money from small-scale compounding to make safety and efficacy testing of their compounded drugs economically feasible.” Id.
19. Id. at 1505. The FDA did not allow compounding that was, for example, the equivalent of making generic drugs without agency approval. Id. at 1502.
20. Id. However, advertising to consumers and doctors about the general availability of compounding services was allowed. Id.
21. Id. at 1505.
22. Id.
C. Majority's Analysis of Ads as Limiting the Scale of Compounding

The majority found that the government had an important interest in preserving the integrity of the new drug approval process and in making as many drugs as possible subject to the process. The Court was also willing to assume that the ad restrictions on compounding might directly advance that interest by precluding the marketing of compounded drugs on the large scale that makes testing affordable. The fatal inadequacy in the government's argument, as often occurs in commercial speech cases, was in the final prong of Central Hudson: the failure to show that the speech restriction was "not more extensive than necessary" in light of other possible alternatives. The Court's discussion illustrates the burden of detailed justification needed to meet this final hurdle.

The Court thought the government's aims in preventing large-scale compounding might have been met by alternative measures, identified in an earlier FDA guidance document as indicators of inappropriate compounding, such as the use of commercial scale manufacturing equipment. The government also might have relied solely on the other restrictions in the statute, such as the limit on the amount made in advance of receiving a prescription. The Court also added the new possibility of capping the amount of compounding for any particular drug by volume, the number of prescriptions, or, remarkably, even by the profit a pharmacy makes in a period of time. The government had failed to discuss why these alternatives, individually or in combination, were not sufficient. There was no showing by the government in the "leg-

23. Id.
24. Id. at 1505-06.
25. See Lorillard Tobacco Co. v. Reilly, 533 U.S. 525 (2001) (finding restrictions on the placement of ads for tobacco on billboards within 1000 feet of schools to be more extensive than necessary); FDA Commercial Speech Restrictions Could Hold Up in Court, Agency Says, F-D-C REP. ("THE PINK SHEET"), Aug. 12, 2002, at 29 [hereinafter PINK SHEET] (reporting an FDA attorney statement that since 1989, the Court has required government entities to weigh costs and benefits to justify speech restrictions, and "in at least recent years they haven't found a case where the government has done that adequately.").
27. Id. at 1502, 1506.
28. Id.
29. Id. at 1506.
30. Id.
islative history . . . or . . . briefs that the ad restriction was a necessary as opposed to merely convenient means."31 This type of justification is needed because, "[i]f the First Amendment means anything," speech restrictions "must be a last—not first—resort."32

D. The Dissent's Identification of a Separate Safety Interest in Restricting Demand

Justice Breyer believed that the majority opinion "seriously undervalue[d]" the importance of protecting the public's health and safety.33 The dissent was not directed at showing that ad restrictions are needed to reduce large-scale compounding. Instead, Justice Breyer found that the ad restrictions promote patient safety for all compounded drugs, regardless of size.34 The ad restrictions make it more likely that an individualized medical need exists, which justifies the added risks from using an untested compound.35 Without consumer ads, the doctor determines the patient's individual medical need, and does not act in response to pressure from consumers who have seen ads about compounds.36 Thus, the ad restriction better ensures that the need for potentially risky unapproved products has been identified on a medical basis by the physician and is not a mere response to an advertised convenience.37

Justice Breyer believed this safety objective was "presumably" why Congress did not simply restrict volume but also restricted ads.38 The dissent cited legislative history to show that Congress was concerned not only with the volume of compounding but also with other appropriate safety assurances.39 To show that ads can

31. Id. at 1507. While the Court called for an express showing, there also is some plausibility that ad restrictions are more readily enforced than limits on the type of equipment, the amount of production, or the amount of profits, information particularly in the knowledge of the producer.
32. Id. at 1507.
33. Id. at 1510 (Breyer, J., dissenting).
34. See id. at 1509–15 (Breyer, J., dissenting).
35. Id. at 1510 (Breyer, J., dissenting).
36. Id. at 1510–11 (Breyer, J., dissenting).
37. Id. (Breyer, J., dissenting).
38. Id. at 1510 (Breyer, J., dissenting).
39. Id. (Breyer, J., dissenting).

"[S]ome of the conditions are intended to ensure that the volume of com-
pressure physicians to prescribe drugs that are mere conveniences, the dissent cited studies in medical journals demonstrating that doctors are pressured by direct-to-consumer ("DTC") ads about approved prescription drugs that appear in magazines and on television.40

Justice Breyer's identification of this separate safety aim of the ad restriction made the alternatives identified by the majority as adequate to restrict large-scale compounding insufficient to address the risks from small-scale compounding. Thus, limits on commercial equipment which the majority believed the FDA had to consider as a way to limit the amount of compounding do not serve to protect consumers of compounded drugs made on a small scale from the added safety risks of ads merely portraying the drugs as convenient alternatives.41

E. The Majority's Response

1. Hypothesized Rationale and the Basis for Identification of the Government's Interest

Justice O'Connor criticized the dissenting opinion for using "hypothesized justifications" to argue that the safety risks from physician-pressuring support the legislation.42 Such hypothesizing can only be used under the rational basis test used for challenges based on substantive due process to Congress's authority to regulate products, but not for First Amendment challenges to restrictions on commercial speech.43 Justice Breyer viewed his ar-

40. Id. (Breyer, J., dissenting) (quoting 143 CONG. REC. S9840 (daily ed. Sept. 24, 1997) (statements of Senator Kennedy)). The history does not, however, refer to the ad restriction or other means as a way of providing this added safety assurance.

41. W. States, 122 S. Ct. at 1513. Breyer also points out that the limit on use of commercial equipment only restricts compounding to production in small batches but does not restrict the total amount produced. Id.

42. Id. at 1507.

43. Id.
argument as "logically related" to Congress's primary aim of "minimizing safety risks," and the general safety concern identified in the legislative history he cited.  With reflection, these sources provide support, even if the steps are not spelled out. The overall sense is that the dissent is willing to buttress the support for legislation by elaborating on the safety rationale that underlies the general aim of the law. Moreover, if that rationale is fairly implied in the statute and its legislative history, judges should be able to rely on it, even if it has not been explicitly raised by the FDA.

While Justice O'Connor criticized hypothesized justifications, she also pointed out that "[n]owhere in its briefs . . . [did] the government argue" that Congress was motivated by the interest identified by Justice Breyer.  It is interesting that the Court seemed to recognize the propriety of relying on the agency to articulate an explanation for a speech restriction not explicit in the legislation. As a result, the agency is not constrained, as may have been thought, to base its position solely on the grounds for the restrictions explicitly identified by Congress. Consequently, even if Justice Breyer's position was not sufficiently based in the legislative history, the FDA could use it to support the scheme, presumably either because Congress relies on agency judgment and discretion in implementation of the statute, or because of the agency's familiarity with the Congress's reasons for adopting the statute.

The majority also noted that the Central Hudson test is "significantly stricter" than the rational basis test in another respect since it requires "the government" to prove that the regulation directly advances the identified interest, and is not more extensive than necessary. Again, the majority criticized Justice Breyer's

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44. Id. at 1510 (Breyer, J., dissenting).
45. Id. at 1507.
46. See Pink Sheet, supra note 25 (quoting an FDA attorney's statement that "in defending the compounding statute, we were not able to locate any statements or other information in the legislative record that Congress had considered alternative speech restrictions or that Congress had weighed the benefit of speech restrictions against their cost").
47. See Chevron U.S.A. Inc. v. Natural Res. Def. Council, 467 U.S. 837 (1984) (recognizing that courts interpret statutory intent independently when clear from the relevant sources, but that courts accept reasonable agency interpretations when the statute is silent and Congress has left the matter to the agency).
48. W. States, 122 S. Ct. at 1507; Skidmore v. Swift, 323 U.S. 134 (1944) (according
reliance on the medical journal articles about the impact of consumer ads for drugs because the studies were not relied on by the government. If the agency simply needed to address whether the studies indicated that ads for unapproved compounded drugs would unduly pressure doctors, the opinion could have been expected to recognize that the ad restriction might be justified if the government gave further attention to the relevant studies. Justice O'Connor, however, identified other difficulties in relying on speech restrictions in this context that strongly state the commercial speech protections.

2. Ad Restrictions and Consumer Choice

The majority found that ad restrictions would not be justified even if adopted to prevent pressure on doctors by consumers to prescribe unapproved compounds that are not needed. The majority noted that nothing showed that physicians could not be relied upon to avoid prescribing drugs needlessly. Moreover, this concern with unnecessary prescribing "amounts to a fear that people would make bad decisions if given truthful information about compounded drugs." Restricting speech to prevent such a response is mere paternalism. The possibility that the ads might confuse consumers about the risks of compounded drugs, as the dissent suggested, did not warrant a preclusion of ads, since the government did not make that argument. Significantly, the majority also found that even if the government had taken that position, the risk of confusion can be dealt with by a "warning" on the label that the compound "had not undergone FDA testing and that its risks were unknown."

Justice O'Connor thus viewed the information provided to consumers, combined with the need for a prescription, as permitting an adequate decision about whether to undertake unknown risks

respect to agency interpretations not made in the exercise of a delegated authority).

49. See W. States, 122 S. Ct. at 1507.
50. Id.
51. Id. at 1507-08.
52. Id. at 1507.
53. Id. at 1508.
54. Id.
55. Id. at 1508. Justice O'Connor's warning was unusually frank for a disclaimer.
from unapproved variations of compounded drugs.\textsuperscript{56} The outcome in the case might be explained as reflecting the special circumstance that compounded drugs are intended to respond to individual circumstances. The numerous difficulties Justice O'Connor found with the government's position, and with Justice Breyer's dissent, also complicate an assessment of how important each one is individually. Still, she stated her positions about the protections accorded to commercial speech as broad principles, and if they are to be applied on that basis, as discussed below, they may have a significant impact on food and drug regulation.

Justice O'Connor also objected to the broad scope of the advertising restriction for compounded drugs since the restriction applied to ads directed toward doctors as well as to consumers.\textsuperscript{57} Ads to doctors about compounding specialized drugs used on a small scale would be banned even though they may, for example, contain information about more convenient ways of administering dosages to children with special medical needs.\textsuperscript{58} Justice Breyer seemed uncertain about restrictions on ads to doctors, and he did not resolve its propriety. Since physicians get information from various sources and the restrictions were not sufficiently dealt with below, he left that question "in abeyance."\textsuperscript{59} This disposition seems appropriate given the interest in avoiding the needless and premature resolution of constitutional issues.\textsuperscript{60}

F. Congress's Role in Regulating Commercial Speech

The differences among the Justices reflect their assessment about the importance of protecting commercial speech from the legislative process. Justice O'Connor viewed protections for commercial speech as "indispensable" since "[i]t is a matter of public

\textsuperscript{56} Id. at 1508–09.
\textsuperscript{57} Id. at 1509.
\textsuperscript{58} Id. Justice O'Connor also gave another example of the impropriety of the scope of the ad restrictions: It would preclude a pharmacy from posting a notice to let parents know about the availability of better tasting formulations of unpleasant medications that children refuse to take. Id. The government's policy allowed pharmacies to advertise compounding service in general without reference to specific products. The general notice might have been viewed as a reasonable means to alert parents to consult with their physicians about alternative compounds when general problems identified in the notice, such as palatability, presented special difficulties. Id.
\textsuperscript{59} See id. at 1515 (Breyer, J., dissenting).
\textsuperscript{60} See Gilhooley, supra note 3, at 1383.
interest that [economic] decisions, in the aggregate, be intelligent and well-informed.” For Justice Breyer, commercial speech restrictions do not warrant the strictest speech protections because they “do not often repress individual self-expression; they rarely interfere with the functioning of the democratic political processes” and often relate to consumer, environmental, and health and safety protections from commercial ventures. Justice Breyer saw the Central Hudson test as “flexible,” and as one that examines the “the restriction’s proportionality, . . . the fit between ends and means.” Justice Breyer also warned that an overly rigid “commercial speech” doctrine will transform what ought to be a legislative or regulatory decision about the best way to protect the health and safety of the American public into a constitutional decision prohibiting the legislature from enacting necessary protections. As history in respect to the Due Process Clause shows, any such transformation would involve a tragic constitutional misunderstanding. Also notable is that Chief Justice Rehnquist was one of the four dissenters. The then former Justice Rehnquist also disagreed with the majority in the first modern commercial speech case, where he urged that the First Amendment should be interpreted as protecting political speech and discussion of public issues, but not purchasing decisions which lack ideological content. The dissenters here, Chief Justice Rehnquist included, did not reject Central Hudson as the governing test, but were more willing to be generous to the statutory purpose in its application. Yet they

62. Id. at 1514 (Breyer, J., dissenting).
63. Id. (Breyer, J., dissenting).
64. Id. at 1515 (Breyer, J., dissenting); see also Margaret Gilhooley, Constitutionalizing Food and Drug Law, 74 Tul. L. Rev. 815, 869–77 (2000) (expressing concern about the rigor of the commercial speech test in limiting Congress from requiring agency approval, and questioning the differences from the rational basis test).
65. See W. States, 122 S. Ct. at 1509 (Breyer, J., dissenting).
66. See Va. State Bd. of Pharmacy, 425 U.S. at 787 (Rehnquist, J., dissenting). In a switch from the line-up in recent 5–4 decisions, Justice Souter joined the majority in Western States. 122 S. Ct. at 1499.
67. See W. States, 122 S. Ct. at 1515 (Breyer, J., dissenting).
are the dissenters. Thus, the validity of other types of commercial speech restrictions are open to question under the Court’s more rigorous test for commercial speech restrictions.

III. IMPACT ON REGULATION OF DRUG AND HEALTH CLAIMS

The most immediate question about *Western States* is the impact it will have on other aspects of food and drug regulation. These issues are highlighted by the FDA’s recent request for comments on the impact of the First Amendment on the FDA’s regulation of claims, a request that has itself been criticized for its breadth. This article examines the relevance of the judicial decision to a contentious and important issue: whether drug manufacturers can distribute medical articles about new off-label uses of drugs to doctors, without FDA approval, but with a disclaimer. The discussion will also deal with other important issues raised in the notice, such as the impact of the First Amendment on direct-to-consumer advertising of approved drugs.

The potential impact of the protections for commercial speech in *Western States*, if broadly read, cuts deeper into the regulatory scheme. As the FDA stated, “much of the operation” of the law “depends on the use of words.” Moreover, the Court objected to the paternalism of restricting truthful commercial speech out of a fear that people will make “bad decisions” with respect to unnecessary drug compounds when they bear a disclaimer that the risks are unknown. The law, however, prohibits the sale of unapproved drugs that have not been proven safe and effective. Consumers and physicians cannot get access to drugs that are untested simply based on a disclaimer about the lack of testing

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69. See William B. Schultz & Michael R. Taylor, Hazardous Hucksters, WASH. POST, May 28, 2002, at A17. The FDA placed public health protections “in jeopardy” when it urged the public and industries “to supply it with arguments” about whether commercial speech limits its power over advertising, an outgrowth of “a movement led by conservative judges, academics and advocacy groups who argue that the First Amendment limits the government’s power to limit advertising even when important public health interests are at stake.” Id.
70. 67 Fed. Reg. at 34,943.
and lack of FDA approval. Indeed, the prescription drug provisions can also be called paternalistic since consumers cannot buy the drugs without a prescription merely based on a disclaimer that the user should consult a physician.

The breadth of the agency’s request for comments and the breadth of the reasoning in the Court’s decision makes it important to examine the reasons for the regulatory scheme, in addition to considering the specific issues. Moreover, an evaluation is needed of what disclosures are necessary to keep consumers and physicians from being misled, assuming that a complete restriction of the speech is not permissible in some cases. My analysis of the impact of commercial speech developments on FDA regulation is given below and is an expansion of my comments to the agency.

The agency also raises the issues as constitutional questions, thus side-stepping the need to consider any statutory questions or administrative law issues that may exist. Avoiding deciding constitutional issues unnecessarily is highly important, and ordinarily these alternative grounds should be the first step in the analysis. However, the issues have been framed by the agency’s request as constitutional ones, and therefore some response on that basis must be made.

A. Justification for Pre-Market Approval of Drug Claims

1. Scope of Agency’s Request

The FDA’s notice asks some very general questions about the basis for drug regulation, in a manner that suggests a wide scope for the agency’s inquiry. The first question is whether there are arguments for regulating speech about drugs more comprehensively than dietary supplements—which have been deregulated—

73. Id.
75. See Gilhooley, supra note 3, at 1383; Gilhooley, supra note 64, at 815.
and what "an administrative record" must contain "to sustain such a position." The agency later asks with respect to products in general whether the First Amendment or social science evidence supports giving the government greater latitude to regulate labels as compared with advertising. These questions could relate to eliciting support for the need for the existing regulation of drug claims. On the other hand, the questions could be read as indirectly putting into question the constitutional validity of the requirement for pre-market approval of drugs, because of the implication of the need for more evidence to regulate claims on labels, as well as in advertisements, that relate to unapproved uses of drugs. These questions, if meant to be read so broadly, are so fundamental that some general comments are needed on the importance of Congress's determinations about the need for drug regulation.

While it is appropriate to consider the implications of the Western States decision and other lower court decisions dealing with commercial speech, I do not believe they should be read as intended to undercut the constitutional validity of the pre-market approval requirements for drugs. Indeed, the majority in Western States found that the new drug approval process is "clearly an important governmental interest, and the government has every reason to want as many drugs as possible to be subject to that approval process." The case can also be seen as dealing with a special situation: when the ordinary drug testing requirements economically cannot be met but there is still a recognized interest in making the compounded drugs available to handle individual circumstances.

2. Differences in Dietary Supplement Statutory Scheme

Dietary supplements are not ordinarily subject to prior safety review, nor is there pre-market approval for their "structure or function" claims when the claim is accompanied by a disclaimer about the lack of FDA approval. Congress established a less rig-
orous system for these products because of a congressional assessment that the supplements are "safe within a broad range of intake, and safety problems with the supplements are relatively rare." Moreover, the claims can relate only to the "structure or function" of the body and not disease prevention and treatment. The line between disease and structure or function claims is debatable, and agency action or legislative change is needed to provide better disclosures and support for the claims, and to assure better substantiation for the safety of the supplements.

Whatever the case is for supplements, the need for strong drug regulation is more imperative. Drugs often use potent chemicals that can cause harm, and they cannot be considered safe unless their effectiveness in treating or preventing disease outweighs these harmful effects. Furthermore, if drugs are ineffective, the delay in getting better treatment can also cause harm. These factors clearly justify Congress's determination that pre-market approval is needed to ensure the safety and efficacy of drugs, notwithstanding its willingness to adopt a less rigorous scheme, with disclaimers, for supplement claims.

3. Support Needed for Speech Restrictions

As noted above, the FDA notice asks if there is social science evidence or an administrative record to support FDA regulation of speech about drugs. FDA drug regulation is not simply an administrative decision; instead, it is based on statutory requirements. Congress's reasons for enacting the requirements, in light of the experience of harm from drugs, provides all the support needed for the scheme. In 1937, a manufacturer changed the drug sulfanilamide to a liquid form by using an ingredient found in antifreeze without testing the safety of the new formulation, a

83. REPORT OF COMMISSION ON DIETARY SUPPLEMENT LABELS, at x, 25 (1997) (discussing access to files and warnings on lack of safety substantiation); Margaret Gilhooley, Deregulation and the Administrative Role, 62 MONT. L. REV. 85, 110–13, 118–19 (2001); see discussion infra Part III.C.5 (discussing significant scientific agreement for substantiation).
change that led to over seventy-three deaths. Congress responded by requiring prior review of the safety of new drugs. The birth defects caused overseas by thalidomide led to the strengthening of the drug laws and a requirement for pre-market approval of the effectiveness, as well as the safety, of drugs. This historical experience with the harm that can occur with insufficient review convinced Congress of the importance of having strong safeguards to protect the public. That determination and value judgment provides sufficient support for the statutory requirements that restrict promotion of drugs for unapproved uses by manufacturers on the labels or in advertising, without the need for additional social science research. Moreover, the Supreme Court found that the statutory requirements for adequate and well-controlled studies as the basis for approving drugs reflected “the conclusion of Congress, based upon hearings, that clinical impressions of practicing physicians and poorly controlled experiments” were not adequate evidence of efficacy. While the constitutional protections for commercial speech were not at issue, it would be anomalous if the Court were now to find Congress’s reasons for requiring scientific testing to be of only marginal significance.

4. Statutory Tests as Benchmarks for Disclaimers

Some may maintain that providing disclaimers about the lack of studies is an alternative to conducting drug testing. Whether disclaimers ought to be used should be a congressional decision. While disclaimers are not an adequate substitute for testing, if they are ever to be used for drugs, the burden should be on the companies who seek to use them to show that consumers—and

86. Id.
89. The FDA notice asks about the administrative record needed to support its positions. 67 Fed. Reg. at 34,943. It should be borne in mind that the administrative record for agency regulations need not always be based on empirical evidence. As the Court of Appeals for the District of Columbia stated, a “regulation that is self-evidently rational is not less legitimate than a regulation whose rationality must depend on elaborate statistical, expert, or other evidence.” Nat’l Confectioners Ass’n v. Califano, 569 F.2d 690, 695 (D.C. Cir. 1978).
busy practicing physicians—can clearly understand the disclaimers, and are not misled. Common experience indicates that users find it difficult to assess small-print complicated qualifications of a claim. When the unapproved claim is in headlines, the disclaimer qualifying it also needs to be simple and comparable to a headline in clarity. The statutory standard for approval should also provide the benchmark for judging the type of disclaimers that are needed. Thus, any disclaimers relating to drugs should indicate the specific ways in which the product lacks the adequate and well-controlled studies needed for approval. In the case of disease claims, we are dealing not merely with economic harm. The need to protect the public from the safety risks and potential ineffectiveness of powerful drugs provides the rational support for the pre-market approval requirement. If, nonetheless, Congress is found to be without the power to provide that safeguard to the American public, the promoter of the unapproved claim should have the burden to show that disclaimers are adequate to alert the user to the specific support that is lacking.

B. Direct-to-Consumer Advertisements

1. Present Policy as Meeting the Constitutional Tests

The FDA asks if its approach to direct-to-consumer (“DTC”) advertising is “consistent with empirical research” and with “relevant legal authority.” Unlike the FDA policy at issue in Western States, the FDA does not preclude all DTC ads for approved drugs. Instead, its approach is geared toward preventing consumers from being misled about the approved use and the important side-effects. Thus, the focus for any re-examination should not be on the constitutional validity of the FDA’s present program, but on whether changes are needed for policy or statutory reasons. Some changes may be appropriate, for example, in the manner of providing information to consumers. The inclusion in consumer magazines of the small print professional labeling for drugs has little value, and more attention to an adequate disclosure in consumer-friendly language of the significant risks would be better. Furthermore, the FDA guidance for the ads does not call for prior

90. 67 Fed. Reg. at 34,943.
review of DTC ads, although it encourages consultation.\textsuperscript{91} Since the statute provides standards for prior review of drug advertisements,\textsuperscript{92} whether such a requirement is appropriate or needed becomes—in the first instance—a statutory question and not a constitutional one.

2. Changes to Limit Over-Prescription

The FDA’s notice also asks if the DTC ads lead to over-prescription and if they encourage treatment for under-diagnosed diseases.\textsuperscript{93} The FDA questions are phrased generally and are broad enough to encompass restricting advertisements for drugs that are over-prescribed.\textsuperscript{94} Any effort to restrict drug advertisements to prevent over-prescription would have to meet the commercial speech tests identified in \textit{Western States}.\textsuperscript{95} Whether an agency initiative could do so would depend on an assessment of the particular proposal and its justification.\textsuperscript{96} Showing that drugs are over-prescribed will be a critical step. Moreover, any regulatory proposal will have to take account of the majority’s position in \textit{Western States} that the government cannot impose speech restrictions to preclude people from making “bad decisions” about drugs that are not needed when the speech is truthful and the risk of deception can be met by a warning about unknown risks.\textsuperscript{97} Still, the FDA has identified an important policy issue with respect to the over-prescription of drugs, and the agency should pursue investigating ways to achieve this aim in ways that meet the Court’s standards.

There has also been an interest in legislation that would restrict or discourage DTC ads because the ads are seen as increasing the costs of drugs, making it more difficult for consumers, in-

\textsuperscript{92} 21 U.S.C. § 352(n) (2000) (providing FDA authority over-prescription drug advertising and specifying that prior review can be required only if there are “extraordinary circumstances”).
\textsuperscript{93} 67 Fed. Reg. at 34,943.
\textsuperscript{94} Id.
\textsuperscript{96} See id.
\textsuperscript{97} See id. at 1507.
surers, employee benefit plans, and the government to cover the costs for prescription drugs.\footnote{PINK SHEET, supra note 25, at 29; see S. 2486, 107th Cong. (2002) (noting that a legislative proposal to limit companies' tax deduction for marketing to no more than its research expenses has been criticized as unconstitutional because it is aimed at preventing truthful ads about drugs); see also NAT'L INST. FOR HEALTHCARE MNGT. RESEARCH & EDUC. FOUND., PRESCRIPTION DRUGS AND MASS MEDIA ADVERTISING, 2000 (2001), available at http://www.nihcm.org/DTCb brief 2001.pdf (last visited Jan. 24, 2003) (maintaining that a relatively small number of prescription drugs that were advertised contributed significantly to the increase in pharmaceutical spending from 1999 to 2000).} While the legislative developments are beyond the scope of this article, any proposals will also have to consider Western States's reasoning that it would be unconstitutional paternalism for the government to bar truthful ads about unapproved drug compounds that have warnings to prevent confusion about unknown risks.\footnote{See W. States, 122 S. Ct. at 1507.} Whether promoting the affordability of drugs counts as a substantial governmental interest presents a new factor that needs to be evaluated in sorting out the Central Hudson prongs in this setting. The government would also need to provide an assessment of why other alternatives are insufficient to address the cost concern. As a consequence, legislative proposals in this area may focus, in the first instance, not simply on the merits of the legislation or its political viability, but on what the Court will allow.

3. Better Disclosures About Physician’s Role

Another approach for the FDA to consider in reassessing DTC ads is the need to provide better disclosures in the ads about the basis for the physician’s decision.\footnote{Request for Comment on First Amendment Issues, 67 Fed. Reg. 34,942, 34,943 (May 16, 2002).} The agency asked if the current approach to DTC advertising creates any impediments to the ability of doctors to give optimal medical advice. The single-drug focus of the DTC ads can lead to special pressures on doctors to prescribe a particular drug. I recommend that the DTC ads state prominently that consumers need to "Consult your doctor about the range of treatment choices that may be available, and their risks, benefits and costs." Disclosure to prevent consumer deception is permissible under the standards governing commercial speech, and this disclosure prevents consumers from being misled when the ad fails to indicate the range of factors that need to be
considered by the consumer and the doctor in making the drug choice.

The role of the physician is to advise patients about the choice of therapies in light of available drug and non-drug treatments, the potential side-effects from these treatments, the patient's particular situation, the relative efficacy of the treatments, and cost factors—including the availability of generic drugs. The survey cited by the dissenting judges in *Western States* indicated that family physicians reported DTC advertisements pressure physicians to prescribe drugs they would not ordinarily prescribe. The majority in *Western States* found this single survey insufficient to support an advertising ban. The FDA should consider whether existing and future surveys provide support for reducing unwarranted pressure on the physician by providing disclosures about the range of advice the patient needs from the doctor.

The typical statement in DTC ads advises the consumer to consult their physician about the drug, and to see if the advertised drug is "right for you," suggests that the decision is drug-specific, dependent on the side effects for the particular drug. If the ads made clearer the fact that drug choices are relative, they would accord greater respect to the physician's role. Additionally, this would help alleviate the pressure doctors feel from consumer advertisements aimed at a single drug. Moreover, there is a need to make consumers aware of the need for advice from their physician on the relative benefits and costs of generic drugs and other treatments.

4. Better Data and Delay in Ads for New Products

Further attention may be needed to discover ways to ensure that physicians have sufficient information to advise consumers about the relative choice between drugs. The FDA does not now base the approval of drugs on their relative efficacy, although it considers relative safety. Under a system used by the FDA to determine priorities for drug reviews, two-thirds of drugs ap-

102. *Id.* at 1507.
proved in the 1990s were simply modified versions of existing drugs and not significant advances in drug therapy.\textsuperscript{104} The development of better data on the relative efficacy of drugs has been identified as important to guide health insurers, doctors, and patients.\textsuperscript{105} A proposal has been made for creating a research institute as a way to do so.\textsuperscript{106}

A delay in the use of the ads in the mass media might also be appropriate if the FDA could show that a phase-in of the wide sale of newly approved drugs is needed for safety reasons to permit physicians and the agency to assess whether the newly-sold drugs pose risks not detectable in the limited size of the clinical studies.\textsuperscript{107} The FDA should take account of the need for better information and disclosures to prevent deception as part of its reassessment of its policy towards DTC ads.

C. Off-Label Uses of Prescription Drugs

1. Relevance of Western States

The FDA asks about the extent of its ability to regulate speech about off-label uses and whether permitting speech by manufacturers about off-label uses would undermine the new drug approval process.\textsuperscript{108} Read broadly, \textit{Western States} can be seen as raising the issue of whether disclaimers can provide a reasonable alternative to restrictions on speech by the manufacturer about

\textsuperscript{104} Melody Peterson, \textit{New Medicines Seldom Contain Anything New, Study Finds}, \textit{N.Y. Times}, May 29, 2002, at C1. The article describes a study by an institute, which receives funding from health insurers, finding that two-thirds of the drugs approved between 1989 and 2000 were modified versions of existing drugs and were the most heavily advertised to consumers. \textit{Id.} The article also reported that a representative of drug manufacturers said that drugs that copy those already on the market could still offer benefits to patients since patients may respond to one medication but not another. \textit{Id.}


\textsuperscript{106} \textit{Id.} at 146–47.

\textsuperscript{107} \textit{Task Force on Risk Mgmt.,} U.S. DEP’T OF HEALTH & HUMAN SERVS., \textit{MANAGING THE RISK FROM MEDICAL PRODUCT USE} 46 (1999) [hereinafter \textit{Task Force on Risk Mgmt.}] (reporting that new products reach consumers so quickly that “often dozens to hundreds of adverse reactions can occur before they are recognized and action is taken to reduce their effects”). \textit{Western States}, however, might be read to permit the distribution of the advertisements so long as they include a warning that the risks are unknown.

off-label uses of drugs. This issue is most relevant with respect to the distribution by pharmaceutical companies to doctors of medical articles about off-label uses of approved drugs.\footnote{109}

In the case of medical journal articles, the FDA recognizes that doctors, as part of the practice of medicine, will discover off-label uses for approved drugs, and that medical researchers investigate these uses and communicate their conclusions to practitioners in accordance with the standards of the profession.\footnote{110} The FDA’s position on the extent to which manufacturers can initiate distribution of medical articles has already been the subject of litigation.\footnote{111} This litigation ended on appeal without reaching the constitutional merits. The FDA withdrew its prior guidance, leaving the FDA policy as reflecting simply its traditional objection to a manufacturer’s distribution of materials intended to promote unapproved uses of drugs.\footnote{112}

In \textit{Western States}, the Court assumed that a statutory preclusion of advertising to physicians and consumers of the willingness of a pharmacy to “compound” specific drugs, without FDA approval of the variation, would promote the valid governmental interest in the integrity of the new drug approval process.\footnote{113} Nonetheless, the Court found that before suppressing speech, the government had to consider other alternatives, and that the potential for misleading advertising about drug risks could be dealt with by a “warning that the drug had not undergone FDA testing and that its risks were unknown.”\footnote{114} The Court, in pointed language, found that “if the First Amendment means anything, it

\begin{footnotes}
\footnote{109}{Promotion of off-label uses by manufacturers that is not based on peer-reviewed medical articles should clearly be considered impermissible—no matter what disclaimers are used—since allowing that promotion would undercut the drug approval process.}
\footnote{110}{This reporting of scientific information is clearly protected by the First Amendment. \textit{See} Alexander Meiklejohn, \textit{The First Amendment Is an Absolute}, 1961 SUP. CT. REV. 245, 256–57 (1961).}
\footnote{111}{Wash. Legal Found. v. Henney, 202 F.3d 331 (D.C. Cir. 2000).}
\footnote{112}{\textit{Id.} at 332; see also Gilhooley, \textit{supra} note 3. \textit{See} Kordel v. United States, 335 U.S. 345 (1948) (finding that statutory prohibitions applied to labeling and advertising that explained the uses of a drug).}
\footnote{113}{Thompson v. W. States Med. Ctr, 122 S. Ct. 1497, 1505 (2002). The law allowed advertisements to consumers and doctors of the general availability of compounding services, but only if no specific drugs were identified. 21 U.S.C. § 353a(c) (2000).}
\footnote{114}{W. States, 122 S. Ct. at 1508. Other alternatives included banning commercial scale manufacturing equipment for compounding. \textit{Id.} at 1506.}
\end{footnotes}
means that regulating speech must be a last—not first—resort.”

The FDA's position about medical articles describing off-label uses may be affected by the Court's treatment of pharmacy compounding if the decision is read broadly. If the First Amendment protects ads for unapproved compounds made to consumers and doctors when the ad has a disclaimer that the risks are unknown, the Constitution could logically also protect the distribution by drug companies of medical articles to doctors about unapproved off-label uses when the distribution is accompanied by a disclosure about the lack of FDA approval. The FDA, though, has not been willing to accept the adequacy of a disclaimer as sufficient to allow the manufacturer to distribute reprints when the distribution would show an intent to make an unapproved drug claim. While there are some similarities, there also are important differences between drug compounding and the promotion of off-label uses. Moreover, there are substantial difficulties in providing adequate disclaimers about the off-label uses.

2. Differences in Need for Review of New Off-Label Uses

Western States dealt with "pharmacy compounding," which primarily relates to making changes in the formulation of an approved drug by using approved ingredients to deal with individual patient needs in light of individual variability. Compound-
ing responds to individualized needs and this focus should help limit the extent to which compounding occurs and the potential for widespread harm to the public.\textsuperscript{120} With off-label uses, promoted by major pharmaceutical companies, wider use can occur on a national basis, with a greater risk that the drugs can pose safety risks and delay effective treatment for wide numbers of people. Moreover, the large market for off-label uses and the involvement of the pharmaceutical company make possible the type of costly testing needed for drug approval, which is not economically viable for the small-scale efforts involved in pharmacy compounding done to meet individual needs.\textsuperscript{121}

The promotion of off-label uses also threatens the integrity of the new drug approval process in a basic way.\textsuperscript{122} If that promotion is permitted, drug manufacturers may obtain agency approval for the least risky use of the drug, and the use with efficacy that is the easiest to establish.\textsuperscript{123} The riskier uses with borderline efficacy and narrow and possibly inappropriate risk/benefit ratios can become widespread based on a journal article with disclaimers.\textsuperscript{124} The government will lose the ability to determine that the public needs to be protected by an independent agency review of the added risks, due to an off-label use promoted by the manufacturer in distributed reprints.\textsuperscript{125} Not only is agency review independent, the FDA also has access to all of the underlying data to support claims, even those that are trade secrets. However, the access of medical journals to information about protocols and data analysis is affected by the manufacturer's interest in the proprietary nature of the database.\textsuperscript{126}

\begin{itemize}
\item \textsuperscript{120} Id. at 1500.
\item \textsuperscript{121} See id. at 1505.
\item \textsuperscript{122} See id.
\item \textsuperscript{123} Id. at 1503–36 (discussing how FDA approved individual drugs for short-term use, but safety complications arose when the unapproved combination of the drugs, referred to as “fen-phen,” came to be used extensively on a long-term basis as a diet aid based on a medical article).
\item \textsuperscript{124} See id.
\item \textsuperscript{125} See id. at 829–31.
\item \textsuperscript{126} PHARM. RESEARCH & MFRS. OF AM., PHRMA PRINCIPLES ON CONDUCT OF CLINICAL TRIALS AND COMMUNICATION OF CLINICAL TRIAL RESULTS 24, available at http://www.PhRMA.org/publications/policy/2002-06-24.430.pdf (last visited Jan. 9, 2003) (stating that “if requested by a medical journal when reviewing a submitted manuscript for publication, the clinical trial sponsor will provide a synopsis of the clinical trial protocol and/or pre-specified plan for data analysis with the understanding that such documents are confidential and shall be returned to the sponsor”). See id. at 22 for a provision
\end{itemize}
3. Obstacles to Making Disclaimers Adequate

A separate difficulty is that providing adequate disclosures about off-label uses presents seemingly insurmountable obstacles. These obstacles become clearer if one tries to envision what would make disclaimers adequate, taking into account the significance that the manufacturer's distribution of the article will have for physicians.\(^\text{127}\)

a. Warning Caption

Disclaimers, if they could be made adequate, would require a bluntness that those seeking them may characterize as unnecessary. This issue can be seen by examining the disclaimer identified by the Supreme Court of the United States as suitable in Western States. The Court found that claims not approved by the FDA should be identified by a “warning” to the consumer.\(^\text{128}\) Use of a “warning” as the introductory signal is also appropriate with respect to off-label uses, given the importance of alerting the physician to the significant responsibility that he or she is undertaking in evaluating off-label uses promoted by the manufacturer.\(^\text{129}\) However, there is likely to be resistance to such a clear signal. Nonetheless, it should be required, and if it is not, the manufacturer should have to provide the evidence that other captions are fully adequate to alert physicians.\(^\text{130}\)

b. Distribution as Endorsement

When a pharmaceutical company distributes a medical article reporting off-label uses, physicians may see the distribution as an endorsement by the company of the new use as adequate to meet the standards of the profession as well as the usual testing standards for drugs. The physician may also assume that if the new

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127. See Gilhooley, supra note 64, at 836.
129. See Gilhooley, supra note 64, at 836–37.
130. Id.
use proves harmful, the manufacturer will be subject to product liability for any inadequacies in the testing or warnings that the manufacturer provides with the medical article on the off-label use.

In the absence of a manufacturer endorsement of the off-label use, the physician would recognize the potential for medical malpractice liability if the new use does not meet professional standards. The physician would exercise the cautions involved in being sure that the off-label use fully meets the standards of the profession. Whether the liability of the manufacturer would replace or lessen professional liability in this setting is a difficult question, and one that the FDA is not in a position to resolve. The relevant point is that the physician's perception of the manufacturer's endorsement can lessen the extent to which the physician will rely solely on professional assessment. Thus, a disclosure would be needed that the manufacturer's distribution is not an endorsement that the article shows that the off-label use meets the professional standards (assuming this to be the manufacturer's position).

c. Specific Differences from FDA Testing Requirements

If a disclosure system were to be used, it would need to indicate the specific ways in which the off-label use did not have the testing normally required for FDA approval. A blanket statement that the risks of the off-label use are unknown, suggested in Western States, is not suitable in this context. The testing reported in the medical journal is likely to have identified some risks associated with the new use, and the FDA labeling for the approved use will indicate others. Instead, the difficulty will be whether the testing in the medical article is sufficient.

An adequate disclosure in this situation also needs to indicate more than the lack of FDA approval. Indeed, the disclosure identified by the Supreme Court of the United States in Western States referred to the lack of FDA testing, not to the lack of FDA

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131. Whether there needs to be any separate disclosures to patients is an important matter not explored in this article.
132. See Gilhooley, supra note 83, at 114.
In dealing with off-label uses promoted by the manufacturer, the physician needs the benefit of knowing how the studies in the medical journal differ from the testing the FDA requires. Individual physicians have limited time to undertake studies about differences reported in the literature, and they are not in a position to determine the efficacy and risks of a drug within the limits of their practice. The variability in the quality of articles in medical journals makes this type of specific disclosure critical.

To adequately inform physicians, there should be a disclosure reporting the extent to which the medical journal article, relied on to support the off-label use, fails to meet the usual FDA standards for drug testing. This disclosure should cover any differences with respect to the number of test subjects and the type of testing and controls. Moreover, if this is the type of situation in which the FDA would call for post-use "Phase IV" studies, the warning should disclose whether any such studies are being undertaken.

d. Material Omissions

The manufacturer should ensure that there is adequate disclosure of any other material information that would affect the assessment of the journal article, such as contradictory results from an unreported study known to the manufacturer.

e. Provision for Post-Market Surveillance

Increasingly, there has been recognition of the need for an adequate post-market surveillance system to detect adverse reactions that are not detectable within the testing limits of reliable stud-

133. W. States, 122 S. Ct. at 1508.
134. See Gilhooley, supra note 64, at 836–37.
135. See Drummond Rennie, Fourth International Congress on Peer Review in Biomedical Publication, 287 JAMA 2759, 2760 (2002) (finding that there continues to be abundant evidence that even with peer review "there are scarcely any bars to eventual publication").
137. Frank Davidoff, et al., Sponsorship, Authorship and Accountability, 345 New Eng. J. Med. 825, 825 (2001) (stating that "the results of the finished trial may be buried rather than published if they are unfavorable to the sponsor's product").
There could be complications in knowing how to deal with adverse reactions attributable to off-label uses in the post-marketing adverse reaction reporting. Reactions based on off-label uses might be discounted as based on misuses of the drug for which the manufacturer has little responsibility. However, when the manufacturer is encouraging the off-label use by distributing medical journal articles, particular attention should be paid, in the reporting system and the disclosure, to reactions associated with these uses.

f. Conflict of Interest and Independent Review

There should also be disclosure about any conflict of interest between those doing the study reported in the medical article and the pharmaceutical company distributing the reprint so that the reader can take account of the potential for bias. Moreover, there should be a disclosure of whether there has been any independent review of the medical testing by those without any conflict of interest. A disclosure approach still suffers the key drawback of not providing the safeguard of an independent review. The FDA’s employees and its advisory committees’s members are subject to requirements that preclude a role when there is a conflict of interest.

4. Notification and Prior Review of Distributions and Disclaimers

If a disclosure system were to be used, the manufacturer should be obliged to notify the FDA of the dissemination by the manufacturer of the reprint from the medical journal, and related material such as cover letters, sent to physicians about off-label

140. See id.
141. Id.
142. The revised standards for the leading peer-reviewed journals call for authors of review articles not merely to disclose conflicts, but to have no conflicts of interest that are "significant." This policy, even as modified, provides an indication of the importance of independent review, and that there are times when mere disclosure is not enough. Jeffrey M. Drazen & Gregory D. Curfman, Financial Associations of Authors, 346 New Eng. J. Med. 1901 (2002); see also Marcia Angell, supra note 139, at 1516.
uses. These cover letters can be important in conveying the manufacturers’ endorsement of the off-label use reported in the medical journal. Without such a notification requirement, the FDA is in a poor position to know about the dissemination and the disclosures, and to take enforcement action to correct misleading disclosures. The FDA has proposed to require that companies provide the agency notice of new uses of biotechnology for foods, and has identified the legal basis for finding such a notification necessary to carry out its authority to efficiently enforce the law. That rationale also seems applicable to the problems presented by promotion of medical articles about off-label uses.

Moreover, the need for FDA prior review of disclaimers for unapproved health claims on dietary supplements has been recognized in *Pearson v. Shalala*, a major commercial speech case. If prior review of the disclaimers for supplements is appropriate, notification of the distributions of articles and related material about off-label uses of drugs is clearly needed. *Pearson* also provides support for prior reviews of the disclaimers to be provided with journal articles about off-label uses. If disclosures alone were to be relied upon, the disclaimer accompanying the distribution of the medical article should indicate any FDA comments and the status of any testing recommended by FDA.

5. GRAS/E Status

The FDA should acknowledge the circumstances when the warning and disclosures described above are not needed. In some cases, it may be that off-label uses described in medical articles may have sufficient scientific support and expert acceptance that they could become Generally Recognized as Safe and Effective ("GRAS/E"). When new drugs are initially developed, they can-

144. 164 F.3d 650, 657–58 (D.C. Cir. 1999).
145. Id. at 658 n.7.
146. In FDAMA, Congress provided an alternative means for manufacturers to distribute reprints about off-label uses, and this “safe harbor” could still provide a framework for obtaining agency comments. The FDAMA process included prior notification of the distribution, a 60-day delay for FDA comments, an undertaking to do additional testing found necessary by FDA, and a filing of a supplemental notification. 21 U.S.C. § 360aaa(b)(c) (2000); see Gilhooley, supra note 64, at 830–31.
147. 21 U.S.C § 321(p) (2000) (defining new drugs as those that are not GRAS/E).
not be GRAS/E because the drug will not have been used for the material time needed for expert recognition.\textsuperscript{148} The standards for GRAS/E are high. As the Supreme Court of the United States has found, experts would not generally recognize a drug as safe and effective without the type of adequate and well-controlled studies needed to obtain FDA approval.\textsuperscript{149} Thus, it may be rare that off-label uses could achieve this status.

The FDA might consider whether it should establish criteria and a process for affirming off-label uses that have attained GRAS/E status based on the adequacy of the studies, extensive use, and expert recognition. When that exists, the product would not need the disclaimers described here. A benefit of establishing this procedure would be to encourage manufacturers to sponsor fuller studies for off-label uses that provide the level of support and safeguards needed for GRAS/E recognition. This would be preferable to having manufacturers distribute medical articles that need extensive disclaimers.

D. Health Claims on Foods

The FDA asks if different standards can be used for health claims on foods than the approach found constitutionally applicable to health claims on dietary supplements.\textsuperscript{150} There are reasons to believe that differences exist. Dietary supplement users seek the products out and may be willing to spend more time studying a disclaimer. In contrast, foods are a necessity and shoppers have limited time to review the details of disclaimers while making selections. Consumers can lose confidence in health claims generally if preliminary and weakly supported claims are frequently put in question by new information. The valid claims that promote healthy dietary choice should not be obscured by weak claims whose validity is continually undercut.

This need for stability and confidence in health claims led to the statutory requirement for agency approval of claims when they are supported by significant scientific agreement based on

\textsuperscript{149} Weinberger, 412 U.S. at 633–34.
\textsuperscript{150} Request for Comment on First Amendment Issues, 67 Fed. Reg. 34,942, 34,943 (May 16, 2002); see also Gilhooley, \textit{supra} note 83, at 110–11.
the totality of the evidence, including well-designed studies.\textsuperscript{151} If
disclaimers are to be used, the best way to provide an adequate
disclaimer would be for the unapproved claims to state that they
do not meet the key statutory requirement of "significant scientific agreement."\textsuperscript{152} However, the \textit{Pearson} court found this stan-
dard vague and remanded for better identification of the stan-
dard.\textsuperscript{153} The FDA should pursue articulating the criteria for
significant scientific agreement. The FDA has already recognized
that the standard does not require the wide degree of consensus
among experts needed for general recognition of drugs. Perhaps
the FDA could make clear that the standard for food health
claims is met if there is majority acceptance by the leading quali-
fied experts, which can be shown by affirmative endorsement by
the leading organizations. Scientific support is especially needed
in this field because the ultimate validity of the claim depends
upon long-term studies and population studies that are difficult
to conduct.\textsuperscript{154} The support of scientific experts serves as a safe-
guard in the absence of full testing. Of course, further experience
and full testing could show that the views of the experts are in-
correct.\textsuperscript{155} Still, unless that happens, the consumer should have
the benefit of knowing whether a majority of experts agree with
the claim.

The alternative form for the disclosure should build on that
used by the FDA for dietary supplements on remand from the
\textit{Pearson} case.\textsuperscript{156} Thus, it should state that the FDA does not en-
dorse the claim, but it should also state that the FDA does not do
so based on the lack of long-term studies and that the claim has

\textsuperscript{151} Weinberger, 412 U.S. at 633–34.
\textsuperscript{152} See Gilhooley, supra note 83, at 111–14.
\textsuperscript{153} Pearson v. Shalala, 164 F.3d 650, 659–60 (D.C. Cir. 1999).
\textsuperscript{154} See Gilhooley, supra note 83, at 111–14 (suggesting that the FDA allow supple-
ment marketers to make "research in progress" claims as a way to encourage high-quality
research programs).
\textsuperscript{155} A dramatic example in the case of drugs has been provided by the studies showing
that estrogen replacement therapy not only fails to provide many of the benefits thought
to exist but causes harm. Gina Kolata & Melody Peterson, \textit{Hormone Replacement Study
\textit{What if the Big Fat Story Is Wrong?}, \textit{Wash. Post.}, Aug. 27, 2002, at F1 (criticizing new
diet that ignores scientific research) \textit{with} Gary Taubes, \textit{What if It’s All Been a Big Fat
Lie?}, \textit{N.Y. Times Mag.}, June 7, 2000, at 22 (questioning the role of carbohydrates and fat
in the diet).
\textsuperscript{156} See Gilhooley, supra note 83, at 112 (summarizing disclosures used on remand).
not been accepted by most experts.\textsuperscript{157} A mere statement that the FDA has not approved the claim could seem to reflect agency delay and inattention. Therefore, a disclaimer that affirmatively reflects the FDA’s non-acceptance is more informative for consumers. The FDA’s prior review of the disclaimers for the food claims should occur, just as the \textit{Pearson} court recognized was necessary for disclaimers for the supplement claims.\textsuperscript{158}

\textbf{E. Resources}

Reviewing notifications for off-label uses and disclosures about the off-label uses and for health claims, on a timely basis, places considerable demands on FDA resources. The administration needs to consider providing additional support to enable the FDA to meet its added review and enforcement responsibilities under a constitutional scheme that relies on disclaimers rather than pre-market review to protect the public. Consideration should be given to legislation that would have those seeking to make claims based on disclaimers pay a fee to cover the added FDA staff costs for enforcement. The model would be the “user fees” that must be paid by those seeking approval of new drug applications, although the fee range would be different.

\section*{IV. CONCLUSION}

The FDA’s request for comments on the impact of \textit{Western States} has put on the table the means of regulating food and drug claims: whether simply providing information and disclaimers about the lack of testing and FDA approval is sufficient, or whether agency review of claims continues to be needed. The decision whether disclaimers supplant the need to obtain agency approval for claims should not be made, however, on a simplistic uniform basis. The determination of what is needed to protect the public health and to meet the constitutional standards must be made with respect to each type of regulatory program.

The agency made that request not simply to explore policy options but as a response to judicial developments that can put the

\textsuperscript{157} See id. at 112–13.
\textsuperscript{158} See \textit{Pearson}, 164 F.3d at 659–61; see also \textit{Gilhooley}, supra note 83, at 110–11.
choice beyond the power of congressional decision. The immediate impact of the agency's reconsideration of the policy will likely be with respect to the position towards the manufacturer's promotion of off-label uses of drugs, direct-to-consumer advertising, and health claims for foods. These are matters of major policy, and their treatment can shape how other regulations are treated. The re-examination now underway by the FDA will test the support that pre-market approval has among health professionals and the public, and how central a role Congress will play in determining the protections provided to the public for food and drugs.