



**Corporate Regulatory and Quality Science**

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September 16, 2002

Dockets Management Branch (HFA -305)  
Food and Drug Administration  
5630 Fishers Lane - Room 1061  
Rockville, MD 20852

**RE:** *Request for Comment on First Amendment Issues*  
*[Docket 02N-0209]*

Dear Sir or Madam:

Abbott Laboratories submits the following comments regarding FDA notice "Request for Comment on First Amendment Issues," published in the Federal Register on May 16, 2002 at 67 FR 34942 with an extended comment period published on July 19, 2002 at 67 FR 45742.

Thank you for the opportunity to provide these comments. We are pleased that the Agency has decided to re-evaluate its regulation of speech, in light of governing First Amendment authority.

The courts have long recognized the importance of free speech, including commercial speech. Commercial speech is distinct from other forms of speech (e.g., scientific) in that it is afforded lesser constitutional protection. For purposes of these comments, we have considered FDA's speech restrictions under the standard established for commercial speech. Commercial speech is expression related solely to the economic interests of the speaker and its audience (Central Hudson Gas & Elec. Corp. v. Public Serv. Comm'n of N.Y., 447 U.S. 557, 562 (1980)).

In deciding whether or not the government's restrictions on commercial free speech are appropriate the Supreme Court developed a four-pronged test to evaluate speech restrictions. Under this test, courts are to assess whether: (1) the speech is lawful and not misleading; (2) the government interest asserted to justify the regulation is substantial; (3) the regulation directly advances the government's interest; (4) the regulation is no more extensive than necessary to serve that interest (Central

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Hudson Gas & Elec. Corp. v. Public Serv. Comm'n of N.Y., 447 U.S. 557,567 (1980)). We relied on this test as we considered our responses to the questions posed by FDA. The questions below are numbered as they appeared in the Federal Register Notice.

**1. Are there arguments for regulating speech about drugs more comprehensively than, for example dietary supplements?**

The principle behind regulating commercial speech should be the same no matter what products are involved. The principle involved here is the importance of presenting truthful and not misleading information.

**Does anything turn on whether the speech is made to learned intermediaries or to consumers?**

Truth should not change depending on the audience. In other words, regulations should not be different for products meant for the professional market as compared to products meant for the consumer market. However, the level of the message may change depending on the educational level or medical sophistication of the audience.

**2. What are the positive and negative effects, if any, of industry's [direct-to-consumer] promotion of prescription drugs, biologics, and/or devices?**

Truthful and not misleading direct-to-consumer advertising is appropriate. Some consumers would use the information to initiate conversations with their own physicians and others will totally ignore the information. Physicians have the ability to assess the merits of a particular drug, biologic, or device and treatment regime. Ultimately, it is the physician who prescribes the product.

There is some evidence that pharmaceutical advertisements raise awareness of conditions and diseases that often go undiagnosed and untreated. Such advertising can raise awareness that treatments are available to populations that have traditionally been undertreated. By informing people about the symptoms of such diseases and the availability of effective treatments, direct-to-consumer advertising can promote discussion between patients and medical professionals, and ultimately improve public well-being. See, e.g., Center for Drug Evaluation and Research, *Attitudes and Behaviors Associated with Direct-to-Consumer (DTC) Promotion of Prescription Drugs: Main Survey Results*, Food and Drug Administration (1999; accessed September 10, 2002 <<http://www.fda.gov/cder/ddmac/dtcindex.htm>>); Kathryn J. Aiken, Ph.D., *Direct-to-Consumer Advertising of Prescription Drugs: Preliminary Patient Survey Results*, Division of Drug Marketing, Advertising and Communications, Food and Drug Administration (April 18, 2002; accessed September 10, 2002 <<http://www.fda.gov/cder/ddmac/DTCnational2002a/sld001.htm>>).

**4. Should disclaimers be required to be in the same (or smaller or larger) size of type and given equal prominence with claims?**

The prominence of the disclaimers should depend on the nature of the risk presented and the importance of the information. A "one size fits all" approach does not make sense here. The size of type and prominence of disclaimers should be considered on a case-by-case basis.

**5. How can warnings be made most effective in preventing harm while minimizing the chances of consumer confusion or inattention?**

Warnings on labels should be worded at a level appropriate for the intended audience to understand.

**6. What arguments or social science evidence, if any, can be used to support distinguishing between claims made in advertisements and those made on labels?**

There should be no distinction between claims made on advertisements and labels in that either should be truthful, non-misleading and supported by scientific evidence. Truthful and non-misleading claims, whether made in advertisements or labels, are protected speech. Furthermore, through truthful and non-misleading labeling and advertisements the regulated industry is able to counterbalance anecdotal opinions from varying sources about its products. We are unaware of social science evidence on this topic.

**7. Would permitting speech by manufacturer, distributor, and marketer about off-label uses undermine the act's requirement that new uses must be approved by the FDA?**

Permitting speech by manufacturer, distributor, and marketer about off-label uses via the dissemination of peer-reviewed journal reprints and textbooks would not undermine the act's requirement that the FDA approve new uses. FDA's goal is to ensure that the public receives truthful and non-misleading information from manufacturers. To serve this end all off-label use statements should come with a disclaimer that such uses have not been cleared or approved by the FDA. There could even be a requirement that such disclaimers precede the off-label use statements.

**8. Do FDA's speech-related regulations advance the public health concerns they are designed to address?**

The FDA's speech-related regulations do, often, advance the public health concerns, but they also, sometimes, deprive, at least, a segment of the public with important information.

Specifically, in the area of analyte specific reagents (ASRs) FDA's speech-related regulations deprive clinicians of important scientific information concerning analytical and clinical information on how best to use the ASR. Under the ASR regulations, manufacturers are prohibited from discussing the analytical and clinical performance of the ASR, which has been interpreted to include how to best use the ASR in a diagnostic test (21 CFR 809.30(d)(4)). This interpretation deprives the clinician of important information, which ultimately impacts the patient.

**9. Are there any regulations, guidance, policies, and practices FDA should change, in light of governing First Amendment authority?**

Relying on the four-pronged test established in Central Hudson, we considered aspects of FDA regulations, guidance, policies, and practices that should change, in light of governing First Amendment authority. Specifically, we considered FDA speech restrictions in the areas of unapproved products, the dissemination of peer-reviewed journal reprints and textbooks, analyte specific reagents (ASRs), pre-approval drug promotion, and financial materials.

#### Unapproved Products

While a product is under FDA review, a manufacturer is very limited in what can be discussed about the product. In light of governing First Amendment authority, it should be permissible to engage in discussions about an investigational medical device that is subject to a pending FDA marketing application, provided the information is truthful, not misleading, and accompanied with a statement that the application is pending FDA approval. Therefore, the regulation at 21 CFR 812.7(a), which prohibits discussion about an investigational product should be changed to allow discussion about the investigational product (e.g., name and area of research) that is subject to a pending FDA marketing application.

Such an approach has worked successfully for medical devices undergoing FDA substantially equivalent determinations under the 510(k) application process. It is permissible to “advertise or display a device that is the subject of a pending 510(k)” (Compliance Policy Guide 7124.9, Section 300.600 Commercial Distribution with Regard to Premarket Notification). In practice, such a display is typically accompanied with a disclaimer “510(k) pending.”

This approach would not undermine FDA’s approval process because the importance of the process is duly noted with the disclaimer. Furthermore, if the product is not on the market for another indication, it does not present a public health risk because there is no product to use. If the medical device is subsequently approved with a different indication, the manufacture should be required to address the difference through a limitation in the product labeling. In this case, the fact that the medical device is not available, a clear identification of the product review status, and limitations in approved product labeling, if necessary, provide sufficient safeguards that it is not necessary to restrict speech about the investigational product.

Similarly, restrictions on speech related to ongoing research of potential new medical devices, are unnecessarily restrictive. Discussions about ongoing research for a product that is not available on the market for another indication and that clearly indicate the product is under research should be permitted. The fact that there is no product available for use provides sufficient safeguards against unapproved use. Furthermore, by including a disclaimer indicating the research status the manufacturer maintains the integrity of the FDA approval process. Limitations on such speech hamper the ability of medical device manufacturers to discuss their current research activities and potential product lines.

Prior to product approval, it is impermissible to discuss product price. For products under FDA review, it should be permissible to discuss price, provided orders are not taken. Decisions to purchase large capital equipment, such as *in vitro* diagnostic instruments, require cost projections, which depend on obtaining a purchase price. This is a time consuming process. Allowing such discussions does not undermine FDA’s

approval process, and because the product is pending approval there is no product for sale.

The above items demonstrate areas in which FDA's interests, preserving the integrity of the approval process and protecting the public from unapproved devices, can be accomplished through means other than restricting speech. As the Supreme Court stated, "if the government could achieve its interests in a manner that does not restrict speech, or restricts less speech, the Government must do so" Thompson v. Western States Medical Center 122 S. Ct. 1497, 1506 (2002). Here, the government's interests are achieved through appropriate notification of the product's regulatory status and by not distributing the unapproved product.

#### Dissemination of textbook and peer-reviewed journal article reprints<sup>1</sup>

The dissemination of peer-reviewed journal articles and textbooks primarily discussing "on-label" uses, should be permitted, even if there is some discussion of an off-label use. Scientifically sound materials are limited from distribution due to anecdotal discussion of an off-label use. Rather, than prohibit all speech, on-label and off-label, inclusion of a notice of the approved use of the product on the material would sufficiently inform the recipient of the product's approved/cleared use(s).

Permitting such off-label speech by manufacturer, distributor, and marketer through the dissemination of peer-reviewed journal article reprints and textbooks would not undermine the act's requirement that the FDA approve new uses. FDA's goal is to ensure that the public receives truthful information from manufactures. To serve this end all off-label use statements could come with a disclaimer that such uses have not been cleared or approved by the FDA.

#### Analyte Specific Reagents

Analyte Specific Reagents (ASRs) are single reagents, which form the building blocks of a diagnostic assay. ASRs are regulated as medical devices and manufactured in accordance with the Quality Systems regulations. Despite the fact that disclaimers about the product's status accompany the product and the test results obtained when using the product, manufacturers are restricted from making any statement regarding analytical or clinical performance (21 CFR 809.30(d)(4)). ASRs and any associated advertising and promotional materials must be accompanied with the statement, "Performance characteristics have not been established." Test results obtained with an ASR must be accompanied with the statement, "This test was developed by (Laboratory Name). It has not been cleared or approved by the Food and Drug Administration" (21 CFR 809.30(e)). Furthermore, manufacturers are restricted to selling ASRs only to laboratories meeting the highest CLIA standards.

By prohibiting manufacturers from making any statement regarding analytical or clinical performance, the Agency has quashed all scientific speech<sup>2</sup> about ASRs, including information that the manufacturer has on how best to use the ASR and minimal analytical characteristics (e.g., test sensitivity and specificity). Restricting scientific

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<sup>1</sup> We do not address here whether off-label speech disseminated through textbooks and peer-reviewed journal article reprints is scientific speech accorded greater constitutional protection than commercial speech.

<sup>2</sup> We do not address here whether such speech would qualify as scientific speech accorded greater constitutional protection than commercial speech.



speech on the optimal use of the ASR does a disservice to the laboratory running the test, the physician ordering the test, and most importantly the patient who is the subject of the test. Through disclaimers, requiring a physician order, and specifying the quality standards of the laboratories permitted to run ASRs, the government's interest of safeguarding the public is achieved. Restriction of scientific speech does not further the FDA's goal of safeguarding the public; rather with ASRs it severely limits the scientific and technical knowledge that is important to developing assays. If FDA is concerned with manufacturers circumventing the product approval process, it could restrict clinical performance claims and clinical utility statements. However, it is not necessary to restrict "any" statement regarding analytical or clinical performance.

#### Pre-Approval Drug Promotion

FDA's "Pre-Approval Promotion Guidance" (June 1994) describes two types of pre-approval promotions for drug products, "Institutional Promotion" and "Coming Soon Promotion." With an "Institutional Promotion" advertisement, the manufacturer may state the drug company name and the area in which it is conducting research, but not the proprietary or established drug name. In "Coming Soon Promotion" advertisements, the manufacturer may state the drug name, but not the area in which the company is conducting research. Assessing these speech restrictions under the Central Hudson test is difficult because the government interest in this policy is not apparent. Furthermore, it is difficult to understand how the government interest would be directly advanced by this policy. Permitting manufacturers to state the drug name and the area in which it is conducting research for phase III drug candidate would better serve the general public, as it would allow individuals to further inquire about specific drugs related to specific therapeutic areas, thereby arming individuals with information about disease conditions and available treatment options.

#### Financial materials

FDA considers financial materials, such as general product portfolios, under its advertisement standards. Such materials have limited purposes, intended to provide product and financial information to investors. Subjecting such materials to FDA's advertisement standards, such as brief summaries and contraindications, prevents manufacturers from discussing important financial information in an unencumbered manner. FDA's interest, protection of the public health, is not served by this policy, and should be modified.

Should you have any questions, please contact April Veoukas at (847) 937-8187 or by facsimile at (847) 938-3106.

Sincerely,

A handwritten signature in cursive script that reads "Douglas L. Sporn".

Douglas L. Sporn  
Divisional Vice President  
Corporate Regulatory Affairs, Abbott Laboratories

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City ABBOTT PARK  
State IL ZIP 60064

2 Your Internal Billing Reference (internal only)

3 To Recipient's Name  
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Does this shipment contain dangerous goods?  
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No  
Shipper's Declaration  
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