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September 13, 2002

Via Facsimile and First Class Mail

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

**Re: Docket Number 02N-0209
Comments on First Amendment Issues**

The Advanced Medical Technology Association (“AdvaMed”) is pleased to respond to FDA’s request for public comment on First Amendment issues. The issues raised by FDA for comment are crucial to ensuring that there are adequate communication lines open between the medical community and industry related to important advances in science and medical technologies. FDA’s policies should encourage, not inhibit, the early communication of important scientific information to health care providers.

AdvaMed is the largest medical technology trade association in the world, representing more than 800 medical device, diagnostic products, and health information systems manufacturers of all sizes. AdvaMed member firms provide annually nearly 90 percent of the \$68 billion of health care technology products purchased in the United States and nearly 50 percent of the \$159 billion purchased worldwide.

AdvaMed supports the manufacturers’ right to exercise their constitutionally protected commercial speech rights. AdvaMed recommends that the agency ensure that its policies comply with governing First Amendment law to ensure that health care providers and patients have access to the most current information regarding advances in medical technology.

AdvaMed’s responses to each of the questions posed in the May 16, 2002 Federal Register Notice follow:

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- 1. Are there arguments for regulating speech about drugs more comprehensively than, for example, about dietary supplements? What must an administrative record contain to sustain such a position? In particular, could FDA sustain a position that certain promotional speech about drugs is inherently misleading, unless it complies with FDA requirements? Does anything turn on whether the speech is made to learned intermediaries or to consumers? What is the evidentiary basis of such a distinction?**

Response to Question 1:

As FDA acknowledged in its request for comment, commercial speech by FDA-regulated industry is entitled to First Amendment protection as long as the speech is truthful and not misleading. Moreover, as FDA discussed, constitutionally protected commercial speech can only be regulated if the restriction is no more burdensome than necessary to directly advance a substantial government interest. See Central Hudson Gas and Elec. Corp. v. Public Serv. Comm. of N.Y., 447 U.S. 557 (1980). This standard is not dependent on the type of product at issue.

As a trade association primarily representing medical device manufacturers, the distinctions between dietary supplement and drug regulation are beyond the scope of our comments. On the other hand, FDA's question regarding its ability to take the "position that certain promotional speech about drugs is inherently misleading" is of concern to our members, because FDA not only takes that position with regard to drugs, but also posits that many types of promotional speech about medical devices are "inherently misleading." Under the standard set forth above, such speech is excluded from First Amendment protection. For example, FDA restricts manufacturer speech regarding off-label uses and unapproved products without any case-by-case analysis of whether the speech at issue is actually misleading. See, e.g., Washington Legal Foundation v. Friedman, 13 F.Supp. 2d 51, 67 (1998) (noting that FDA argued that an industry-supported continuing medical education program regarding an off-label use is "inherently misleading"). This approach infringes on First Amendment protections.

To be "inherently" misleading, the very nature of the speech itself must mislead. Yet, FDA's current policies would ban or permit the exact same speech depending on the identity of the speaker. For example, we question how a scientific presentation regarding an off-label use of a product is "inherently misleading" when sponsored by a manufacturer, but not misleading when sponsored by a third-party. If the speech is "inherently" misleading, would it not mislead in both instances? We would argue that such speech is not "inherently" misleading in either instance. While such programs could be potentially misleading, FDA should be required to proffer appropriate evidence in such instances and initiate enforcement action on a case-by-case basis. The District Court for the District of Columbia noted a similar inconsistency in determining that FDA could not sustain a position that scientific

journal articles regarding off-label uses are “inherently misleading” when disseminated unsolicited by a manufacturer, but not misleading when disseminated in response to a health care provider’s request. In the words of the court, “[o]bviously, the exact same journal article or textbook reprint cannot be inherently conducive to deception and coercion when it is sent unsolicited, yet of significant clinical value when mailed pursuant to a request.” Id.

Similarly, although one factor that courts consider in determining whether speech is misleading is “the ability of the intended audience to evaluate the claims made,”¹ FDA cannot merely ignore First Amendment concerns when a category of speech is targeted to consumers as opposed to learned intermediaries, *i.e.*, physicians. While we concede that certain types of speech, *e.g.*, clinical data, may be more appropriately targeted to health care providers, we question whether even that type of speech would necessarily be “inherently misleading” if provided to consumers. To the contrary, FDA should be required to proffer evidence that the speech is “more likely to deceive the public than to inform it.” See Central Hudson, 447 U.S. at 563.

FDA has a right -- and, in fact, an obligation -- to prevent misleading speech regarding medical products from being disseminated. FDA should be required, however, to demonstrate that the speech is actually misleading before excluding it from First Amendment protections.

- 2. Is FDA’s current position regarding direct-to-consumer and other advertisements consistent with empirical research on the effects of those advertisements, as well as with relevant legal authority? What are the positive and negative effects, if any, of industry’s promotion of prescription drugs, biologics, and/or devices? Does the current regulatory approach and its implementation by industry lead to over-prescription of drugs? Do they increase physician visits or patient compliance with medication regimes? Do they cause patient visits that lead to treatment for under-diagnosed diseases? Does FDA’s current approach and its implementation by industry lead to adequate treatment for under-diagnosed diseases? Do they lead to adequate patient understanding of the potential risks associated with use of drugs? Does FDA’s current approach and its implementation by industry create any impediments to the ability of doctors to give optimal medical advice or prescribe optimal treatment?**

Response to Question 2:

We are not aware of any empirical research regarding the effects of FDA’s direct-to-consumer advertising policy. We do not, however, believe such evidence is relevant or necessary where there exists a violation of First Amendment protections.

¹ See Association of Nat’l Advertisers v. Lungren, 44 F.3d 726, 731 (9th Cir. 1994).

In response to FDA's questions regarding the benefits and potential risks of direct-to-consumer advertising, we contend that the arguments offered in opposition to the consumer advertisements are often paternalistic. That is to say, out of fear that the disseminated information might be misused, opponents argue that it is better not to inform the public. The Supreme Court has consistently taken a dim view of paternalistic speech restrictions. See, e.g., 44 Liquormart, Inc. v. Rhode Island, 517 U.S. 484, 503 (1996) (“[b]ans against truthful, non-misleading commercial speech usually rest solely on the offensive assumption that the public will respond irrationally to the truth. The First Amendment directs us to be especially skeptical of regulations that seek to keep people in the dark for what the government perceives to be their own good.”) FDA's first specific question on this issue, for example, highlights one of these paternalistic concerns, i.e., that direct-to-consumer advertising may lead to over-prescription. We believe this concern is likely unfounded. We do not believe that health care providers make their prescribing decisions based on television advertisements or what their patient may have learned about a drug or device through a direct-to-consumer advertisement. As a result, we do not believe that permitting direct-to-consumer advertisements creates impediments to the ability of health care providers to give optimal medical advice or prescribe optimal treatment. To the contrary, health care providers are certainly more than capable of evaluating whether a particular treatment that a patient learned about through an advertisement is appropriate for the patient and, if necessary, explaining why the treatment is inappropriate.

Furthermore, FDA has recognized the numerous benefits of direct-to-consumer promotion including, for example: (1) increasing health care provider visits and compliance with medication regimes; and (2) encouraging patients to seek treatment for under-diagnosed diseases. We would simply add that at the heart of First Amendment commercial speech protections is the belief that broad dissemination of truthful information only serves the public good. See, e.g., Bates v. State Bar of Arizona, 433 U.S. 350, 364 (1977) (“the free flow of commercial speech ... serves individual and societal interests”).

As a result, we believe that any paternalistic concerns regarding direct-to-consumer advertisements are significantly outweighed by the benefits and encourage CDRH to issue a policy allowing “coming soon” advertisements.

- 3. May FDA distinguish claims concerning conventional foods from those relating to dietary supplements, taking into account limits on claims that can be made about foods in the Nutrition Labeling and Education Act, 21 U.S.C. 301, 321, 337, 343, 371? What must an administrative record contain to sustain or deny claims on food labels? How can information best be presented in a succinct but non-misleading fashion? To what extent do assertions in claims need qualifications or disclaimers added to the label to avoid any misconceptions that consumers may draw? Is there a basis to believe that consumers approach claims about conventional foods and dietary supplements differently?**

Response to Question 3:

As a trade association that principally represents medical device manufacturers, this question pertains to issues beyond the scope of our comments.

- 4. Should disclaimers be required to be in the same (or smaller or larger) size of type and given equal prominence with claims? Is there any relevant authority or social science research on this issue?**

Response to Question 4:

The concept of truthful, non-misleading speech is best served when disclaimers are considered on a case-by-case basis. 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. We are unaware of any social science research on this issue, but do not believe any is necessary to answer these questions.

- 5. How can warnings be made most effective in preventing harm while minimizing the chances of consumer confusion or inattention? Is there any evidence as to which types of warnings consumers follow or disregard?**

Response to Question 5:

We believe that current warnings both in content and prominence are adequate to prevent consumer confusion or inattention. We believe that no additional warnings or any changes to the process by which warnings are developed are necessary at this time.

- 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? Does the First Amendment and the relevant social science evidence afford the Government greater latitude over labels?**

Response to Question 6:

This issue involving claims made in labels and advertising is a First Amendment issue and therefore the analysis should be based on First Amendment principles and doctrines rather than references to social science evidence. There are no arguments under the First Amendment that justify distinguishing between claims made in advertisements and those made on labels. Assuming the claims are truthful and non-misleading, both types of claims are constitutionally protected commercial speech. Admittedly, the Bolger method for determining whether speech is “commercial speech” includes as one of its factors whether the speech is concededly an advertisement. See Bolger v. Youngs Drug Prods., 463 U.S. 60, 66 (1983). At one time, the existence of this factor could have supported a *prima facie* argument that claims on labels -- as opposed to in advertisements -- may not be constitutionally protected commercial speech. In the wake of Pearson v. Shalala,

however, this argument is no longer viable. In Pearson, the court found that “it is undisputed that FDA’s restrictions on [a product’s labeled] health claims are evaluated under the commercial speech doctrine.” See Pearson, 164 F.3d 650, 655 (1999) (citing Bolger); see also Friedman, 13 F. Supp. 2d at 62 (“Typical ‘commercial speech’ is authored and/or uttered directly by the commercial entity that wishes to financially benefit from the message. A purveyor of goods or services makes claim about his products in order to induce a purchase.”) Therefore, First Amendment commercial speech protections apply equally to both claims made on product labels and in advertisements.

- 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? If so, how? If not, why not? What is the extent of FDA’s ability to regulate speech concerning off-label uses?**

Response to Question 7:

No, permitting certain types of truthful non-misleading speech regarding off-label uses would not in any way undermine FDA’s ability to preserve the Federal Food, Drug and Cosmetic Act’s new product approval processes. Assuming FDA limits the scope of such speech, as described in greater detail below, to: (1) the dissemination of scientific journal articles (either the full text or a truthful, non-misleading summary of a peer-reviewed article) and reference text excerpts; and (2) the sponsorship and determination of content, speakers and invitees for continuing medical education (CME) programs, a manufacturer would retain a significant incentive to pursue FDA approval for the new use. Specifically, it would need FDA approval to make safety and effectiveness claims. In fact, we would argue that not only should certain types of speech regarding off-label uses be permitted, but also certain types of speech regarding unapproved products. After all, the fear of misuse of the disseminated information is far less, and the incentive for obtaining FDA approval far greater, in the context of unapproved products because they are not commercially available. Therefore, the information would be purely educational for the recipient. Moreover, with FDA-approved products, some courts have recognized federal preemption defenses with state law claims in connection with medical devices subject to approved premarket applications. See, e.g., Mitchell v. Collagen Corp., 126 F.3d 902 (7th Cir. 1997); see also 21 U.S.C. § 360k(a) (federal preemption provision in Medical Device Amendments). This protection from certain state law claims provides an additional incentive for manufacturers to seek FDA approval for their products.

As noted above, FDA has asserted in the past that certain types of off-label use speech are “inherently misleading,” and therefore are excluded from constitutional protection. As discussed in greater detail above, we disagree with this position. Where the speaker (1) discloses its financial interest in the product discussed; (2) discloses that the use or product discussed is not FDA-approved; and (3) targets its

speech to those trained in the art, such as physicians, we believe the following types of speech are constitutionally protected:

- the dissemination to health care providers of truthful and non-misleading (1) peer-reviewed scientific journal articles and/or abstracts and (2) reference text excerpts that discuss an off-label use or unapproved product (Note: FDA has always recognized that these items could be disseminated by a manufacturer upon receiving a request for that information from a health care provider);
- the dissemination of letters or brochures to health care providers providing: (1) the citation(s) of journal article(s) discussing an off-label use or an unapproved product and/or (2) a truthful and non-misleading summary of the article(s);
- the propagation of advertisements in scientific or medical journals, or information on webpages clearly designated as intended “for health care providers” that provide: (1) the citation(s) of journal article(s) discussing an off-label use or an unapproved product and/or (2) a truthful and non-misleading summary of the article(s);
- a CME program sponsored by a manufacturer which would generally conform to FDA’s Guidance for Industry on Industry-Supported Scientific and Educational Activities (December 1997), except that the manufacturer would be permitted to develop CME program content and generate a list of speakers and invitees, even when the manufacturer was not requested to do so by a third party.

Assuming that a manufacturer disseminates, in one of the forms described above, truthful and non-misleading information regarding an off-label use or unapproved product, FDA only should be able to constitutionally regulate the speech or take enforcement action if it: (1) proffers evidence that, in fact, the speech is untrue or misleading; or (2) can satisfy the Central Hudson standard. Based on recent commercial speech decisions, however, we believe that FDA’s current policies restricting a manufacturer’s ability to engage in off-label use and unapproved product speech would not withstand constitutional scrutiny.

As mentioned above, under Central Hudson, a restriction of constitutionally protected speech is permissible only if: (1) a substantial interest is served by the regulation; (2) the regulation directly advances the asserted interest; and (3) the regulation is not more extensive than is necessary to serve that interest. See Central Hudson, 447 U.S. at 566. When this standard is applied to FDA’s regulations of off-label use and unapproved product speech, FDA’s speech restrictions would be found unconstitutional even if the agency was successful in asserting that preserving the new product approval process is a substantial interest advanced by

the regulation. The restrictions are unconstitutional because they are more extensive than necessary. As mentioned above, FDA need only prohibit manufacturers from making safety and effectiveness claims to preserve the new product approval process. Therefore, by prohibiting significantly more speech than just safety and effectiveness claims, the restrictions on off-label use and unapproved product speech are more extensive than necessary. Moreover, this final element of the Central Hudson standard has consistently been FDA's downfall in recent cases. See Thompson v. Western States Medical Center, 122 S. Ct. 1497, 1506 (2002); Pearson v. Shalala, 164 F.3d 650, 656 (D.C. Cir. 1999); Friedman, 13 F. Supp. 2d at 72-74. It would be FDA's Achilles heel once again if the agency's policies regarding off-label use and unapproved product speech were challenged in the current judicial climate. As a result, to ensure it complies with First Amendment protections, FDA should permit manufacturers to engage in the limited forms of off-label use and unapproved product speech described above.

8. Do FDA's speech-related regulations advance the public health concerns they are designed to address? Are there other alternative approaches that FDA could pursue to accomplish those objectives with fewer restrictions on speech?

Response to Question 8:

No, generally FDA's speech-related regulations do not advance the public health concerns that they are designed to address. Moreover, FDA has several less burdensome alternatives to achieve the aims that supposedly are sought by its current speech restrictions. For example, as discussed above, FDA could significantly reduce restrictions on off-label use and unapproved product speech while still preserving the new product approval process. Specifically, FDA would accomplish its objective of preserving incentives for manufacturers to pursue FDA approval by (1) prohibiting manufacturers from including safety and effectiveness claims in their speech regarding off-label uses and unapproved products; (2) limiting oral communications between the company personnel (i.e., the sales force) and health care providers that would relate to off-label uses or unapproved product information. Instead, all information related to off-label uses and unapproved product would be provided in written form by company personnel to health care providers (i.e., the sales force could directly hand out a copy of the peer-reviewed scientific journal article during a sales call). Company medical directors and other medical or scientific personnel would continue to be able to answer physician questions on off label use as is currently permitted; (3) requiring manufacturers to disclose relevant information to assist health care providers in evaluating such speech (including the fact that FDA has not approved the product for the use described). Moreover, it would accomplish this objective without trampling on First Amendment protections.

In addition, FDA currently has certain policies that appear to restrict speech without advancing any discernable public health purpose. For example, the Food and Drug Modernization Act of 1997 ("FDAMA") permitted a manufacturer to include a

statement in its promotional materials that its product is FDA approved. See FDAMA § 421 (November 21, 1997). As a result, a medical device manufacturer is permitted to state that its product is the subject of an approved PMA. FDA continues, however, to prevent device manufacturers from representing that their products have been 510(k)-cleared by FDA. See 21 C.F.R. § 807.97. Assuming such a statement is truthful, we question the purpose served by barring manufacturers from informing health care providers and/or consumers that their device is legally marketed in the United States. Certainly, it would only promote FDA's public health mission to assist health care providers and consumers from distinguishing between legally marketed devices and those that may be on the market illegally. Moreover, by permitting manufacturers to inform health care providers and consumers of their 510(k) clearance, FDA would be advancing the intent of both FDAMA and the First Amendment.

Therefore, we believe that FDA could reduce restrictions on constitutionally protected speech without harming any of its public health objectives. Moreover, we encourage the agency to take this opportunity to do so.

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

Response to Question 9:

As discussed in greater detail above, to ensure FDA does not infringe on the First Amendment rights of regulated industry, we recommend the following changes to its policies:

- In light of recent commercial speech cases, FDA should not rely on unsupported assertions that certain categories of speech are “inherently misleading” as a means of avoiding constitutional scrutiny of its regulations. Instead, FDA should analyze speech on a case-by-case basis and proffer evidence that the particular speech at issue is actually untrue or misleading before claiming that it is beyond First Amendment protections.
- CDRH should adopt a pre-approval promotional policy (i.e., the use of “institutional” and “coming soon” promotion).
- FDA should permit manufacturers to disseminate truthful and non-misleading information regarding off-label uses and unapproved products. Specifically, FDA should permit the following types of speech as long as there is no evidence that the speech at issue is untrue or misleading, and the speaker (1) discloses its financial interest in the product discussed; (2) discloses that the use or product discussed is not FDA-approved; (3) does not utilize oral communications between company personnel (i.e., the sales force) and health care providers that

would relate to off-label uses or unapproved product information. Instead, all information regarding off-label uses and unapproved products would be provided in written form by company personnel to health care providers (i.e., the sales force could directly hand out a copy of a peer-reviewed scientific journal article during a sales call) and; (4) targets its speech to those trained in the art, such as physicians. Therefore, the following speech should be allowed:

- the dissemination to health care providers of truthful and non-misleading (1) peer-reviewed scientific journal articles and/or abstracts and (2) reference text excerpts that discuss an off-label use or unapproved product;
 - the dissemination of letters or brochures to health care providers providing: (1) the citation(s) of journal article(s) discussing an off-label use or an unapproved product and/or (2) a truthful and non-misleading summary of the article(s);
 - the propagation of advertisements in scientific or medical journals, or information on webpages for healthcare professionals that provide: (1) the citation(s) of journal article(s) discussing an off-label use or an unapproved product and/or (2) a truthful and non-misleading summary of the article(s); and
 - a CME program sponsored by a manufacturer which would generally conform to FDA's Guidance for Industry on Industry-Supported Scientific and Educational Activities (December 1997), except that the manufacturer would be permitted to develop CME program content and generate a list of speakers and invitees, even when the manufacturer was not requested to do so by a third party.
 - FDA should also permit manufacturers to inform physicians and consumers when they have received 510(k) clearance for a medical device.
- FDA should revise its intended use regulation in 21 C.F.R. § 801.4, which is the provision that defines the "intended use" of a product based on a manufacturer's knowledge of an off-label use. As drafted, the so-called "catch 22" provision potentially conflicts with a manufacturer's ability to freely disseminate information about off-label uses or unapproved products. In its current form, this provision could be invoked to require a manufacturer to provide labeling on those off-label uses or unapproved product information contained in the peer-reviewed journal article or abstract---- effectively requiring the manufacturer to

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submit a marketing application to FDA for that off-label use or unapproved product upon dissemination of this type of information. This regulation should be revised to allow a manufacturer to disseminate truthful non-misleading information without imposing restrictions on speech.

AdvaMed appreciates the opportunity to comment on these important issues and looks forward to the policy changes implemented by the agency in response to the public's comments.

Sincerely,

A handwritten signature in cursive script that reads "Nancy Singer". The signature is written in black ink and is positioned above a horizontal line.

Nancy Singer
Special Counsel
AdvaMed