

September 12, 2002

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

7251 02 19 16 14:35

RE: Request for Comments (Docket 02-N0209)

To Whom It May Concern:

I have provided comments in response to the request for comment by the Food and Drug Administration regarding First Amendment Issues (Docket 02N-0209).

This response provides a general overview of the application of the First Amendment Rights to commercial speech, and addresses some of the nine specific questions posed by the agency. My background is in medical devices; where I feel that it is not pertinent to comment, I will reference the general comments.

These responses are my own personal opinion, and do not reflect the opinion of any company for which I may work.

Should you wish to contact me regarding the response, please feel free to contact me directly at (714) 899-8345 or via the Internet at [lovepoohbear@socal.rr.com](mailto:lovepoohbear@socal.rr.com). However, I respectfully request that this personal information remain confidential within the agency, and that any personal and confidential information such as address, telephone number, and Internet mailing address be redacted in the event that any of these comments are published.

Thank you.

With best regards,



Yvette Lloyd  
Senior Regulatory Affairs Specialist

02N-0209

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## I. General Statutory Background:

The First Amendment provides that “Congress shall make no law.....abridging the freedom of speech”. This fundamental right has generally been broadly interpreted in recent years to allow for the unrestricted public dissemination of all protected speech. Protected speech may be regulated, but the government must establish a higher burden of proof to allow for the regulation.

The concept of commercial speech has generally been defined as ‘no more than propose a commercial transaction’. *Virginia State Board of Pharmacy v. Virginia Citizens Consumer Council*, 425 U.S. 748 (1976). Initially, the Supreme Court held that commercial speech was outside the auspice of First Amendment Protection, and therefore could be regulated by government. *Valentine v. Chrestensen*, 316 U.S. 52 (1942). Modernly, commercial speech, has been regarded as being semi-protected speech. It may be said that this form of speech is not as protected as political speech, which is given the highest form of protection; rather, commercial speech is proffered a ‘mid-level’ form of protection based on the holding in *Central Hudson Gas and Electric Corporation v. Public Service Commission*, 447 U.S. 557, 100 S. Ct. 2343, 65 L. Ed. 2D 241 (1980), discussed *herein*. The Court in *Virginia Pharmacy* recognized that commercial speech is an essential element to maintain economic due process, and that commercial speech was required to assist in creating a well-informed consumer. In that holding, Justice Blackmun remarked:

“It is a matter of public interest that those decisions, in the aggregate, be intelligent and well informed. To this end, the free flow of commercial information is indispensable. And if it is indispensable to the proper allocation of resources in a free enterprise system, it is also indispensable to the formation of intelligent opinions as to how that system ought to be regulated or altered.”

## II. Impact of Case law on First Amendment Rights:

As stated above, commercial speech is generally given the mid-level amount of protection, and the government may regulate on the basis on ensuring continuing public safety.

However, the level of regulation must be balanced against the need to not unduly burden the right of industry to advertise.

This balancing calculus was brought forth in the US Supreme Court holding of in *Central Hudson Gas and Electric Corporation v. Public Service Commission*, 447 U.S. 557, 100 S. Ct. 2343, 65 L. Ed. 2D 241 (1980) which provided the following 4-prong test in order to determine whether the government may regulate commercial speech:

1. The speech or message may not be false, misleading or involve illegal activity;
2. The government interest served by the regulation at issue must be substantial;
3. The regulation must directly advance that interest; and,

4. The regulation must not be more extensive than necessary to serve the governmental interest. (i.e., that regulation must be narrowly tailored).

Thus it may be inferred from the 4-part *Central Hudson* calculus, that the government may regulate commercial speech which is truthful, but which may involve dissemination of potentially harmful activities, if it is narrowly tailored to meet a specific governmental interest, and the regulation must directly advance the government's substantial interest in ensuring public safety. Of course, any speech that is misleading or fraudulent is unprotected. The Agency currently has authority to deal with these issues, as evidenced by the 'police' powers that are expressed in the Federal Food and Drug Cosmetic Act.

### III. Specific First Amendment Issues:

Note: These are the nine questions posed by the agency. In order to facilitate the reading, the questions have been reprinted in italic type, while my comments are directly beneath in regular type.

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?*

In general, logic would dictate that a prescription drug should be regulated more comprehensively than a dietary supplement. Because prescription drugs are generally in a higher risk classification by virtue of their harmful potential side effects, it is only natural that these product are more comprehensively regulated. In addition, it would seem logical that prescription drugs are more likely to be discussed with a learned intermediary than would be a dietary supplement.

However, in recent years, information has surfaced that may indicate certain over-the-counter dietary supplements may have potential serious side effects. One only has to perform a simple search on recent warning letters to verify this. Because dietary supplements currently are not strictly regulated as a prescription drug, perhaps the Agency can view their regulation similar to an over-the-counter drug or device. In general, those products are likely to be purchased by a consumer, without the assistance of a learned intermediary. As such, the advertising should be sufficient to create a well-informed consumer. Therefore, the advertising should be truthful, and should strive to make claims that are in accordance with the research and data on file to support such performance claims.

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?*

This questions appears to lean more towards direct to consumer information regarding drug products. Please refer to general comments, as I do not have sufficient expertise in drug regulations to answer this question.

- 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?*

Please refer to general comments, as I do not have sufficient expertise in food regulations to answer this question.

- 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?*

Section 502(c) of the Federal Food, Drug, and Cosmetic Act (the Act) provides express guidelines regarding the prominence of statements required by or under the Authority of the Act, indicating that if there is a lack of prominence, the Agency may deem that drug or device misbranded. The objective test as suggested in Section 502(c) of the Act, is that misbranding may occur when text is "not prominently placed thereon with such conspicuousness (as compared with other words, statements, designs, or devices, in the labeling) and in such terms as to render it likely to be read and understood by the ordinary individual under customary conditions of purchase and use."

Therefore, by derogation of Section 502(c) of the Act, logic would dictate that disclaimers should be given equal prominence as claims. The Agency may have further discretion to require that certain disclaimers be given more prominence if for example, there is a high risk of death or serious injury from use of a product. The higher prominence can be done for example, by bolding the statement, or by placing it at the beginning of the labeling to ensure that it would be read first. The Agency may find such a requirement based on pre-market clinical trial data or from post-market surveillance information (e.g. MDRs, recalls). If the Agency finds that certain products lend themselves to more prominent disclaimers, then I would recommend that the Agency promulgate such requirement via product specific Guidance document. This is a practice that the Agency currently follows

for certain high-risk products, and therefore, it would not add additional burden on the part of the Agency.

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?*

The purpose of a warning statement emanates from the concept of Informed Consent: a consumer via direct reading of the labeling, or via a learned intermediary must understand the warnings so that all material risks are well comprehended, and absent exigent circumstances, the consumer will make a knowingly, voluntary, and intelligent choice about using the product in spite of the inherent risks.

In my opinion, a consumer is likely to disregard a warning statement if it is hidden in the text, or may disregard it if the product labeling dilutes the material risk such that it becomes seemingly innocuous. Additionally, a consumer may fail to read a warning statement if the text is substantially smaller than the surrounding text.

As stated *supra*, the Agency has authority to require equal prominence of any statements required by or under the authority of the Act, and may as part of the Agency's police powers, require a higher prominence of certain statements as discussed *supra*.

In addition, the Agency may want to consider reasonable alternatives to text in order to satisfy the prominence requirement of Section 502(c) of the Act. For example, in lieu of the text "do not resterilize", the Agency may require that the text can either be supplanted or supplemented by the International harmonized symbol, as found for example in EN 980: Graphical symbols for use in the labelling of medical devices. The use of symbols as a pictorial representation of the text may give the meaning of the text more prominence as the symbol, is likely to be seen first before any text might be seen. In addition, because our Nation is filled with such cultural diversity, the use of symbols may be beneficial to those consumers where English is not understood, or where it is not the primary language.

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?*

In my own personal opinion, I view advertisements along the same level as labeling. Because a consumer is more likely to view an advertisement before a label on the product, advertisement should follow the labeling requirements that are appropriate for the product, but allow for some limited flexibility in the spirit of economic due process; such flexibility will allow for the latitude necessary to remain competitive in the free enterprise marketplace.

An advertisement should be regulated to the degree that the claims made on an advertisement are supported by retained objective evidence supporting such performance claims. It should provide the consumer with all material risk

information, such that the consumer can make a well-informed decision as to whether it should be purchased and used in spite of inherent risks. However, an advertisement should not supplant the labeling required for a product. I would argue that an advertisement should be a distilled version of a package insert; if the consumer would like more comprehensive information, they should consult a learned-intermediary or be provided with company contact information to inquire about the product. Finally, in the spirit of free enterprise, an advertisement should be allowed to be given some latitude in the means in which the information is presented. For example, while the Agency may regulate the content of such information, and may in some cases regulate the manner in which it is presented (e.g. prominence of material risks and warnings), any part of the advertisement which is not related to the product per se, such as artwork, should not be regulated by the Agency.

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?*

Modern case law as evidenced by *Tommy G. Thompson, Secretary of Health and Human Services, et al. v. Western States Medical Center, et al.* 535 U.S. S Ct. No. 01-344 (April 29, 2002), seems to suggest that the FDA may be over-regulating commercial speech. While the court acknowledged in *Thompson* that the Agency had a substantial interest in the regulation of unapproved drug uses, and such regulation directly advanced that governmental interest, Section 503(a) of the FDAMA was deemed to be unconstitutional for it failed to meet a part of the *Central Hudson* test. In that analysis, the court held that the regulation was too restrictive, and that the same result could be achieved in a less restrictive manner.

While the case law invalidates Section 503(a) of the FDAMA, it thus leaves open the interpretation of what type of 'off-label' use a company may disseminate, and the extent to which the Agency may regulate that speech.

An objective reading of the Act suggests that the Agency has inherent authority to regulate such off-label use, as evidenced by the requirements in Chapter V – Subchapter D—The Dissemination of Treatment Information. Rather than create new regulation, perhaps the Agency should evaluate the efficacy of the industry's use of that option. It would seem that Subchapter D certainly provides industry adequate means to disseminate off-label uses, however, there is certainly a high amount of Agency regulation involved in that mechanism, as evidenced for example, by the discretion of the Secretary when authorizing the dissemination of unapproved use. For example, could industry perform a type of 'self-certification' by complying with the provisions of that subchapter, minus the submission to the Agency? Or, may industry simply perform a 'simple notification' to the Agency of the intent to disseminate such information, with the understanding that such information is openly reviewable?

Additional options for industry to disseminate off-label use may also be found in Chapter V – Subchapter E—Section 561 Expanded Access to Unapproved Therapies and Diagnostics, where patients may directly access the information

from the manufacturer. However, as with Subsection D, the Secretary is given much discretion to approve such dissemination.

The Agency should evaluate if such discretionary power is more restrictive than necessary and directly advances the government's interest in promoting the health and safety of consumers.

Finally, it should be noted that technology is changing dynamically. It seems logical that industry may promote an 'approved' use of a product, only to find that some practitioner has found a way to use the product in an 'off-label' use and has found success with the 'off-label' use. Furthermore, Section 906 of the Act as added by the FDAMA, promulgates that that "nothing in this Act shall be construed to limit or interfere with the authority of a health care practitioner to prescribe or administer any legally marketed device to a patient for any condition or disease within a legitimate health care practitioner-patient relationship." Therefore, if a practitioner deems it medically necessary to use a product in an 'off-label' use, because the clinical benefits outweigh the inherent risks, the practitioner is essentially provided that opportunity via Section 906 of the Act.

In the future, undoubtedly, practitioners will find more 'off-label' uses with the medical 'tools' they are given, and it will only be natural for industry to want to capitalize on such discoveries and disseminate the information. Furthermore, the Agency should realize that often times, 'off-label' uses domestically, are 'approved' uses abroad. While the Agency's jurisdiction is the domestic marketplace, industry will want to strive for harmonized labeling; as such, the Agency will have to be prepared to deal with these types of situations.

I would encourage the Agency to research the current outcomes of dissemination of 'off-label' use; for example, if the Agency finds a nexus between a higher rate of death or serious injury as a direct result of 'off-label' use, then the Agency is justified in restricting such dissemination. Where such outcomes are statistically insignificant compared to expected incident rates for death or serious injury, there is likely not to be any direct harm from the dissemination of 'off-label' use, and therefore, the Agency may be able to ease the restrictions via Guidance document.

Based on the discussion, *supra*, I do not believe that these regulations will undermine the Agency's ability to regulate unapproved uses. The means describes above, are temporary means for industry to disseminate 'off-label' use. In my opinion, if an 'off-label' use would be economically beneficial for the company to market the 'approved' version, industry will likely perform the necessary clinical work to support safety and efficacy claims of the products in order to obtain the necessary pre-market approval from the Agency.

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?*

The Supreme Court has acknowledged in *Thompson* that the Agency has a significant governmental interest in regulating commercial speech of the products

directly regulated by the Act. Therefore, by derogation, the commercial speech regulations do directly advance public health concerns.

However, the Agency's dilemma will be finding the least restrictive means to directly advance public health concerns. As discussed supra, the Agency appears to have much discretionary power when regulating commercial speech. While such discretion may not be inherently unconstitutional, the Agency should verify if the same means may be advanced without the Agency discretion. In the alternative, the Agency may find that certain high risk products may still require discretionary regulation, while other products may enjoy less restrictions based on the lower risk classification. The agency has already done this similarly by down-classifying many products, and relegating Class I products to general controls.

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

Symbols:

As stated supra, the Agency may want to consider the use of symbols as a means to supplant or supplement the text required by or under the Authority of the Act. The use of symbols is encouraged by the European harmonized standards required to CE Mark a product, as evidenced in the labeling requirements in the Essential Requirements of the various medical devices standards. Given that there are many recognized languages in the European Union, the use of symbols bridges the language barriers and may be thought of as a 'common' international language in unto itself. Symbols are currently utilized in the labeling of many regulated products, and there has been discussion that the ability to utilize symbols is inherent in Chapter V of the Act.

I realize that there is currently joint working groups within the Agency addressing this issue, and I hope that the Agency will see the benefits and realize the low risk in using symbols.

IV. Conclusion:

It is certain that the Agency has a substantial government interest in regulating commercial speech. As an individual working in an industry regulated by the Food and Drug Administration, I can appreciate the difficulty that the Agency must face when attempting to seek harmony between regulating products on the basis of public safety, and not over-regulating such that economic due process is threatened, and it impairs the ability of learned intermediaries and consumers to make a well-informed decision about the use of such products.

As with any First Amendment issue, there can be no law that the Agency would create that would satisfy all parties, since this is a dynamic field, and advertising will continually evolve as the people who create it will strive to continually meet the demands of a well-informed consumer. As such, I would encourage the Agency to set firm basic rules regarding advertising, and more importantly to ensure consistent application of those rules. However, I would encourage the Agency to always look for reasonable alternatives to allow for the future evolution of this information. The Agency should evaluate such alternatives based on a

recognized risk assessment process to ensure that the Agency has performed due diligence when evaluating the impact of such alternatives.

I applaud the agency for opening the dialogue with the public regarding First Amendment issues. Such a move will only strengthen the Agency's power to regulate because the public may be more receptive to complying with the regulation knowing that they have had a chance to voice their opinion and possibly assist with the changing of any regulations, guidance, policies, and practices that govern the way products are advertised or labeled.

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