

# Medical Device Labeling and Advertising: An Overview

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## I. INTRODUCTION

The Food and Drug Administration (FDA) has the authority under the Federal Food, Drug, and Cosmetic Act (FDCA)<sup>1</sup> to regulate the labeling of all medical devices. This statement, however, is not as simple as it appears. The regulation of medical device labels and labeling, closely linked to the advertisement of medical devices, is a dynamic area, and FDA is struggling to address the new issues that arise daily in this area. This article seeks to: 1) provide the background necessary to understand the current law and FDA's regulation of medical devices; 2) summarize the law and regulations governing medical devices; 3) define "intended use" and explain its importance; and 4) discuss several areas that are of particular interest to FDA, including promotion of uncleared or unapproved devices and uses, Internet promotion, press releases, and comparative claims.

## II. BACKGROUND

### A. *Labels and Labeling*

The FDCA defines "label" as "a display of written, printed, or graphic matter upon the immediate container of any article. . . ."<sup>2</sup> Therefore, "label" applies only to what is affixed to the container that holds the actual product. Labeling, however, has a broader definition in the statute. Labeling includes: "all labels and other written, printed, or graphic matter (1) upon any article or any of its containers or wrappers, or (2) accompanying such article."<sup>3</sup> Labeling includes more than the package insert and the label for a device; it may include brochures, detail aids, promotional mailings, posters, "Dear Doctor" letters, and scientific journal articles.<sup>4</sup> For example, reprints of medical articles distributed with a device are categorized as labeling, when the articles supplement or explain the device.<sup>5</sup> Labeling is understood generally to include any written material that supplements or explains the product, is disseminated by the manufacturer, and reaches the customer, doctor, or patient, either before, with, or after the product.<sup>6</sup>

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<sup>1</sup> Pub. L. No. 75-717, 52 Stat. 1040 (1938) (codified as amended 21 U.S.C. §§ 301 et seq. (1994)).

<sup>2</sup> 21 U.S.C. § 321(k) (FDCA § 201(k)).

<sup>3</sup> *Id.* § 321(m) (FDCA § 201(m)).

<sup>4</sup> *See United States v. Kordel*, 335 U.S. 345 (1948) (defining "labeling" to include all printed matter accompanying the drug).

<sup>5</sup> *See United States v. Diapulse Mfg. Corp.*, 389 F.2d 612 (2d Cir. 1968), *cert. denied*, 392 U.S. 907 (1968).

<sup>6</sup> *See United States v. Urbeteit*, 335 U.S. 355 (1948) (holding descriptive leaflets constituted labeling even though the shipment of leaflets did not accompany the shipment of devices); *United States v. 47 Bottles, More or Less, Jenasol RJ Formula "60,"* 320 F.2d 564 (3d Cir. 1963), *cert. denied*, 375 U.S. 953 (1963) (defining test for determining when literature is considered labeling as whether it supplements or explains the article to the prospective purchaser and no physical attachment is necessary).

## B. Advertising

Advertising is not defined in the FDCA, but it is a central issue in medical device law and regulation. Typically, FDA understands advertising to include media-based activities that appear in magazines, newspapers, professional journals, and on radio and television. Thus, there is no clear distinction between advertising and labeling, and many advertisements meet the definition of labeling and can be regulated as such. FDA regulates medical device advertising that does not meet the definition of labeling in two ways: 1) by regulating advertising for restricted devices;<sup>7</sup> and 2) by regulating statements regarding the intended use<sup>8</sup> of a device.<sup>9</sup>

As a post-approval requirement to all premarket approval application (PMA) approvals, FDA declares the device to be restricted and thus has authority to regulate the advertising of all PMA devices.<sup>10</sup> FDA does not have the authority to regulate advertising for 510(k)-cleared devices unless the device has been deemed restricted by regulation or the advertising also constitutes labeling or relates to intended use.

## C. Misbranding

Section 502 of the FDCA governs misbranded devices.<sup>11</sup> FDA deems a device to be misbranded: 1) if its labeling is false or misleading; 2) if any information required by the FDCA to appear on the label or labeling is not prominently placed thereon “with such conspicuousness . . . 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”;<sup>12</sup> 3) if its label does not bear the device’s established name prominently printed in type, at least half as large as that used for any proprietary name or designation for such device; 4) if its labeling does not bear “adequate directions for use and such adequate warnings against use in those pathological conditions or by children where its use may be dangerous to health, or against unsafe dosage or methods or duration of administration or application, in such manner and form, as are necessary for the protection of users”;<sup>13</sup> or 5) if it is dangerous to health when used in the manner suggested in the labeling.<sup>14</sup>

<sup>7</sup> Although the regulations provide no definition of a restricted device, the Secretary of the Department of Health and Human Services (DHHS) may require by regulation that a device be restricted to sale, distribution, or use only on the written or oral authorization of a practitioner licensed by law to administer or use such device or on

such other conditions as the Secretary may prescribe in such regulation, if, because of its potentiality for harmful effect or the collateral measures necessary to its use, the Secretary determines that there cannot otherwise be reasonable assurance of its safety and effectiveness. A restricted device is misbranded, if (1) its advertising is false or misleading in any particular. . . .

or

[i]n the case of any restricted device distributed or offered for sale in any State, unless the manufacturer, packer, or distributor thereof includes in all advertisements and other descriptive printed matter issued or caused to be issued by the manufacturer, packer, or distributor with respect to that device — (1) a true statement of the device’s established name as defined in section 502(e), printed prominently and in type at least half as large as that used for any trade or brand name thereof, and (2) a brief statement of the intended uses of the device and relevant warnings, precautions, side effects, and contraindications . . . .

21 U.S.C. §§ 352(q),(r) (FDCA §§ 502(q),(r)). FDA was supposed to implement restricted device restrictions by regulation but never did so successfully.

<sup>8</sup> See Section IV, *infra*.

<sup>9</sup> The Federal Trade Commission regulates all other advertising.

<sup>10</sup> 21 U.S.C. §§ 352(q),(r).

<sup>11</sup> *Id.* § 352.

<sup>12</sup> *Id.* § 352(c).

<sup>13</sup> *Id.* § 352(f).

<sup>14</sup> See *id.* § 352 (this is not an all-inclusive list).

In determining whether a device is misbranded due to false or misleading labeling or advertising, FDA considers not only representations made or suggested about the device, but also the extent to which the labeling or advertising fails to reveal facts material to the representations made or consequences that may result from the use of the product.<sup>15</sup> The FDCA states that:

. . . in determining whether the labeling or advertising is misleading there shall be taken into account (among other things) not only representations made or suggested by statement, word, design, device, or any combination thereof, but also the extent to which the labeling or advertising fails to reveal facts material in the light of such representations or material with respect to consequences which may result from the use of the article to which the labeling or advertising relates under the conditions of use prescribed in the labeling or advertising thereof or under such conditions of use as are customary or usual.<sup>16</sup>

With regard to labeling, what qualifies as false or misleading is determined by the effect the label and labeling will have on prospective purchasers to whom claims are addressed.<sup>17</sup> Information about the use, benefits, and risks stated in advertising must be consistent with the approved product labeling.

It is important to note that labeling can be “false and misleading” even if it is not technically false or literally untrue.<sup>18</sup> The labeling and advertising must present a “fair balance” of information relating to the side effects and effectiveness of the product. The fair balance concept applies to the content of the materials and the format or manner in which risk information is presented. In this regard, the presentation of risk and benefit information in labeling and advertising comes under scrutiny. For example, although risk and benefit information may be of the same print size, it still may not achieve fair balance if the color and contrast highlight the benefit information more than the risk information.<sup>19</sup>

Prior to 1998, the FDCA prohibited the “use, on the labeling of any drug or device or in any advertising relating to such . . . device, of any representation or suggestion that approval of an application with respect to such drug or device is in effect. . . .”<sup>20</sup> The Food and Drug Administration Modernization Act (FDAMA)<sup>21</sup> amended the FDCA so that a company may indicate in its labeling that its device is “PMA approved.”<sup>22</sup> Doing so no longer constitutes misbranding.

### III. GENERAL LABELING PROVISIONS

#### A. *Name and Place of Business of Manufacturer, Packer, or Distributor*

As a general rule, the label of every device in package form shall “specify conspicuously the name and place of business of the manufacturer, packer, or distribu-

<sup>15</sup> *Id.* § 321(n) (FDCA § 201 (n)).

<sup>16</sup> *Id.*

<sup>17</sup> See *United States v. Articles of Drug*, 263 F. Supp. 212 (D. Neb. 1967).

<sup>18</sup> See *United States v. One Device, More or Less, Ellis Micro-Dynameter*, 224 F. Supp. 265 (E.D. Pa. 1963) (expanding definition of “misleading” to include instances when the total effect of labeling is to deceive or mislead).

<sup>19</sup> See Letter from John W. Thorsky, FDA Acting District Director, Philadelphia District Office to Merck & Company, Inc. (June 16, 1998). This letter is available at <[www.fda.gov/foi/warning\\_letters/d1209b.pdf](http://www.fda.gov/foi/warning_letters/d1209b.pdf)>.

<sup>20</sup> 21 U.S.C. § 310(l) (1997).*Id.*

<sup>21</sup> Pub. L. No. 105-115, 111 Stat. 2296 (1997).

<sup>22</sup> See FDAMA § 421.

tor.”<sup>23</sup> The statement of the place of business must include the street address, city, state, and zip code; the street address may be omitted if it appears in a current city or telephone directory.<sup>24</sup>

### B. Adequate Directions for Use

A device is misbranded unless its labeling bears adequate directions for use.<sup>25</sup> The regulations state that the phrase “adequate directions for use” means “directions under which the layman can use a device safely and for the purposes for which it is intended.”<sup>26</sup> Directions for use may be inadequate because they omit information or provide incorrect information regarding intended use, quantity of dose, frequency of administration or application, duration of administration or application, time of administration or application, route or method of administration or application, or preparation for use.<sup>27</sup>

There are, however, some exemptions from adequate directions for use.<sup>28</sup> For example, prescription devices, which are defined by regulations as “device[s] which, because of any potentiality for harmful effect, or the method of its use, or the collateral measures necessary to its use is not safe except under the supervision of a practitioner licensed by law to direct the use of such device,”<sup>29</sup> are exempt from the statutory requirement of adequate directions for use<sup>30</sup> as long as they meet the conditions set out in the regulations.<sup>31</sup>

### C. Prominence of Required Label Statements

Section 502 of the FDCA<sup>32</sup> requires that any word, statement, or other information required to appear on the label or labeling must be placed prominently with such conspicuousness 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.”<sup>33</sup> Information required by the FDCA to appear on the label or labeling will be deemed to lack the requisite prominence if: 1) the information does not appear on the part of the label presented or displayed under customary conditions of purchase; 2) the label does not extend over the area of the container or package available so as to provide sufficient label space for the prominent placing of such information; 3) the label does not provide enough space for such information because of the use of label space for informa-

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<sup>23</sup> 21 C.F.R. § 801.1(a) (1996). If the name on the label of a device is not the name of the manufacturer, the name must include a phrase that reveals the connection between the name on the device and the device itself, such as “Manufactured for \_\_\_\_\_,” or “Distributed by \_\_\_\_\_.” *Id.* § 801.1(c).

<sup>24</sup> *Id.* § 801.1(d). If a device is manufactured, packed, or distributed at a place other than the principal place of business, the label may state the principal place of business in lieu of the actual place where such device was manufactured or packed or is to be distributed, “unless such statement would be misleading.” *Id.* § 801.1(e).

<sup>25</sup> 21 U.S.C. § 352(f)(1) (FDCA § 502(f)(1)).

<sup>26</sup> 21 C.F.R. § 801.5; *see* Section IV, *infra*, regarding “intended use.”

<sup>27</sup> 21 C.F.R. §§ 801.5(a)-(g).

<sup>28</sup> *See id.* § 801, pt. D.

<sup>29</sup> *Id.* § 801.109.

<sup>30</sup> *See* 21 U.S.C. § 352(f)(1) (FDCA § 502(f)(1)).

<sup>31</sup> 21 C.F.R. § 801.109. Other exemptions from adequate directions for use include: medical devices having commonly known directions; medical devices for processing, repacking, or manufacturing; medical devices for use in teaching, law enforcement, research, analysis; and cigarettes and smokeless tobacco. *See id.* §§ 801.116, 801.122, 801.125, 801.126.

<sup>32</sup> 21 U.S.C. § 352(c) (FDCA § 502(c)).

<sup>33</sup> *Id.*

tion not required by or under the authority of the FDCA; or 4) the information is presented in type that is too small, fades into the background, is obscured, or crowded with other graphic matter.<sup>34</sup>

#### D. Labeling Requirements for Over-The-Counter Devices

The principal display panel of an over-the-counter (OTC) device is the part of the label that is “most likely to be displayed, presented, shown, or examined under customary conditions of display for retail sale.”<sup>35</sup> It must be large enough to accommodate all the mandatory label information required to be placed “with clarity and conspicuousness and without obscuring designs, vignettes, or crowding.”<sup>36</sup>

The principal display panel of an OTC device in package form must bear, as one of its principal features, a statement of the identity.<sup>37</sup> The statement of identity should include the common name of the device and an accurate statement of the principal intended action or actions of the device.<sup>38</sup> The statement of identity must be presented in bold face type on the principal display panel in a size reasonably related to the most prominent printed matter on the panel, and must be in lines parallel to the base on which the package rests as it is designed to be displayed.<sup>39</sup> The label of an OTC device in package form also must contain a declaration of the net quantity of the contents,<sup>40</sup> and this declaration must appear on the principal display panel of the label.<sup>41</sup>

### IV. INTENDED USE

A device is cleared or approved for marketing based on its “intended use.” Intended use refers to the “objective intent of the persons legally responsible for the labeling of devices.”<sup>42</sup> Intent is determined by “such persons’ expressions” or “by the circumstances surrounding the distribution of the article.”<sup>43</sup> FDA provides examples of how objective intent may be shown by stating that “[t]his objective intent may, for example, be shown by labeling claims, advertising matter, or oral<sup>44</sup> or written statements by such persons or their representatives.”<sup>45</sup>

The regulations further provide that intended use may be shown “if the article is, with the knowledge of such persons or their representatives, offered and used for a purpose for which it is neither labeled nor advertised. . . . [I]f a manufacturer knows, or has knowledge of facts that would give him notice that a device introduced into interstate commerce by him is to be used for conditions, purposes, or uses other than the ones for which he offers it, he is required to provide adequate labeling for such a device which accords with such other uses to which the article is to be put.”<sup>46</sup> This

<sup>34</sup> See 21 C.F.R. § 801.15(a) (1998). All information required by or under the authority of the FDCA to appear on the label or labeling must be in English. See *id.* § 801.15(c)(1). There are a few exceptions to this rule. See *id.*

<sup>35</sup> *Id.* § 801.60.

<sup>36</sup> *Id.*

<sup>37</sup> *Id.* § 801.61(a).

<sup>38</sup> *Id.* § 801.61(b).

<sup>39</sup> *Id.* § 801.61(c).

<sup>40</sup> *Id.* § 801.62(a).

<sup>41</sup> *Id.* § 801.62(d).

<sup>42</sup> *Id.* § 801.4.

<sup>43</sup> *Id.*

<sup>44</sup> See *V.E. Irons v. United States*, 244 F.2d 34, 44 (1st Cir. 1957); *United States v. El Rancho Adolphus Prods.*, 243 F.2d 367 (3d Cir. 1952); *United States v. 3 Cartons, More or Less, No. 26 Formula GM*, 132 F. Supp. 569, 574 (S.D. Cal. 1952).

<sup>45</sup> 21 C.F.R. § 801.4.

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

latter provision rarely has been used by FDA and has not been tested in the courts. It may attempt to extend FDA's authority beyond the FDCA. Nevertheless, manufacturers should know that FDA may invoke this authority if doing so is considered necessary.

As FDAMA explicitly states, FDA does not have the authority to interfere with a health care practitioner's ability to prescribe any legally marketed device to a patient for any condition or disease within a legitimate health care practitioner-patient relationship.<sup>47</sup> This provision is referred to as the "practice of medicine" exception to FDA regulation of unapproved uses of devices. This provision allows a physician to prescribe a device for a purpose not approved by FDA, and therefore not listed as an "intended use" in the product labeling. Physicians also may prescribe the device to patients in groups other than those for whom FDA approved it, for periods exceeding the labeled recommended use, or in combination with other FDA-approved drugs.<sup>48</sup> Health care practitioners enjoyed broad latitude in their prescribing practices prior to the passage of FDAMA.<sup>49</sup> FDAMA, however, affirmed that FDA's regulatory authority regarding unapproved uses is limited to manufacturers.

## V. CURRENT ISSUES IN MEDICAL DEVICE LABELING AND ADVERTISING

### A. Advertising of Unapproved/Uncleared Devices

FDA's general rule is that medical device firms are not permitted to promote devices if they are not approved or cleared.<sup>50</sup> There are, however, some exceptions to this rule.

#### 1. Prohibition of Commercialization of Investigational Devices

FDA's investigational device exemption (IDE) regulations are detailed regarding the promotion of investigational devices. They prohibit a sponsor, investigator, or any person acting on behalf of these parties, from promoting an investigational device until after FDA has approved or cleared the device for commercial distribution.<sup>51</sup>

In addition, the IDE regulations expressly prohibit representing or implying that an investigational device is safe or effective for the investigational use.<sup>52</sup> Accordingly, any materials that represent or suggest safety and efficacy for an investigational device — whether via labeling, advertising on television, or Internet communication — would violate this regulation.

The following practices are considered to be improper commercialization of investigational, unapproved, or uncleared devices: enrolling excess investigators or patients in an investigational study; orchestrating undirected mass mailings; giving volume discounts on investigational devices, offering pricing information, or charging a

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<sup>47</sup> 21 U.S.C. § 396.

<sup>48</sup> See Steven R. Salbu, Off-Label Use, Prescription, and Marketing of FDA-Approved Drugs: An Assessment of Legislative and Regulatory Policy, 51 FLA. L. REV. 181, 189 (1999).

<sup>49</sup> See, e.g., Rhone-Poulenc Rorer Pharm., Inc. v. Marion Merrell Dow, Inc., 93 F.3d 511, 514 n.3 (8th Cir. 1996); Weaver v. Reagen, 886 F.2d 194, 198 (8th Cir. 1989); United States v. Evers, 453 F. Supp. 1141, 1149-50 (M.D. Ala. 1978), *aff'd*, 643 F.2d 1043 (5th Cir. 1981).

<sup>50</sup> FDA "approves" pre-market approval applications (PMA), but only "clears" 510(k) submissions. FDA's regulations prohibit the use of the term "approved" with regard to a 510(k) clearance because it implies that the clearance is a finding of the safety and effectiveness of the device, whereas it is only a conclusion of "substantial equivalence." See 21 C.F.R. § 807.97.

<sup>51</sup> *Id.* § 812.7.

<sup>52</sup> See *id.* § 812.5(b).

price in excess of the amount necessary to recoup manufacturing, research and development, and handling; and unduly prolonging an investigational study.<sup>53</sup>

Although FDA prohibits promotion of investigational devices, FDA does permit manufacturers of Class III investigational devices to distribute “Notices of Availability of an Investigational Device” to recruit investigators for clinical studies.<sup>54</sup> FDA strictly circumscribes the type of information that sponsors of Class III investigational devices can disseminate through Notices of Availability. One critical point is that the manufacturer must not state, suggest, or imply that the investigational device is safe or effective for its investigational indication.<sup>55</sup>

Another essential point is that Notices of Availability must target potential investigators, qualified to evaluate the safety and effectiveness of the Class III investigational device.<sup>56</sup> Notices of Availability to broad audiences are viewed as promotional by FDA.<sup>57</sup> Information disseminated on the Internet reaches broad audiences, instead of targeting investigator candidates and, thus, would constitute promotion. As such, FDA would consider the Internet, among other information sources, to be inappropriate for recruiting investigators for clinical studies of investigational devices.<sup>58</sup> In contrast, it is likely that FDA would consider scientific or medical journal pieces targeting physicians appropriate for dissemination of such Notices of Availability.

FDA permits advertisements intended to recruit patients, but they are considered part of the informed consent and subject selection process; thus, review by the institutional review board is necessary to ensure that the information provided is not misleading.<sup>59</sup> Here again, neither the sponsor nor the investigator may make any claims that the device is safe or effective for the purposes under investigation.<sup>60</sup> According to FDA’s guidance, “FDA believes that any advertisement to recruit subjects should be limited to the information the prospective subjects need to determine their eligibility and interest.”<sup>61</sup>

## 2. *Display of Devices Pending 510(k) Clearance*

Some display and advertising of devices pending 510(k) clearance is permitted.<sup>62</sup> For example, manufacturers are permitted to advertise or show uncleared products at trade shows. Materials should be limited to objective, factual statements regarding the device, its features, and how it operates. Any description of the device should not include comparisons to competitor’s devices, as FDA is likely to view any comparisons as illegal claims. Manufacturers may not make safety or effectiveness claims about the device, and manufacturers may not take any orders or be prepared to take orders that might result in contracts for sale of the uncleared device.<sup>63</sup>

<sup>53</sup> See *id.* § 812.7.

<sup>54</sup> See *Guidance for Industry and FDA Staff: Preparing Notices of Availability of Investigational Medical Devices and for Recruiting Study Subjects* (Mar. 19, 1999).

<sup>55</sup> *Id.*

<sup>56</sup> *Id.*

<sup>57</sup> *Id.*

<sup>58</sup> See *id.*

<sup>59</sup> See *id.*

<sup>60</sup> See *id.*

<sup>61</sup> *Id.*

<sup>62</sup> See Sec. 300.600 COMMERCIAL DISTRIBUTION WITH REGARD TO PREMARKET NOTIFICATION (§ 510(k)) (Compliance Policy Guide 7124.19) (Sept. 24, 1987) (“Although a firm may advertise or display a device that is the subject of a pending 510(k) — in the hope that FDA will conclude that the device is substantially equivalent to a pre-amendments device — a firm may not take orders, or be prepared to take orders, that might result in contracts of sale for the device unless limited to research or investigational use.”).

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

## B. *Promotion of Unapproved/Uncleared Uses of an Approved or Cleared Device*

### 1. *General Promotion of Unapproved/Uncleared Uses*

FDA's general rule is that manufacturing firms are not permitted to promote devices for uses that have not been cleared or approved. FDA has issued warning letters for violations of this rule. For example, FDA issued a warning letter to a company for advertising its device for uses for which it had not submitted a 510(k) containing valid scientific evidence supporting those uses.<sup>64</sup> The sponsor promoted the device for "stereotactic functional neurosurgery/intraoperative microelectrode guidance during pallidotomy, thalamotomy, and the implantation of deep brain stimulators for the treatment of Parkinson's Disease and essential tremor,"<sup>65</sup> but the device was cleared only for "recording of intracranial neural activity and for stimulation at subsurface levels of the brain during surgery."<sup>66</sup> In the warning letter, FDA stated that as a result of this promotion, the device was "adulterated within the meaning of section 501(f)(1)(B) of the Act<sup>67</sup> in that it was a Class III device under section 513(f), and [did] not have an approved application for premarket (PMA) [*sic*] in effect pursuant to section 515(a), or an approved application for investigational device exemption (IDE) under section 520(g)."<sup>68</sup> FDA also stated that the device was "misbranded within the meaning of section 502(o)<sup>69</sup> of the Act, in that a notice or other information respecting the modification in the intended use of the device was not provided to FDA as required by 21 C.F.R. 807.81(a)(3)(ii), and the device was not found to be substantially equivalent to a predicate device."<sup>70</sup>

FDA issued a warning letter to another company for promoting its device for the treatment of specific conditions when FDA had not approved or cleared the use of the device for the treatment of specific conditions.<sup>71</sup> The iontophoresis drug delivery system at issue had been cleared under Section 510(k) for "the local administration of ionic drug solutions into the body for medical purposes and [for use] as an alternative to injections."<sup>72</sup> The sponsor was promoting the device for use with a specific drug without FDA approval of the drug for iontophoretic administration.<sup>73</sup> In this letter, FDA stated that:

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<sup>64</sup> Letter from Lillian J. Gill, Director, Office of Compliance, Center for Devices and Radiological Health (CDRH) to Axon Instruments, Inc. (Sept. 1, 1999). This letter is available at <[www.fda.gov/foi/warning\\_letters/m2910n.pdf](http://www.fda.gov/foi/warning_letters/m2910n.pdf)>.

<sup>65</sup> *Id.*

<sup>66</sup> *Id.*

<sup>67</sup> Section 501(f)(1)(B) states that a device is adulterated if it is a Class III device "which was classified under section 513(f) into Class III, which under section 515(a) is required to have in effect an approved application for premarket approval, and which is not exempt from section 515 under section 520(g), and . . . which has an application which has been suspended or is otherwise not in effect . . ." 21 U.S.C. § 351(f)(1)(B).

<sup>68</sup> Gill, *supra* note 64.

<sup>69</sup> FDCA § 502(o) states that a device is misbranded if:

it was manufactured, prepared, propagated, compounded, or processed in an establishment in any State not duly registered under section 510(k), if it was not included in a list required by section 510(j), if a notice or other information respecting it was not provided as required by such section or section 510(k), or if it does not bear such symbols from the uniform system for identification of devices prescribed under section 510(e) as the Secretary by regulation requires.

21 U.S.C. § 352(o).

<sup>70</sup> Gill, *supra* note 64.

<sup>71</sup> Letter from Lillian J. Gill, Director, Office of Compliance, CDRH to Empi, Inc. (Aug. 31, 1999). This letter is available at <[www.fda.gov/foi/warning\\_letters/m2906n.pdf](http://www.fda.gov/foi/warning_letters/m2906n.pdf)>.

<sup>72</sup> *Id.*

<sup>73</sup> *Id.*

[m]arketing the [device] for treatment of the specific conditions listed above, or any other claims for uses which have not been cleared by FDA, and labeling or promoting [the] device for use with specific drugs . . . without FDA approval of an NDA (new drug application) for such use, causes the device to be adulterated within the meaning of section 501(f)(1)(B) of the Act in that it is a Class III device under section 513(f), and does not have an approved application for premarket approval (PMA) in effect pursuant to section 515(a), or an approved application for investigational device exemption (IDE) under section 520(g).<sup>74</sup>

In addition, FDA stated that the device was “misbranded within the meaning of section 502(o) of the Act, in that a notice or other information respecting the modification in the intended use of the device was not provided to FDA as required by 21 C.F.R. 807.81(a)(3)(ii), and the device was not found to be substantially equivalent to a predicate device.”<sup>75</sup>

## 2. *Dissemination of Scientific Journal Articles and Reference Texts and Scientific Symposia*

The dissemination of scientific journal articles and reference texts, as well as the sponsorship of scientific symposia, discussing unapproved or uncleared uses of a medical device currently are concerns of FDA. The dissemination of this information and the sponsorship of scientific symposia constitute labeling or an oral statement of intended use, and if the use discussed is not approved or cleared, FDA has determined that these activities misbrand the product.

The Washington Legal Foundation (WLF) brought suit against FDA in the Federal District Court in the District of Columbia challenging FDA’s policies, rules, and regulations in this regard.<sup>76</sup> In July 1998, the court held that FDA’s policies, rules, and regulations violated the First Amendment of the Constitution.<sup>77</sup> The court granted WLF’s motion for summary judgment and issued an order enjoining FDA from enforcing policies restricting certain forms of manufacturer communication of off-label uses for drugs and devices.<sup>78</sup>

The court, looking at three specific Guidance Documents,<sup>79</sup> found that FDA could not seek to limit any medical device manufacturer or any other person:

- from disseminating or redistributing to physicians or other medical professionals any article concerning prescription drugs or medical devices previously published in a bona fide peer-reviewed professional journal, regardless of whether such article includes a significant or exclusive focus on uses of medical devices other than those approved by FDA . . . ;
- from disseminating or redistributing to physicians or other medical professionals any reference textbook . . . or any portion thereof published by a bona fide inde-

<sup>74</sup> *Id.*

<sup>75</sup> *Id.*

<sup>76</sup> Washington Legal Found. v. Friedman, 13 F. Supp. 2d 51 (D.D.C. 1998).

<sup>77</sup> *Id.* at 74.

<sup>78</sup> *Id.* at 74-75.

<sup>79</sup> The specific Guidance Documents at issue were: Guidance to Industry on Dissemination of Reprints of Certain Published, Original Data, 61 Fed. Reg. 52,800 (Oct. 8, 1996); Guidance for Industry Funded Dissemination of Reference Texts, 61 Fed. Reg. 52,800; and Final Guidance on Industry Supported Scientific and Educational Activities, 62 Fed. Reg. 64,074 (Dec. 3, 1997).

- pendent publisher and otherwise generally available for sale in bookstores or other distribution channels where similar books normally are available, regardless of whether such reference textbook includes a significant or exclusive focus on uses of drugs or medical devices other than those approved by FDA; or
- from suggesting content or speakers to an independent program provider in connection with a continuing medical education seminar program or other symposium, regardless of whether uses of drugs and medical devices other than those approved by FDA, are to be discussed.<sup>80</sup>

The court did say that FDA could require the manufacturer to disclose that the uses have not been approved.<sup>81</sup> In addition, the court noted various limitations on a manufacturer's rights. For example, manufacturers still are "proscribed from producing and distributing any internally-produced marketing materials to physicians concerning off-label uses, or from involvement with seminars not conducted by an 'independent program provider.'"<sup>82</sup> Nor may medical device manufacturers "initiate person-to-person contact with a physician about an off-label use," and they may not "advertise off-label uses for previously approved [products] directly to the consumer."<sup>83</sup>

In July 1999 the court denied the defendant's motion to exclude FDAMA from the scope of *Friedman*, and amended its order to reflect the unconstitutionality of the FDAMA provisions and implementing regulations.<sup>84</sup> The court found that the FDAMA provisions perpetuated in part, and modified in part, the policies that were held unconstitutional in its July 1998 opinion.<sup>85</sup> Specifically, the court examined FDAMA's requirement that a manufacturer satisfy the following conditions before disseminating journal articles and reference texts: 1) the device must be subject to an approved application or otherwise lawfully marketed; 2) the disseminated scientific journal articles or reference texts must be unabridged, not false or misleading, and not pose a significant risk to public health; 3) the material presented in the scientific article or reference text must not be derived from clinical research by another manufacturer without that manufacturer's permission; 4) the manufacturer must submit an advance copy of the journal article or reference text to be disseminated to FDA along with any clinical trial information and reports of clinical experience; 5) the manufacturer must submit a supplemental application for the off-label use or have certified that such an application will be submitted; 6) the disseminated scientific journal article or reference text must include certain disclosures about the off-label uses; and 7) the manufacturer must prepare and submit semi-annually to FDA lists of the articles and reference publications disseminated and categories of recipients.<sup>86</sup>

The court did not consider whether its permanent injunction order in the July 1998 decision covered these FDAMA provisions. Instead, it framed the issue as "whether the changes in FDA policy effected by the FDAMA have brought the FDA

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<sup>80</sup> *Friedman*, 13 F. Supp. 2d at 74-75.

<sup>81</sup> *Id.* at 73.

<sup>82</sup> *Id.*

<sup>83</sup> *Id.*

<sup>84</sup> The court declared "FDAMA and its implementing regulations" unconstitutional without clarifying that only the relevant provisions of FDAMA are unconstitutional. In its final amended order, however, the court declared 21 U.S.C. §§ 360aaa-360aaa-6 unconstitutional, which are the provisions that describe FDAMA's requirements for the dissemination of treatment information regarding drugs and devices. Therefore, despite the imprecise wording, the opinion should be interpreted as applying only to the relevant provisions.

<sup>85</sup> *Washington Legal Found. v. Henney*, 56 F. Supp. 2d 81 (D.D.C. 1999).

<sup>86</sup> 21 U.S.C. § 360aaa. The court found that FDA regulations implementing this section of FDAMA do not differ materially from the statute itself and, therefore, only discussed the statute in its opinion. Slip op. at 7.

into compliance with the First Amendment.”<sup>87</sup> This is an important distinction because instead of simply relying on its original opinion to determine whether its injunction order applied to the FDAMA provisions, the court conducted a new analysis under the *Central Hudson* test for judicial review of commercial speech regulations.<sup>88</sup>

The court did not repeat its legal reasoning, set forth in earlier opinions, for concluding that *Central Hudson* was the appropriate standard for assessing the constitutionality of the policies.<sup>89</sup> The court did, however, discuss its reasoning in rejecting FDA’s argument that the commercial speech standard is inapplicable. The defendants argued that the FDAMA provisions in question do not restrict speech, but rather “affirmatively permit” speech, when concurring with the statute.<sup>90</sup> The court found this argument “preposterous” and contrary to the First Amendment which protects the people’s right to “engage in truthful, nonmisleading speech about lawful activity.”<sup>91</sup> The court, therefore, analyzed the FDAMA provisions under the *Central Hudson* test which protects lawful, nonmisleading commercial speech unless: 1) the government’s interest in regulating the speech is substantial; 2) the regulation directly advances the government’s interest; and 3) the regulation is not more extensive than necessary to advance the government’s interest.<sup>92</sup> To receive protection under *Central Hudson*, the commercial speech at issue must not be unlawful or inherently misleading; the court found that the scientific journal articles and reference texts at issue met this threshold.

The court acknowledged two government interests in regulating the dissemination of the scientific journal articles and reference texts at issue. First, the government has an interest in ensuring that physicians receive a “balanced” flow of accurate and unbiased information upon which to make prescription decisions. Second, the government has an interest in encouraging drug and device manufacturers to seek FDA approval of off-label uses. Despite acknowledging the first governmental interest, the court rejected it as “paternalistic,” noting that the physicians receiving the journal articles and reference texts are “sophisticated listener[s] trained extensively in the use of such information.”<sup>93</sup> Therefore, the court found the first interest insufficient to satisfy the “substantial interest” prong of *Central Hudson*. When analyzing the government’s second interest, however, the court noted that Congress has mandated that all drug and device uses be approved by FDA for the benefit of public health. The court relied on this congressional judgment in finding that encouraging manufacturers to seek FDA approval for new uses is a “substantial” government interest.<sup>94</sup>

The court found that only one FDAMA restriction on dissemination, the supplemental new drug application requirement,<sup>95</sup> directly advances the government’s substantial interest in encouraging manufacturers to seek FDA approval for new uses.<sup>96</sup> The court rejected the position that many FDAMA prerequisites advance FDA’s inter-

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<sup>87</sup> Slip op. at 6.

<sup>88</sup> See *Central Hudson Gas & Elec. Corp. v. Public Serv. Comm’n*, 447 U.S. 557 (1980).

<sup>89</sup> Slip op. at 7. In *Friedman*, the court examined why the dissemination of journal articles and reference texts is speech as opposed to conduct, and why it is commercial speech as opposed to pure speech in order to determine that *Central Hudson* was the appropriate standard. 13 F. Supp. 2d at 59-64.

<sup>90</sup> Slip. op. at 8.

<sup>91</sup> *Id.*

<sup>92</sup> *Id.* at 7.

<sup>93</sup> *Id.* at 11.

<sup>94</sup> *Id.* at 11-12.

<sup>95</sup> As discussed above, FDAMA requires a manufacturer to: 1) submit a supplemental new drug application for the off-label use discussed in the disseminated journal article or reference text; 2) certify that such an application will be submitted; or 3) be declared exempt from the requirement by the DHHS Secretary in order to disseminate the article or reference text on the off-label use. *Id.* at 4.

<sup>96</sup> *Id.* at 12.

est in ensuring that physicians receive a balanced flow of information, because that interest was insufficient to meet the “substantial interest” prong of the test.<sup>97</sup> The court also dismissed the argument that generally restricting speech about off-label uses creates an incentive for manufacturers to seek FDA approval for the use, thereby advancing the government’s interest. The court noted that even if true, encumbering speech does not advance the government’s interest directly.<sup>98</sup> Thus, the court found that the government’s substantial interest in encouraging manufacturers to seek FDA approval is advanced directly only by requiring a supplemental new drug application (NDA) as a prerequisite to disseminating scientific journal articles or reference texts on off-label uses.<sup>99</sup>

The court held that the FDAMA provisions and implementing regulations restricting a manufacturer’s dissemination of scientific journal articles or reference texts regarding off-label uses are unconstitutional under the First Amendment. FDA has appealed this decision, and the decision could be stayed pending appeal and that the district court’s opinion could be reversed. Thus, FDA’s policy regarding the dissemination of these materials currently is in flux.

### C. *Internet Advertising and Promotion*

#### 1. *FDA Regulation of Promotion and Advertising on the Internet*

The Internet presents novel issues that FDA’s regulations and guidance originally did not contemplate. Specific differences include the interactive potential of the Internet; the capability to create links to other websites not associated with the manufacturer of a regulated product; the global nature of the Internet that allows American Internet users access to information initiated abroad, and vice versa; and the accessibility of the Internet to all types of users, including consumers, investors, and medical professionals.

FDA has not issued any formal guidance that addresses specifically the novel promotional issues presented by increasing use of the Internet, and has not determined when it will finalize a written guidance document. Until a formal guidance is published, FDA’s warning letters are the main source of observations regarding FDA’s current policies. Because FDA has not finalized its Internet policies, this article offers only general observations, based on current policies and regulations governing labeling, conversations with the Center for Devices and Radiological Health’s Promotion and Advertising Policy Staff (Office of Compliance), and other research.

#### 2. *Restrictions on Internet Promotional Practices*

FDA consistently has taken the position that information published on the Internet will be treated as labeling and subject to all of the misbranding provisions applicable to labeling. This is evidenced by several warning letters that have been issued by the agency regarding Internet promotion.

For example, FDA issued a warning letter to a manufacturer of microcannulas whose microcannulas were cleared for passage into a surgically created body cavity for removal of fluids and tissues by suction. The Internet site for the product, however, contained, “the impermissible promotion of [the] products for use in the tumescent

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<sup>97</sup> *Id.*

<sup>98</sup> *Id.* at 12-13.

<sup>99</sup> *Id.* at 13.

liposuction procedure.”<sup>100</sup> FDA stated in the warning letter that “[t]he claims for tumescent liposuction procedures have misbranded and adulterated, within the meanings of sections 502(o) and 501(f)(1)(B), respectively, of the Act, the [device]. . . .”<sup>101</sup> The language in this letter is similar to the language used in FDA’s warning letters to manufacturers that promote their products for unapproved or uncleared uses through more traditional media than the Internet.

FDA also issued a warning letter to a manufacturer of a uterine balloon therapy system being promoted on the manufacturer’s home page as safe and effective for the treatment of menorrhagia.<sup>102</sup> The device had not been cleared for menorrhagia, and thus FDA stated that such promotion rendered the device adulterated under the FDCA.<sup>103</sup> In addition, FDA found that this Internet promotion constituted commercialization of an investigational device.<sup>104</sup>

Internet links are an area of concern, but they have yet to be addressed definitively by FDA. It is safe to assume that links between sites that discuss approved/cleared devices and their approved/cleared uses do not create regulatory issues. FDA recently issued a warning letter, however, to the manufacturer of a transurethral injection needle system and injection/aspiration needle device concerning the links it provided on its website.<sup>105</sup> FDA stated that the material presented on the website modified the manufacturer’s products’ intended use, requiring the submission to FDA of a PMA, and resulted in the misbranding and adulteration of both devices.<sup>106</sup> FDA specifically pointed out a link on the website to an article which included a statement that “the delivery of adenoviral vectors directly to the prostate provided the ‘best route to treat local regional prostate cancer by viral-based gene therapy.’”<sup>107</sup> In spite of the fact that there was no explicit reference to the manufacturer’s products in the article, FDA concluded that the implication created by the link to the article, along with a picture of the device after the article, was that the device could be used to deliver adenoviral vectors to the prostate in the treatment of cancer.<sup>108</sup> According to FDA, however, the 510(k) record for the device clearly stated that the device should not be marketed for the treatment of benign or malignant prostate conditions.<sup>109</sup> In addition, the website contained a link to a website entitled “Gene Therapy.”<sup>110</sup> The “Gene Therapy” website linked to several websites referring to various aspects of gene therapy, as well as a picture of the device with a caption reading, “Gene Therapy Delivery Systems.”<sup>111</sup> FDA found that the “Gene Therapy” page further implied that the device could be used in gene therapy, a component of some cancer treatments.<sup>112</sup> As a result, FDA found the device to be misbranded and adulterated.<sup>113</sup>

<sup>100</sup> Letter from Lillian Gill, Director, Office of Compliance, CDRH to HK Surgical, Inc. (Aug. 11, 1999). This letter is available at <[www.fda.gov/foi/warning\\_letters/m2858n.pdf](http://www.fda.gov/foi/warning_letters/m2858n.pdf)>.

<sup>101</sup> *Id.*

<sup>102</sup> Letter from Lillian J. Gill, Director, Office of Compliance, CDRH to Gynecare, Inc. (Feb. 5, 1997). This letter is available at <[www.fda.gov/foi/warning\\_letters/d1163b.pdf](http://www.fda.gov/foi/warning_letters/d1163b.pdf)>.

<sup>103</sup> *See id.*

<sup>104</sup> *See id.*; *See also* Section V.A.1, *supra*.

<sup>105</sup> Letter from Lillian Gill, Director, Office of Compliance, CDRH to Ximed Medical Systems/ Prosurg, Inc. (July 22, 1999). This letter is available at <[www.fda.gov/foi/m2783n.pdf](http://www.fda.gov/foi/m2783n.pdf)>.

<sup>106</sup> *Id.*

<sup>107</sup> *Id.*

<sup>108</sup> *See id.*

<sup>109</sup> *See id.*

<sup>110</sup> *See id.*

<sup>111</sup> *See id.*

<sup>112</sup> *See id.*

<sup>113</sup> *See id.*

Regulatory issues also arise when a company uses the Internet to promote a device or an indication that has been approved in a foreign country, but not in the United States. It is unclear whether FDA has the authority to control this information. FDA may take the position that a company has violated FDA's regulations by linking to a specific site discussing unapproved uses or products.

Thus far, FDA has taken action against only blatant violations on the Internet because: 1) FDA's authority over foreign communications is questionable; 2) constitutional free speech issues may circumscribe the control that FDA would like to assert over promotion on the Internet; and 3) FDA is faced with the daunting task of monitoring all regulated industry websites to ensure compliance with FDA's regulations and policies. In addition, there are non-promotional reasons a manufacturer would want to put information on its website; for example, to tell investors of a product in the pipeline. FDA's authority over such information is debatable. The above-mentioned letters are examples of FDA's criticism of firms for traditional and/or blatant violations that appear on companies' websites.

#### D. *Comparative Claims*

The regulations state that, "[a]mong representations in the labeling of a device which render such device misbranded is a false or misleading representation with respect to another device or a drug or food or cosmetic."<sup>114</sup> These are referred to as "comparative claims" and currently are a major interest of FDA's.

FDA discourages advertising or promotional materials that compare one device with another. All comparative claims must be supported by reliable scientific data, including a study that directly compares the products. That study must be presented in full and must point out the negative aspects of the study, in addition to the positive. In recent years, FDA has written many warning letters to medical device manufacturers for making unsubstantiated comparative claims. For example, FDA issued a warning letter to the manufacturer of a ventricular assist device for making comparative claims to a device that was approved for indications different from its own.<sup>115</sup> FDA described the comparisons as "meaningless" and "misleading."<sup>116</sup> Thus, FDA found the device to be misbranded and adulterated.<sup>117</sup>

#### E. *Press Releases and Investor Relations Materials*

Product specific press releases, including those targeted to investors and regulated by the Securities and Exchange Commission, may be subject to FDA scrutiny, for example, as labeling or advertising for restricted devices and/or material that demonstrates a manufacturer's intended use. FDA does not hesitate to issue warning letters based on information that appears in press releases. For example, FDA issued a warning letter to a manufacturer of a non-rebreathing mask and valve because the manufacturer's press release contained the statement that its device was, "the only CPR (cardiopulmonary resuscitation) mask to be awarded an FDA 510(k) number. . . ."<sup>118</sup> Because there are other CPR masks that have received clearance from FDA, this state-

<sup>114</sup> 21 C.F.R. § 801.6.

<sup>115</sup> See Letter from Lillian Gill, Director, Office of Compliance, CDRH to Thoratec Laboratories Corp. (Aug. 12, 1999). This letter is available at <[www.fda.gov/foi/warning\\_letters/m2863n.pdf](http://www.fda.gov/foi/warning_letters/m2863n.pdf)>.

<sup>116</sup> *Id.*

<sup>117</sup> See *id.*

<sup>118</sup> Letter from Lillian Gill, Director, Office of Compliance, CDRH to Emergency Filtration Products, Inc. (Apr. 29, 1999). This letter is available at <[www.fda.gov/foi/warning\\_letters/m2572n.pdf](http://www.fda.gov/foi/warning_letters/m2572n.pdf)>.

ment was found to be misleading.<sup>119</sup> Another example is a warning letter written to the manufacturer of an in vitro diagnostic test. The press release started with the title, "Heart Attack-Detection Breakthrough . . ." and continued with the subtitles, "Human Clinical Trial Shows New FDA-Cleared Blood Clot Test . . . May Facilitate Early, Cost-Effective Detection of Thrombosis and Thereby Reduce Mortality and Morbidity in Patients with Acute Cardiac Symptoms" and "An Accurate, Rapid and Reliable Clinical Test for Detecting a Blood Clot Will Assist in the Early Diagnosis of Acute Myocardial Infarction (Heart Attack)."<sup>120</sup> The press release also stated that the manufacturer's device was "at least three times more sensitive in a clinical study than commercially available biochemical markers currently used for diagnosing heart attacks."<sup>121</sup> FDA found that the titles and the comparison to heart attack markers implied that the test could be used to diagnose heart attacks though the device had not been cleared for that use.<sup>122</sup> FDA stated that these claims misbranded the device.<sup>123</sup>

These examples demonstrate that FDA will review press releases and take action when it concludes that the press release is not accurate, is inconsistent with the approved labeling, or contains indications and claims that have not been approved or cleared for a product. Press releases that announce information about uncleared or unapproved products (i.e., press releases regarding the results of clinical trials) for investment purposes should not suggest that the product is safe or effective for the uncleared or unapproved use. Although a manufacturer may promote a device that has been PMA-approved as approved by FDA, an informal "one bite of the apple" policy for announcing 510(k) clearances in a press release has been adopted. Thus, a company only may say that its device is 510(k)-cleared in the first press release issued at the time the device is cleared.

## VI. CONCLUSION

This article provides an overview of the laws and regulations impacting medical device advertising and labeling. Medical device labeling and advertising is a dynamic area that continues to present new challenges to FDA and medical device manufacturers. The issues that arise on a daily basis, such as the promotion of investigational devices and unapproved uses, along with the new issues like Internet promotion, constantly present new questions that FDA has to address. How FDA chooses to answer these questions will have an enormous impact on medical device manufacturers in the years to come.

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<sup>119</sup> *See id.*

<sup>120</sup> Letter from Lillian Gill, Director, Office of Compliance, CDRH to American Biogenetic Sciences, Inc. (Mar. 6, 1997). This letter is available at <[www.fda.gov/foi/warning\\_letters/d1240b.pdf](http://www.fda.gov/foi/warning_letters/d1240b.pdf)>.

<sup>121</sup> *Id.*

<sup>122</sup> *See id.*

<sup>123</sup> *See id.*

