Displaying Investigational and Unapproved Medical Devices According to FDA Policy

Manufacturers who follow FDA's policies when showing investigational or unapproved devices—whether at a trade show or on a Web site—can avoid arousing the agency's suspicions.

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DISPLAYING INVESTIGATIONAL and unapproved devices at trade shows, in directed mailings, and on the Internet is important to the vitality of the medical device industry. For instance, to attract investment capital,manufacturers need to educate potential investors about the kinds of technology under development. In addition,new devices often require substantial capital outlays by purchasers, who can use advance knowledge of upcoming devices to plan for this type of purchase. Finally, product development can benefit from early feedback from potential users and the scientific community. Even the display of a device with a pending 510(k) submission—that is, a device that may be a new brand of an existing technology—allows the manufacturer to hit the ground running with sales after receiving clearance and thus to compete better with existing brands.

Aware of the importance of such premarket exhibition, FDA permits the display of investigational and unapproved medical devices. But the agency has its concerns and therefore limits such display. One concern is that a sponsor of an investigational device may be a biased source of information with an interest in making claims for the device beyond what the clinical trial data support. Allowing sponsors to put their own spin on research results, the agency believes, could undermine the impartial scientific evaluation of investigational devices. It also could allow sponsors to create false or misleading impressions about a device among potential users, impressions that the agency fears could be difficult to dispel if the device is later approved for more limited use.

Another concern applies to the display of marketed devices that are under investigation for a new use or that have a 510(k) pending for such a use. Because FDA does not regulate the practice of medicine, users can engage in off-label uses without interference from the agency. FDA fears that displaying marketed devices for new uses may encourage such off-label uses before the agency has evaluated their safety and efficacy.

FDA's approach to the display of investigational and unapproved devices represents an attempt to balance these competing concerns. This article discusses FDA's current policies, possible revisions to them as part of a comprehensive trade show compliance policy guide (CPG) now under review at the agency, and the emerging question of how the policies apply to the Internet.

DEVICES WITH 510(k) SUBMISSIONS PENDING

Since 1978, FDA has permitted the display and advertising prior to clearance of devices with pending 510(k) submissions. This policy is set forth in FDA's CPG 7124.19, which states:

> 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 preamendment device—a firm may not take orders or be prepared to take orders that might result in contracts for sale for the device unless limited to research or investigational use.[1]

FDA is considering requiring devices with pending 510(k)s be labeled "Pending 510(k), not available for sale within the United States. "

Thus, a device with a pending 510(k) may be displayed and advertised if the manufacturer does not solicit or accept any purchase orders. In addition, all claims made about the device must adhere to the intended use for which the 510(k) notification is pending.

FDA is considering revising the CPG to require that devices with pending 510(k)s be displayed with the label "Pending 510(k), not available for sale within the United States."[2] This revised label would send a clear message to potential purchasers about the status of the device. Some manufacturers already use such a label to prove they are not soliciting sales.

FDA is also reviewing whether to liberalize its policy by allowing the display of uncleared devices before the submission of 510(k) notifications, so long as manufacturers are prepared to provide upon request "reasonable assurances" of intent to submit them.[3] Such a relaxation makes sense because there is little reason to prohibit display while a manufacturer prepares a 510(k) notification, as opposed to requiring the manufacturer to wait until after it has been submitted. However, the revised policy will not be worth much to manufacturers if they must produce a mountain of evidence to prove their intention to submit 510(k) notifications. For instance, FDA has considered requiring manufacturers to produce their substantial equivalence data.[4] But, as a practical matter, this approach would preclude manufacturers from displaying devices until their 510(k) notifications were almost complete and might even deter them from taking advantage of the policy at all for fear of opening themselves up to a potentially intrusive presubmission review of their data. A better solution would be to require manufacturers to provide upon request written certification of intent to submit 510(k)s for displayed devices. The certification would prove a manufacturer's intent while eliminating the need for an unwieldy evaluation of its substantial equivalence data.

INVESTIGATIONAL DEVICES

Under the *Code of Federal Regulations,* 21 C.F.R. 812.7, a device studied under an approved investigational device exemption (IDE) application may not be represented as safe and effective for its investigational use or otherwise promoted until after FDA has approved it for commercial distribution. In 1985, FDA issued a guideline clarifying that a sponsor may publicize the availability of an investigational device to recruit clinical investigators for proposed or ongoing clinical trials.[5] The recruiting process can include, among other activities, displaying the device. The guideline indicates that a sponsor should:

1. Announce the availability of the device only in medical and scientific publications or at medical or scientific conferences whose readership or audiences are composed primarily of experts qualified by scientific training and experience to investigate the safety and effectiveness of devices.
2. State in clear terms that the purpose is only to obtain investigators and not to make the device generally available. Enrolling more investigators or subjects than necessary to evaluate the safety and effectiveness of the device will be considered promotion or commercialization of the device. In addition,promoting availability of the device to obtain additional sponsors may be considered promotion or commercialization of the device.
3. Limit the information presented in any notice of availability to the following: the name and address of the sponsor, how to apply to be an investigator, and how to obtain the device for investigational use. The notice should further list the investigator's responsibilities during the course of the investigation:namely, to await Institutional Review Board (IRB) and FDA approval before allowing any subject to participate, to obtain informed consent from subjects, to permit the device to be used only with subjects under the investigator's supervision, to report adverse reactions, to keep accurate records,and, more generally, to conduct the investigation in accordance with the signed agreement with the sponsor, the investigational plan, FDA's regulations, and whatever conditions of approval are imposed by the reviewing IRB or FDA.
4. Use direct mailing for the sole purpose of soliciting qualified experts to conduct investigations. (Note: An undirected mass mailing will not be considered an appropriate means of soliciting clinical investigators. Such a mailing will be considered promotion.)
5. Include the following statement displayed prominently and in print at least as large as the print in the notice: "Caution—Investigational Device, Limited by Federal (or United States) Law to Investigational Use." (Note: a clear, unequivocal statement that the device is under investigation and is available only for investigational uses should be made in oral presentations.)
6. Make only objective statements concerning the physical nature of the device.
7. Ensure that no claims are made which state or imply, directly or indirectly, that the device is reliable, durable, dependable, safe, or effective for the purposes under investigation or that the device is in any way superior to any other device.
8. Not present comparative descriptions of the device with other devices but may include reasonably-sized drawings or photographs of the device.
9. Not include information regarding pricing data but may include information stating where such data may be obtained. A sponsor or investigator should not offer volume discounts for an investigational device. FDA would regard such discounts as the promotion of an investigational device.

It would be naive to assume that sponsors display devices pursuant to the guideline solely to recruit investigators. In fact, even FDA generally accepts that a device may be dis-

played while a PMA application is pending, even if the IDE study has closed and there is no longer any need to recruit investigators. FDA's chief concern is that sponsors should observe the key provisions of the guideline—for example, that the device should be labeled as investigational and that accompanying written and oral statements do not claim that the device is safe and effective for its investigational use. FDA is also likely to object if a sponsor conveys price information, solicits or accepts orders in anticipation of approval, or discusses the prospects for approval. These practices are likely to lead the agency to conclude that the sponsor is promoting the device.

FDA's revised trade show CPG may explicitly permit the display of investigational devices with an approved IDE if labeled "Work in progress." It also may allow the display of devices with a pending PMA application if labeled "Pending PMA,not available for sale within the United States." These revisions would help end the current pretense in FDA's written policy that investigational devices are displayed solely to recruit clinical investigators.

FDA's concern regarding a new use doesn't apply if the preapproved device needs manufacturer modification.

If FDA requests clinical data in support of a 510(k) submission, the prohibition in section 812.7 against promoting a device until after FDA has approved it for commercial distribution takes effect when the sponsor obtains an IDE, even if the IDE is for a nonsignificant-risk study that does not require advance approval from FDA. As a legal matter, section 812.7 probably overrides CPG 7124.19, which allows display and promotion of a device with a pending 510(k). The safest course for the sponsor, therefore, would be to follow the rules for displaying investigational devices rather than those for devices with a pending 510(k).

Regulatory Status	*Type of Acceptable Labeling and Promotion while on Display*
510(k) submission pending (no IDE and device not available for sale in the United States)	Promote only for intended uses covered by pending 510(k) submission.
Approved IDE	Follow 1985 guideline and add label, "Caution—Investigational Device, Limited by Federal Law to Investigational Use."
PMA application pending	Follow 1985 guideline and add label, "Caution—Investigational Device, Limited by Federal Law to Investigational Use."
510(k) pending (IDE)	Follow 1985 guideline and add label, "Caution—Investigational Device, Limited by Federal Law to Investigational Use."
Already available for sale in the United States but a new use is under investigation or FDA review	Promote only for previously cleared or approved uses unless the device would require modification by the manufacturer to perform the new use.
Foreign approval only (noIDE,510(k), orPMA application pending)	Label device as "Not Available for Sale in the United States." If the device is manufactured abroad, may import with certification that it is for testing and evaluation and will be reexported or destroyed afterward.
Foreign approval for a use different from use approved in United States	Promote only for U.S.–approved use.

Summary of current FDA requirements for the display of investigational or unapproved devices.

PREVIOUSLY APPROVED OR CLEARED DEVICES UNDER INVESTIGATION FOR NEW USES

If a device has received 510(k) clearance or premarket approval, it may be displayed and promoted only for its cleared or approved uses. There can be no promotional display of investigational or unapproved new uses. The agency fears that because the device is already available for sale, the spread of information about a new use is likely to encourage it. This concern does not apply if the marketed device cannot be converted to the new use without modification by the manufacturer. The revised trade show CPG is almost certain to continue these policies.

DEVICE WITH FOREIGN APPROVAL ONLY

One issue FDA has not addressed with published guidance is whether a foreign manufacturer that does not intend to seek clearance or approval in the United States can display its foreign-approved device at an international trade show held in the United States. However, the agency has stated in an unpublished writing that such a device may be brought into the country if certain conditions are met.[6] First, the device must be accompanied by entry forms that disclose its unapproved status. Next, the manufacturer must indicate that the device is being imported solely for "testing or evaluation" and include a statement that remaining product will be destroyed or exported. Furthermore, when the device is actually on display in the United States, it must be labeled "Not available for sale in the United States," and no sales orders may be taken. FDA's current approach will probably be formalized in the revised trade show CPG.[7] Presumably, the same policy will apply to a device manufactured here for export only. Otherwise, domestic manufacturers would be unable to show their devices while foreign manufacturers could. Such unequal treatment would only encourage domestic manufacturers to move offshore.

An important caveat is that this policy remains subject to the prohibition against off-label promotion. Thus, if a device is cleared or approved in this country for one use, it cannot be displayed at trade shows for another use that is only approved abroad. To be displayed, the device must be completely unavailable for sale in the United States for any intended use.

THE INTERNET

The Internet's interactive browsing capability and the multitude of Web pages that have sprouted for medical device manufacturers create an environment strikingly similar to a trade show. One could analogize Web pages to exhibit booths, with "handouts" now downloaded by modem and oral discussion at the booth replaced by E-mail. For the most part, FDA probably does not need special rules to address the display of investigational and unapproved devices on the Internet. For example, sponsors should be permitted to display investigational devices on Web pages intended to recruit clinical investigators as long as they follow the 1985 guideline.

Although FDA is revising its trade show policy, its fundamental concerns are unlikely to change.

There are some aspects of the Internet, however, that will complicate efforts to apply existing law. For one thing, information on the Internet cannot easily be restricted to specific audiences. For example, because laypersons have free access to sites that are intended for recruiting clinical investigators, sponsors cannot honor the 1985 guideline's requirement to "[a]nnounce the availability of the device only in medical and scientific publications or at medical or scientific conferences whose readership or audiences are composed primarily of experts qualified by scientific training and experience to investigate the safety and effectiveness of devices." It is possible to restrict access to a Web site, but only by prearrangement with those who are permitted access by being given a password. But this kind of arrangement undercuts one of the most useful features of the Internet—the ability to coordinate the activities of anonymous individuals who did not know about each other's existence.

The Internet also crosses international boundaries, thereby creating problems when approvals in the United States lag behind those in foreign markets. Vidamed, Inc. (Menlo Park, CA), received a warning letter issued in July 1996 because its Web page made safety and efficacy claims about its TUNA System for treatment of benign prostatic hyperplasia (BPH), which did not yet have 510(k) clearance from FDA. According to Vidamed, however, the device had received foreign approval for BPH and the company was using its Web page to communicate with foreign distributors. Nonetheless, Vidamed discontinued its Web page until it received 510(k) clearance for BPH from FDA in late 1996. Judging from the warning letter to Vidamed, FDA's position appears to be that a firm with a device cleared or approved for use in the United States may not display a new use for it on the Internet prior to clearance or approval, even if that new use has foreign approval. This position is in line with FDA's existing rule that a device already on the market in this country may be displayed at trade shows only for its cleared or approved uses. Unfortunately, as the Internet becomes ever more integral to commerce, this restriction could increasingly hamstring U.S. companies in foreign markets. Unable to display foreign-approved uses on their Web sites, U.S. manufacturers will have to compete against foreign manufacturers not subject to this restriction. Nonetheless, FDA is unlikely to back down, because it is most concerned about a manufacturer's dissemination of off-label information when a product is already on the market in the United States. There is no obvious solution to this dilemma.

Finally, the easy linkage among sites on the Internet tends to blur the distinction between the display of the device at the manufacturer's Web site and at other ones. If a manufacturer provides a link to a site that it controls, that linked site probably should be treated as part of the manufacturer's display, much like a second booth set up in a different part of a convention center. On the other hand, prohibiting manufacturers from establishing a link to an independent Web site arguably infringes upon the First Amendment rights of the manufacturer and of Web browsers.[8] To a lesser degree, the same is true of sites that a manufacturer underwrites but does not purport to control.

This tension is not unique to the Internet. The same issue is at the heart of the intense controversy over FDA's policy toward industry support for continuing medical education and scientific conferences and distribution of journal articles and textbook reprints.[9,10] Whatever the final shape of FDA's policy in this area, it should be feasible to extend it relatively unchanged to Internet links.

CONCLUSION

Although its trade show policy will be revised when the final CPG is issued, FDA's fundamental concerns are unlikely to change. They can be summarized as follows: First, if a device is on the market, it should be displayed and promoted only for cleared or approved uses. Second, investigational devices should not be promoted or otherwise represented as safe or effective. And finally, if a device has a 510(k) pending, it should be displayed only for the intended uses covered by the submission. Manufacturers who observe these three tenets almost certainly will avoid running afoul of the agency when showing an investigational or unapproved device—whether the display takes place in a downtown convention center or in cyberspace.

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