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Approvals

Revising Premarket Notification: The Canadian Process as a Model

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A recent Government Accountability Office study, mandated by the Food and Drug Administration Amendments Act of 2007, and released in January 2009 (3 MELR 75, 1/28/09), represents the culmination of over a year's worth of speculation on what changes to the medical device approval process in the United States should be made. Many in the industry thought that the focus of the final report would be on the 510(k) premarket notification process and debates about reforming the ''substantial equivalence'' methodology for approving class I and class II medical devices dominated the conversation leading up to the release of the GAO report. Congress heard testimony from consumer advocates in late 2007 and early 2008 criticizing the FDA's use of the 510(k) process because some complex medical devices are cleared for marketing without clinical evaluation of safety and effectiveness. This central theme of needing stronger scientific evidence (such as clinical trials) before a product can be cleared for marketing also has played a central role in the recent congressional investigation of the FDA Center for Devices and Radiological Health (CDRH). The calls for more clinical data to be submitted with 510(k) submissions speaks to a continuing concern that devices with new materials, operating principles and fundamental technology are able to be cleared for marketing through a ''substantial equivalence'' analysis rather than rigorous testing.

Perhaps the primary fear of many in the medical device industry was that the GAO report would recommend splitting class II devices and ''up-classify'' certain categories of class II devices into class III (such as implantable or life sustaining devices). Additional predictions were that the GAO report would recommend requiring more performance data and increase postmarket evaluation obligations.

But, the final GAO report was somewhat of a letdown after all the lead-up and after much anticipation of reformist recommendations. In short, the GAO recommends that the FDA immediately take steps to ensure that high-risk class III medical devices not be permitted to enter the market through the less rigorous 510(k) process. The GAO found that FDA had not complied with the requirements of the Safe Medical Devices Act of 1990 to reclassify or require premarket approval (PMA) for class III devices. As of October 2008, 20 class III devices could still get to market through the 510(k) process rather than premarket approval.

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This does not mean, however, that the discussions about 510(k) reform should be dropped or that the industry should expect that 510(k) process to continue to operate as-is under the new administration. Rather, now might be a good time to evaluate other regulatory systems used for ensuring that medical devices are safe and effective for their intended uses. A review of the Canadian regulation of medical devices may provide insight into alternative ways to regulate medical devices in the United States. Such a comparison may also highlight key components of the 510(k) process in the United States that are uniquely effective and worth preserving, whatever reform looms on the horizon.

Canadian Regulation of Medical Devices

The Canadian system of regulating medical devices is similar to its U.S. counterpart in many ways. The regulation of health products, including medical devices, is governed by Health Canada, pursuant to the Canadian Food and Drugs Act. Medical devices are grouped into four risk-based classes. The lowest-risk class (class I) does not need to be licensed, but manufacturers of a medical device in any of the other three classes, must submit applications for review and approval by Health Canada prior to importation or sale.

Medical device license applications must contain the basic information about the manufacturer, product and uses for which licensure is sought as well as how it will be labeled. In addition, evidence must be submitted to establish how the device will meet a prescribed set of safety and effectiveness requirements relating to the design, manufacture and performance of devices. The level of substantiation of the safety and efficacy of a device required depends on the device's class. For example, applications for class II device licenses must contain a declaration that the device meets the safety and effectiveness standards set out in the Regulations. For the highest-risk class (class IV), detailed information of all studies on which the manufacturer relies, including pre-clinical and clinical studies, must be submitted.

Notwithstanding the many similarities between the Canadian and U.S. systems of regulating devices, there are a number of differences. (See Chart 1).

One such difference is that whereas the FDA relies upon its regulations in 21 C.F.R. Part 820 to address quality, Health Canada relies on ISO standards. Applications for class II medical device licenses must be submitted with a certificate asserting that the device meets a quality standard (ISO standard 13488:2003) developed by the International Organization for Standardization. Class III and IV devices must meet ISO standard 13485:2003, which deals with both design and manufacturing standards.

Chart 1

United States - FDA

Class	Device Examples	Approval Pathway	Key Approval Criteria
I	Examination gloves, tongue depressors, hand-held surgical instruments	Premarket Notification(510(k)); Most are Exempted*	Finding of ''substantial equivalence'' to a previously cleared device
II	Infusion pumps, surgical drapes, powered wheelchairs	Premarket Notification(510(k));Some are Exempted	Finding of ''substantial equivalence'' to a previously cleared device
III	Pacemakers, replacement heart valves, breast implants	Premarket Approval (PMA)**	Independent demonstration of safety and efficacy, usually though clinical trials

*Exempt devices are not subject to FDA review prior to marketing

**Approximately 20 Class III devices can receive approval through the 510(k) process

Canada - Health Canada

Class	Device Examples	Approval Pathway	Key Approval Criteria*
I	Tongue depressors, gowns, bandages	Compliance with Safety and Efficacy Requirements	None; not subject to Health Canada licensure review prior to marketing
II	Contact lenses, pregnancy test kits, endoscopes	Licensure, Compliance with Safety and Efficacy Requirements	Attestation to safety and efficacy, quality management system, and labeling requirements, and standards used
III	Glucose monitors, orthopedic implants	Licensure, Compliance with Safety and Efficacy Requirements	Similar to Class II, plus: information on sales outside Canada, summaries of all studies, copy of device label
IV	Pacemakers, cranial shunts	Licensure, Compliance with Safety and Efficacy Requirements	Similar to Class III, plus: manufacturing process, risk assessment, quality plan, clinical studies

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*In vitro devices for all Classes are subject to additional criteria

The recent GAO report highlights one of the other significant differences between the Canadian and U.S. medical device regulatory systems, namely that there is no Canadian equivalent to the 510(k) process for market approval. In Canada, each device (other than a class I device) must obtain a license by way of application to, and approval by, Health Canada. By contrast, the U.S. approach is to require all devices to use the 510(k) premarket notification process unless specifically exempted or required to use the more onerous premarket approval process. Although the absence of the 510(k) process may seem, at first blush, onerous to industry, there are avenues available in the Canadian process to expedite the device license application process:

Conformity with Recognized Standards—As noted above, the crux of device licensure in Canada is the establishment that the device meets the safety and effectiveness requirements as well as the labeling requirements. For particular kinds of devices, national or international standards have been developed by standards writing organizations such as ISO. Standards recognized by Health Canada are published on a list on its Web site, and updated from time to time. If a device meets a particular standard, a declaration of conformity can be submitted with the device license application, which will at least partially fulfill the requirement of establishing safety and effectiveness. To the extent that a specific device has qualities or properties that are not addressed by the recognized standard, additional substantiation including clinical testing in some cases, may be required. Where there is no applicable standard, independent evidence of safety and effectiveness must be provided, the nature and extent of which will depend on the class of the device as well as its particular characteristics.

The standards conformity process in Canada highlights one of the key issues raised by critics of the current 510(k) process in the United States. Calls for clinical testing for each and every medical device prior to marketing are thought to be overly burdensome and costly by those in the medical device industry. Currently, FDA makes use of consensus standards (and declarations of conformity) to support reasonable assurances of safety and effectiveness for certain aspects of a medical device. However, FDA reviewers are given flexibility to identify instances where a consensus standard alone is insufficient to address specific safety or effectiveness concerns or where substantial equivalence is not established through the consensus standard alone. FDA reviewers may then require additional information beyond the consensus standards, including clinical trial evidence if required elsewhere in the FDA regulations. The Canadian model provides additional support for continued use of recognized, consensus standards as a way to streamline review of medical devices, yet retain the flexibility to address specific safety and effectiveness concerns.

Private License—In recognition that many devices will be sold by way of private license, Health Canada has an expedited application process for such applications. Applications for private label device licenses are submitted with a letter of authorization from the original manufacturer granting permission for the cross-referencing of the safety and effectiveness information and quality systems certificate that formed the application for the original device. Key to this process is the consent and cooperation of the original manufacturer, because the private label device license is, in essence, an extension of the original device's license. The applicant seeking private license is essentially requesting to label the identical device, licensed by Health Canada to the original manufacturer, under a different name. This requires a letter of authorization granting permission from the original manufacturer. By way of example, once approved, a private label device's license is automatically amended if an amendment is made to the original manufacturer's device license.

The concept of private license is handled quite differently in the United States. In many cases, the individual or company who received the 510(k) clearance in the first instance may wish to license the rights to market the device to another. The 510(k) holder is required by the regulations to notify the FDA that the ownership of the 510(k) has changed, but the FDA does not track this information and does not include it in publicly available databases.

Conclusion

The contrast between the Canadian and U.S. regulation of medical devices demonstrates that there are varying options for ensuring the safety and effectiveness of medical devices. That Canada and the United States have taken different approaches to regulating the same types of medical devices is evidence that the current U.S. system is not necessarily the only option available. The medical device industry should be proactive in evaluating other regulatory models and prepare to provide viable options to policymakers and regulators in the United States.