

Beyond the US > Submission Process

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After expending considerable effort to comply with United States (US) marketing authorisation regulations, a company launched its first product on the US market. Unfortunately, the company failed to comply with other applicable US regulations, which led to a delay in the US product introduction and FDA postmarketing enforcement actions against the product. This article discusses ways that companies can prevent this from happening.

Range of regulations

Companies marketing medical devices in the United States (US) should have a clear understanding of the range of US regulations that apply to their products. Instead, some companies concentrate primarily on complying with the regulations related to the authorisation process. Failure to comply with other applicable regulations can lead to delays in market introduction, increased costs related to regulatory enforcement actions, and possibly lost sales due to negative publicity resulting from US enforcement actions. Thus, it is critical that companies allocate the needed resources to develop a comprehensive regulatory programme that identifies and complies with all applicable US regulations.

The Food and Drug Administration (FDA) Center for Devices and Radiological Health (CDRH) maintains a website, Device Advice, (www.fda.gov/cdrh/devadvice) that provides a useful overview of US regulation of medical devices and radiation-emitting products with links to more detailed information. In contrast, the CDRH homepage (www.fda.gov/cdrh/) provides extensive and useful information on US medical device regulations and requirements, but sometimes overwhelms companies unfamiliar with US regulation. Some companies needing an introduction to the regulations find the Device Advice site easier to understand when initiating this effort.



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Registration and listing

Companies are sometimes surprised to learn that unless they have fulfilled US registration and listing requirements, their products cannot be imported into the US. NonUS establishments must register, name a US agent and list their devices before exporting their medical devices to the US. The role of the US agent is discussed below. Therefore, companies need to complete these processes in a timely fashion to avoid shipment and distribution delays. No registration or listing fee is required.

The requirements for registration and listing are described in US 21 Code of Federal Regulations (CFR) Part 807, Establishment Registration and Device Listing for Manufacturers and Initial Importers of Devices. Registration and listing requirements apply to companies that

- initiate or develop device specifications
- manufacture a device for itself or for another person; however, a company that only manufactures devices according to another company's specifications, for commercial distribution by the company initiating specifications, is not required to list those devices
- repackaging or relabel a device
- act as initial importers
- manufacture components or accessories that are ready to be used and packaged or labelled for commercial distribution such as haemodialysis tubing or ophthalmic lenses blanks.

The establishment registration process and instructions for completing the establishment registration form FDA-2891 are found at www.fda.gov/cdrh/devadvice/341.html. The device listing process and instructions for completing the device listing form FDA-2892 are found at www.fda.gov/cdrh/devadvice/342.html. These forms may be completed online, but must be printed and mailed to FDA. If an establishment is registering for the first time, the registration form must be mailed to FDA with the medical device listing form. The establishment registration forms have been recently updated and obsolete forms cannot be used. In addition to the information provided by the Device Advice site, registration and listing information, including requirements applicable to nonUS establishments can be found at www.fda.gov/cdrh/reglistpage.html

Designating a US agent


As mentioned previously, nonUS establishments must name a US agent before exporting their medical devices to the US. These establishments must notify FDA of the name, address and phone number of their US agent who must reside in the US or maintain a place of business in the US. In addition, the US agent cannot use a post office box as an address, cannot use an answering service and must be available to answer the phone or have an employee available to answer the phone during normal business hours. The responsibilities of the US agent include

- assisting FDA in communications with the nonUS establishment,
- responding to questions concerning the nonUS establishment's products that are imported or offered for import into the US
- assisting FDA in scheduling inspections of the foreign establishment.

In addition, if FDA is unable to contact the foreign establishment, FDA may provide information or documents to the US agent. If this is necessary, FDA will consider this action equivalent to providing that information or documents to the foreign establishment. In future, form FDA-2891 (b) will be used for reporting US agent information; however, this form is not yet available. Therefore, nonUS establishments must notify FDA of its US agent by sending a letter to FDA. The information that must be provided and a sample letter can be found at www.fda.gov/cdrh/devadvice/341.html#USA

If the nonUS establishment is registering for the first time, the registration form FDA-2891 should be mailed with the US agent notification letter. FDA states that forms FDA-2891 or FDA-2892 cannot be used to identify a US agent.

Quality system regulation

Unless exempt, manufacturers of medical devices imported into the US must comply with the requirements described in 21 CFR Part 820, Quality System Regulation (QSR). Manufacturers are reminded of this obligation when they receive authorisation from FDA to market their products. In spite of this, some companies fail to fully comply with the QSR when they begin marketing their products in the US. In some cases, this is due to a lack of awareness of the regulation because of inadequate resources being allocated to ensure awareness of, and compliance with, applicable regulations. In other cases, companies believe that conformity with the European quality system standards will suffice, which it does not. At times, inadequate resources are allocated for assessing compliance needs and implementing required procedures. In any case, companies failing to fully comply with the QSR risk US enforcement actions if serious compliance failures become evident; this happens most commonly during FDA plant inspections. Problems can occur when companies are forced to conduct last-minute compliance assessments and institute rushed corrective actions when notified of an imminent FDA plant inspection. For these reasons, companies need to begin planning full compliance with the QSR as early as possible so that this is achieved from the time that their products enter the US market. This effort should also include a programme to evaluate and comply with FDA requirements for the control of electronic records and signatures specified in 21 CFR Part 11. A guidance document that explains FDA's current policies on these requirements can be downloaded from www.fda.gov/cder/guidance/5667fml.doc and www.fda.gov/cder/guidance/5667fml.pdf 

→ Labelling

An understanding of European labelling requirements is insufficient for ensuring compliance with US requirements. Companies need to carefully review FDA labelling regulations and guidance documents before approving final versions of labels and labelling materials for products being shipped to the US. Failure to do so could lead to a costly product or labelling recall. Thus, companies should be aware that the requirements for medical device labelling are found in the following US regulations:

- General Device Labelling 21 CFR Part 801
- In Vitro Diagnostic Products 21 CFR Part 809
- Investigational Device Exemptions 21 CFR Part 812
- Good Manufacturing Practices 21 CFR Part 820
- General Electronic Products 21 CFR Part 1010

Links to these regulations and other information related to US labelling requirements can be found on the Device Advice site at www.fda.gov/cdrh/devadvice/33.html

Medical Device Reporting

Incidents in which a device may have caused or contributed to a death or serious injury must be reported to FDA under the Medical Device Reporting (MDR) programme. Certain types of malfunctions must also be reported. The MDR requirements are specified in 21 CFR Part 803. Although there are similarities between the European and US requirements for reporting adverse incidents, important differences

exist. For example, the European concept of a near incident and its definition in European guidance documents is similar to, but not identical with, the US term “malfunction.” In addition, the timeframes for reporting incidents in Europe differs from that of the US. For this reason, companies exporting to the US need to ensure that written procedures specifically cover US MDR requirements. Comprehensive information on the MDR process can be found at www.fda.gov/cdrh/devadvice/351.html

Corrections and removals

Under 21 CFR 806, Medical Device Correction and Removals, manufacturers and importers are required to submit a report to FDA of any correction or removal of a medical device if the correction or removal was initiated to reduce a risk to health posed by the device or to remedy a violation of the Act caused by the device that may present a risk to health.

Companies should also be aware of US policies regarding recalls that are not related to risk to health. For example, in most cases, medical device recalls are voluntary actions that manufacturers conduct under 21 CFR Part 7, Enforcement Policy. However, where a manufacturer or importer fails to voluntarily recall a device that is a risk to health, FDA may issue a recall order to the manufacturer under 21 CFR 810, Medical Device Recall Authority.

Information on FDA requirements and policies regarding medical device recalls and corrections and removals can be found at www.fda.gov/cdrh/devadvice/51.html

Radiation-emitting products

Companies that export medical devices that also emit radiation must meet specific requirements intended to prevent unnecessary exposure to radiation resulting from the use of these products. These requirements may include the need to retain certain types of records and submission of product reports to CDRH and are specified in 21 CFR Parts 1000–1299.

The Device Advice site www.fda.gov/cdrh/devadvice/311.html includes the definition of “electronic product radiation,” examples of electronic products subject to FDA regulation, record and reporting requirements by product type, guidance documents and labelling requirements.

Avoiding unnecessary risks

Companies must often expend considerable effort and resources when entering the US market. Therefore, any risks that could jeopardise the success of these projects should be avoided. Prudent companies will allocate adequate resources for identifying and complying with all applicable US regulations, not just those related to the submission process, to avoid those risks. **mdt**

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