FDA's New Device Registration and Listing Requirements

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2 Management Summary

FDA introduced some device listing and establishment registration changes that took effect on October 1, 2012. The main changes are: proprietary names must be listed with the FDA AND contract manufacturers and sterilizers must be registered with the FDA.

What will be the impact an on contract manufacturers. A contract manufacturer's job is to manufacture a finished device with another establishment's specifications. A finished device is defined in 21 CFR 820.3(l) as any device, or accessory to any device, that is suitable for use or is capable of functioning, whether or not it is packaged, labeled, or sterilized. In consequence, any company producing medical devices, according to the specifications of a second company which is distributing the device in the U.S., must now register with the FDA. The annual costs in 2013 are $2,575, rising in the following years to an estimated $ 3,872. Furthermore, every company registered with the FDA must agree to comply with U.S. law and FDA guidelines, and they must expect and prepare for an FDA inspection. FDA inspections could result in legal actions. These actions range from warning letters to automatic detention of product entering the United States.

The FDA does not expect a manufacturer to have a perfect quality system; however, failure to recognize major gaps could lead to costly corrections. Depending on a company's quality system, the cost to prepare in advance of an FDA Inspection could range from 60 to 100k swiss francs. If the inspection reveals major deviations, the corrective actions required to address the non-conformities might easily exceed and possible multiply the cost many times. Besides the cost of correcting the non-conformities, the cost could also include loss of revenue from the US market.

3 Introduction

The FDA Safety and Innovation Act (FDASIA) was signed into law on July 9, 2012. This law includes the Medical Device User Fee Amendments of 2012 (MDUFA III), as well as other medical device provisions. These provisions affect the standard for FDA approval of clinical trials, provide an alternative de novo review pathway for risk-based classification of devices, expand FDA's post-market surveillance capabilities, shorten timelines for scheduling appeal meetings and issuing decisions, and change the process for reclassification of devices. (21CFR807).

The Medical Device User Fee Amendments of 2012 (MDUFA III) were enacted as part of FDASIA. MDUFA III took effect on October 1, 2012 and will sunset in five years, on October 1, 2017. MDUFA III mandates that an annual registration user fee has to be paid for all types of establishments. The fee for FY2013 is $2,575. Please note that the FY2013 annual registration period that was scheduled to end on December 31, 2012, will now end on January 31, 2013. The registration period is being extended to allow industry more time to comply with the new requirements of federal law.

4 Establishment registration

Owners or operators of places of business (also called establishments) that are involved in the production and distribution of medical devices, intended for use in the U.S., are required to register annually with the FDA. This process is known as establishment registration.

4.1 What are the changes to device registration and listing requirements

1 All proprietary names, under which a device is marketed, must be reported, at a minimum, when a device is first listed and during the annual update of registration and listing information.
2 Combination products – products comprising of a device and a biological product, or a drug – must be identified as a combination product, and the type of combination product (for example: convenience kit, prefilled drug delivery device, etc.) must be selected from the list displayed in the FDA Unified Registration and Listing System (FURLS).
3 All contract manufacturers and sterilizers of finished devices must register and list, regardless of whether they put the device into commercial distribution or return the device to the manufacturer or specification developer.
4 Initial importers must identify the manufacturers of the devices they are importing.
5 Foreign establishments that are exporting devices, or offering devices for export to the United States, must identify all known U.S. importers of their devices.
6 A device must be listed by the manufacturer, specification developer, single-use device re-processor, remanufacturer, or re-packer/re-labeler before a foreign exporter, contract manufacturer, or contract sterilizer can list it.
7 Establishments that only handle complaints, and previously registered as manufacturers or specification developers, should change their establishment type to "Complaint File Establishment" as required by 21 CFR 820.198.
8 Establishments located in foreign trade zones must now register and list, as well as identify themselves as being located in a foreign trade zone.

9 All establishments that are required to register must now pay the annual registration user fee, as required by the Food and Drug Administration Safety and Innovation Act (FDASIA)3.

4.2 Who must register?

Foreign Establishments must register as follows:

Activity	Register	List	Pay Fee
Foreign Manufacturers (including Kit Assemblers)	YES 807.40(a)	YES 807.40(a)	YES
Foreign Exporter of devices located in a foreign country	YES 807.40 (a)	YES 807.40(a)	YES
Contract Manufacturer (including contract packagers)	YES 807.40(a)	YES 807.40(a)	YES
Contract Sterilizer	YES 807.40(a)	YES 807.40(a)	YES
Re-processor of Single-use Device	YES 807.20(a)	YES 807.20(a)	YES
Custom Device Manufacturers	YES 807.20(a)	YES 807.20(a)	YES
Re-labeler or Re-packager	YES 807.20(a)	YES 807.20(a)	YES
Device Being Investigated under IDE	NO 812.1 (a)	NO 812.1(a), 807.40(c)	NO
Specification Developer	YES	YES	YES
Remanufacturer	YES	YES	YES
Manufacturer of components that are distributed only to a finished device manufacturer	NO 807.65(a)	NO	NO
Manufacturer of accessories or components that are packaged or labeled for commercial distribution for health-related purposes to an end user	YES 807.20(a)	YES 807.20(a)	YES
Maintains complaint files as required under 21 CFR 820.198	YES	YES	YES

4.3 What does it cost

The schedule of annual registration user fees for fiscal years 2013 through 2017 is as follows:

Year	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Fee	$2,575	$3,200	$3,750	$3,872	$3,872

4.4 Consequences of registration

Once the establishment is registered, annual fees, as indicated above, must be paid.
Any company registering with the FDA must agree to comply with ALL guidelines and acts published by the FDA. The FDA inspects companies to assure, compliance with U.S. law.

4.4.1 Preparing Phase

Your efforts to comply with the FDA requirements should start immediately. A full gap analysis should be conducted that covers all aspects of the quality system. Corrective action plans should be established to correct gaps in compliance with FDA requirements. Failure to identify and correct high risk gaps could lead to FDA legal action.

FDA's audits are different in scope and approach in comparison to audits by notified bodies. FDA is focused on high risk areas like CAPA, Design Controls and Management Review. FDA is a law enforcement agency that collects documentation and records to support legal action. Clearly communicating and explaining your quality system is key to your success. Practice audits and coaching will help develop subject matter experts for the "real" audit. This approach allows management to review the corrective actions implemented to comply with FDA as well as the FDA "readiness" of their employees.

4.4.2 FDA Inspections

The FDA published the QSIT (Quality System Inspection Technique) in 1999. For establishments in Switzerland, the FDA usually announces 2-3 months in advance. A standard QSIT inspection starts Monday and terminates Thursday with a presentation of the observations made, collected in the form 483. Depending on the severity of the observations, a series of corrective actions, including continuous progress reporting to the FDA, can avoid a warning letter.

To prepare for an FDA inspection companies should budget 60,000 to 110'000 CHF.

Details:	
Preparation phase (3 months):	
60 man days @ CHF 500.-	CHF 30'000
10 consultant days	CHF 20'000
During Inspection (4 days)	
5-10 employees over 4 days	
Equal 20-40 man days @ CHF 500-1000.-	CHF 10-40'000
Total	CHF 60-110'000

The estimate above is based on average efforts to ensure FDA readiness. Companies with large gaps could increase the cost significantly.

4.4.3 US Agent

A United States agent is a person residing or maintaining a place of business in the United States, and whom a foreign establishment designates as its agent. This definition excludes mailboxes, answering machines or services, or other places where an individual acting as the foreign establishment's agent is not physically present.

There are consultants in the US offering this service for foreign establishments.

4.4.4 Official correspondent

An Official correspondent is the person designated by the owner or operator of an establishment. They are responsible for the following:

1 The annual registration of the establishment;
2 Contact with the Food and Drug Administration for device listing;
3 Maintenance and submission of a current list of officers and directors to the Food and Drug Administration, upon the request of the Commissioner;
4 The receipt of pertinent correspondence from the Food and Drug Administration directed to, and involving, the owner or operator and/or any of the firm's establishments;
5 The annual certification of medical device reports required by 804.30 of this chapter, or forwarding the certification form to the person designated by the firm as responsible for the certification.

In a standard case, the official correspondent of a foreign establishment is a designated person working within the company, eg. the quality manager.

4.4.5 Warning letter

When the observations identified during the inspection are severe, the FDA will issue a warning letter. A company under a warning letter cannot register new products. It also applies to manufacturers with a contract manufacturer under a warning letter. In addition, the company must present and implement corrective actions. Some warning letters may be closed via documentation only route and some will be closed by a re-inspection of the facility. The timeframe between the warning letter and the re-inspection may easily be, or exceed12 months.

5 Conclusion

These new requirements directly affect many European companies. Those companies affected should take quick action to minimize exposure to the FDA. As mentioned above, nonconformities found by the FDA can lead to products on "automatic detention" which means the products are stopped at the US border until corrective actions are in place to ensure the devices are safe for use. Wise and far-seeing decision makers are needed. Once registering is completed, the company must align their quality management system with FDA's requirements. Get ready for an FDA inspection!

6 About us

Axxos GmbH is a Swiss based consultant firm, with its core business in quality management systems for medical device companies. Experienced local consultants, along with ex-FDA inspectors, are able to prepare and accompany manufactures through the FDA inspections with highly effective and efficient guidance. US-agent services and Mock audits will be provided via exclusively contracted US based consultants.

For more information visit www.axxos.ch or contact the owner markus.wipf@axxos.ch.

7 Addendum

7.1 Definitions

7.1.1 Contract Manufacturer

Manufactures a finished device to another establishment's specifications.

7.1.2 Finished Device

Any device, or accessory to any device, that is suitable for use, or is capable of functioning, whether or not it is packaged, labeled, or sterilized.

7.1.3 Contract Sterilizer

Provides a sterilization service for another establishment's devices.

7.1.4 Foreign Exporter

Exports or offers for export to the United States (U.S.), a device manufactured, prepared, propagated, compounded, or processed in a foreign country, including devices originally manufactured in the United States. A foreign exporter must have an establishment address outside the U.S.

7.1.5 Initial Importer

Takes first title to devices imported into the U.S. An Initial Importer must have a U.S. address.

7.1.6 Manufacturer

Creates by chemical, physical, biological, or other procedures any article that meets the definition of "device" in Section 201(h) of the Federal Food, Drug, and Cosmetic (FD&C) Act.

7.1.7 Repackager

Packages finished devices from bulk, or re-packages devices made by a manufacturer into different containers (excluding shipping containers).

7.1.8 Relabeler

Changes the content of the labeling from “that supplied by the original manufacturer” to “distribution under the establishment's own name”. A re-labeler does not include establishments that do not change the original labeling, but merely adds their own name.

7.1.9 Remanufacturer

Any person who processes, conditions, renovates, repackages, restores, or does any other act to a finished device that significantly changes the finished device's performance, safety specifications, or intended use.

7.1.10 Re-processor of Single Use Device

Performs remanufacturing operations on a single use device.

7.1.11 Specification Developer

Develops specifications for a device that is distributed under the establishment's own name, but performs no manufacturing. This includes establishments that, in addition to developing specifications, also arrange for the manufacturing of devices labeled with another establishment’s name, by a contract manufacturer.

7.1.12 US manufacturer of export only devices

Manufactures medical devices that are not sold in the U.S. and are manufactured solely for export to foreign countries.

7.2 References

http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/RegistrationandListing/default.htm