

# Addressing US and European Device Testing Requirements

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Medical device companies do not always realise that United States and European test requirements can be significantly different. Not addressing these differences can be costly when retesting or device redesign becomes necessary. This article discusses some of these differences and ways to help avoid repeat testing.

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## US testing requirements

The United States (US) Food and Drug Administration (FDA) requires that companies provide sufficient evidence to demonstrate that medical devices are safe and effective. In many cases, test data must be supplied to meet this requirement.

The vast majority of US regulatory submissions for medical device marketing authorisation are premarket notifications, termed 510(k)s, which are required for most Class II devices. The purpose of test data in a 510(k) is to demonstrate that a device to be marketed in the US has an equivalent safety and effectiveness to a product that is already on the US market; the latter device is termed a “predicate device.”

The premarket approval (PMA) process, which is required for most Class III devices, demands that FDA receive sufficient valid scientific evidence to ensure that the device is safe and effective for its intended use(s). Test data often represent an important part of this evidence.

FDA has developed general and specific guidance documents, many of which describe the manner in which test data should be presented in US regulatory submissions. In addition, FDA recognises that many US and international consensus standards address aspects of safety and/or effectiveness relevant to medical devices. Many of these standards have been developed with the participation of staff from FDA’s Center for Devices and Radiological Health (CDRH). Thus, under the CDRH Standards Programme, FDA allows the use of recognised consensus standards in satisfying premarket review requirements. A distinct benefit of this

programme to companies marketing their products in both Europe and the US is that some of the recognised standards are the same as those adopted as European harmonised standards. Detailed information on the CDRH Standards Programme can be found on the FDA website: [www.fda.gov/cdrh/stdsprog.html](http://www.fda.gov/cdrh/stdsprog.html)

## US general guidance on test data

The FDA guidance document on the preparation of traditional and abbreviated 510(k)s<sup>1</sup> describes the manner in which test data should be presented in a traditional 510(k) submission. For example, Chapter II of this guidance document indicates the information that should be provided for bench testing, animal testing and clinical studies.

The section on bench testing lists the information that should generally be provided. This includes a list of the specific bench tests conducted, a description of each test protocol, a summary of the results, a description of the analysis performed and a discussion of the conclusions reached. The test protocols should identify the objective of the test, articles used in the test, test methods and procedures (including any specific test conditions), study endpoint (specific parameter measured), and predefined acceptance or pass/fail criteria. The guidance document also recommends that the summary of results and analysis should include a brief description of the data derived from testing that is presented clearly and concisely such as in a table format. In addition, the conclusions should describe any comparison testing with the predicate device in terms of substantial equivalence. →



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→ The guidance document also states that if relevant device-specific guidance is available, the recommendations in that guidance document should be followed. This is important because some companies follow the general guidance, but fail to search for device-specific guidance, which is discussed later in this article. This omission can lead to significant delays in the review of the submission and risks regarding the clearance or approval of the submission.

Similarly detailed advice is provided regarding the presentation of animal test data. Appendix B of the guidance document provides links to performance testing information for in vitro diagnostic devices. Detailed guidance on the general aspects of presenting test data in PMA applications can be found on the FDA Device Advice website: [www.fda.gov/cdrh/devadvice/pma/](http://www.fda.gov/cdrh/devadvice/pma/)

### US guidance on specific devices

FDA has specific ideas regarding the information that must be provided in US regulatory submissions for many types of devices. For example, FDA has developed 33 guidance documents for cardiovascular devices; 28 for ophthalmic and ear, nose and throat devices; 59 for obstetrics/gynaecology, urology and lithotripsy, gastroenterology, renal

and radiological devices; 56 for plastic and reconstructive surgery, orthopaedic joint and spine devices and restorative devices; 64 for anaesthesiology, general hospital, infection control and dental devices; and 92 for in vitro diagnostic devices, including 23 for chemistry and toxicology devices, 30 for immunology and haematology, and 17 for microbiology devices.

Many of these guidance documents contain specific information on the type of test data that FDA expects to receive in premarket submissions, including 510(k)s and PMA applications. It should be noted that FDA guidance documents contain a prominent statement at the beginning of each, which says that the guidance represents FDA's current thinking on the topic; however, an alternate approach may be used if the approach satisfies the requirements of the applicable statutes and regulations.

### CDRH Office of Science and Engineering

The Office of Science and Engineering Laboratories (OSEL) develops independent laboratory information for regulatory and other public health activities of CDRH. In addition to providing consultation to the Center's regulatory experts, OSEL researchers are involved in test method development, risk assessments, forensic investigations,

product evaluations and technology assessment. According to the OSEL Annual Report for 2007, laboratory research is the cornerstone on which OSEL provides the regulatory support function. Furthermore, the Annual Report states that laboratory research is largely based on investigations related to the mechanistic understanding of device performance or test procedures to enable the Center and device manufacturers to gain an improved understanding of issues related to safety and efficacy.

The OSEL regulatory support function is provided through “consults” that support both premarket decisions and postmarket actions using expertise developed in the laboratory. A consult is a request for expert advice or information of a specific nature, where it is perceived that expertise is more discipline-related than medical device related. For example, in 2007, OSEL consulted on 1494 premarket issues and 257 postmarket issues. It reports 405 activities related to standards.

The OSEL Annual Report also states that for many post-market and premarket regulatory issues, the reviews and investigations conducted by OSEL independently assess the claims made by manufacturers or other parties concerning safety or effectiveness. In other cases, OSEL reviews may assess the adequacy of a design, a failure investigation, a production process or a quality process employed by the manufacturer. These reviews and analyses rely on inhouse expertise and are often augmented by expertise solicited from colleagues in academia, other government laboratories, or even other industry sectors. OSEL laboratory investigations may be undertaken in cases where the veracity of a performance claim needs to be independently verified by testing, or when the claimant lacks the resources to conduct the investigation.

Why is this important? Medical device companies preparing to submit 510(k)s or PMA applications to FDA, in particular for the first time, should understand the importance that FDA places on test data and the resources that FDA has to assess these data. FDA reviewers are not only aided by their own experience in reviewing many different regulatory submissions, but may also request assistance from OSEL when they deem this type of support is needed. For these reasons, adequate attention should be paid to the presentation of test data in US premarket submissions.

### US review process

It should also be mentioned that the FDA process of reviewing premarket submissions is a formal process that is subject to a number of FDA guidance documents developed to assist FDA reviewers in using uniform review methods and in minimising variability among reviewers. For example, there are 93 Office of Device Evaluation (ODE) guidance documents that are not specific to any particular Division within ODE. Some of these documents specifically instruct reviewers to refer to applicable FDA guidance documents related to a specific device or category of device. →

### → European testing requirements

The European Directives on medical devices provide a general framework and essential requirements that need to be met to place medical devices on the European market. Under this system, manufacturers must be able to demonstrate compliance with the essential requirements related to safety and performance, which are listed in the first Annex of each of the medical device Directives. In many cases, this includes test data.

Conformity to applicable voluntary European harmonised standards, which contain detailed technical specifications, and test requirements provide manufacturers with a presumption of conformity with the related essential requirements of the relevant Directive. Companies planning to market their products in Europe need to refer to the list of European harmonised standards, which are maintained on the European Commission website: <http://ec.europa.eu/enterprise/newapproach/standardisation/harmstds/reflist.html>. Unlike the list of FDA guidance documents, the list of harmonised standards is not divided into types of device; therefore, companies need to check carefully to identify both general and device-specific standards that may be applicable to their products.

In some cases, a European harmonised standard may not exist to cover a particular requirement related to a medical device. When this occurs, companies may rely on European guidance documents (MEDDEVs), national pharmacopeias, international standards, nonharmonised European standards, standards from other geographic regions or other guidance documents.

To date, one draft device-specific MEDDEV has been made available: "Draft Guideline on Clinical Evaluation of Coronary Stents." The document was developed by the Medical Device Clinical Evaluation Task-Force and is intended to be an annex to MEDDEV 2.7.1 on the "Evaluation of Clinical Data: A Guide for Manufacturers and Notified Bodies." The document was offered for public consultation and comments were requested to be submitted by 22 April 2008. The document has been removed from its initial location on the European Commission website, but at the time of writing can be downloaded from [http://ec.europa.eu/enterprise/medical\\_devices/questionnaires/comments\\_coronary\\_stent.htm](http://ec.europa.eu/enterprise/medical_devices/questionnaires/comments_coronary_stent.htm). The purpose of the guideline is to provide more uniform practices regarding the clinical evaluation of coronary stents; however, the document also contains a section on preclinical assessment, which includes general advice on the type of testing that should be performed before conducting the clinical investigation.

### European review process

The European regulatory review process differs significantly from that of the US. In Europe, medical device technical documentation is reviewed by the particular European Notified Body (NB) selected by the manufacturer if the device is in a class that requires the involvement of a NB.


Some NBs have developed detailed and formal review processes, others are less formal in the manner in which technical documentation is reviewed. Some NBs are large enough to employ staff with specialised areas of expertise; others rely on external support. In any case, each NB is allowed to operate under its own procedures, which means that the manner and depth of technical documentation reviews can vary among NBs.

In some cases, a NB review may be similar to a review conducted by FDA in terms of depth and expectations on the type of test data provided in the technical documentation; however, in general, this is not the case. There are instances where NB expectations are more stringent with regard to the test data provided to support medical device European safety and performance requirements, but FDA expectations tend to be more stringent.

### Avoiding costly retesting and redesign

Until true global harmonisation of device requirements becomes a reality, companies intending to market their products in the US and Europe need to be aware from the earliest stages of device design or modification of the differences that may exist between the US and Europe regarding testing and related device specifications. Of course, differences may also exist in other jurisdictions, and these should also be addressed if companies plan to market in these other regions.

### References

1. US CDRH Guidance for Industry and FDA Staff, Format for Traditional and Abbreviated 510(k)s, 12 August 2005. Downloadable from [www.fda.gov/cdrh/ode/guidance/1567.pdf](http://www.fda.gov/cdrh/ode/guidance/1567.pdf)
2. Office of Science and Engineering Laboratories (OSEL) Annual Reports are downloadable from [www.fda.gov/cdrh/osel/annualreports/](http://www.fda.gov/cdrh/osel/annualreports/) 

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