

Regulatory Submissions for Medical Devices and Diagnostics: The Basics

By Carey G. Smoak

Abstract

Medical devices and diagnostics are an important part of the healthcare industry. The number of device approvals by the FDA has increased by 52% in the past decade. Devices are different than pharmaceutical products in terms of the FDA approval process, and the use of CDISC standards. In May 2006 an SDTM Device sub-team was formed. The team was expanded in February 2009 to include CDASH. The Device sub-team is working towards the goal of modifying existing domains (as needed) and developing new domains, which will be incorporated into CDASH and SDTM standards.

Introduction

Devices are different than pharmaceutical products in many respects (Smoak, 2008). Differences include, how the products are developed, their mechanism of action, their intended use and their lifespan on the market. Other differences include, the regulatory approval process and CDISC. This paper will cover basic information about the medical device and diagnostic industry, including the importance of devices, regulatory approval of devices and CDISC.

In this paper, the term devices refers to both medical devices and diagnostic products.

The Importance of Devices

Devices are an important part of the healthcare industry. Examples of devices that are important to health care include heart stents, which may save peoples' lives and blood screening instruments that test blood for the presence of viruses like HIV, Hepatitis B and Hepatitis C to keep the blood supply safe.

Devices also work in conjunction with other products (drug/device combination products), which are important to the healthcare industry. Devices that work in conjunction with other products include contrast agents used in imaging devices that may be used to monitor therapeutic agents. Drug eluting heart stents may be used to treat cardiovascular disease. Diagnostic assays may be used to determine if a therapeutic product will work in a patient. This last area includes targeted therapies and companion diagnostics in which a diagnostic test may be used to identify when a targeted therapy may work in a particular patient.

Figure 1 shows that during the past decade, the number of device approvals (PMAs – Pre-Market Approvals) by the Center for Devices and Radiologic Health (CDRH) at the FDA has increased from 488 in the year 2000 to 740 in 2009 – an increase of 52% (<http://www.fda.gov/cdrh/pmapage.html> January 27, 2010).

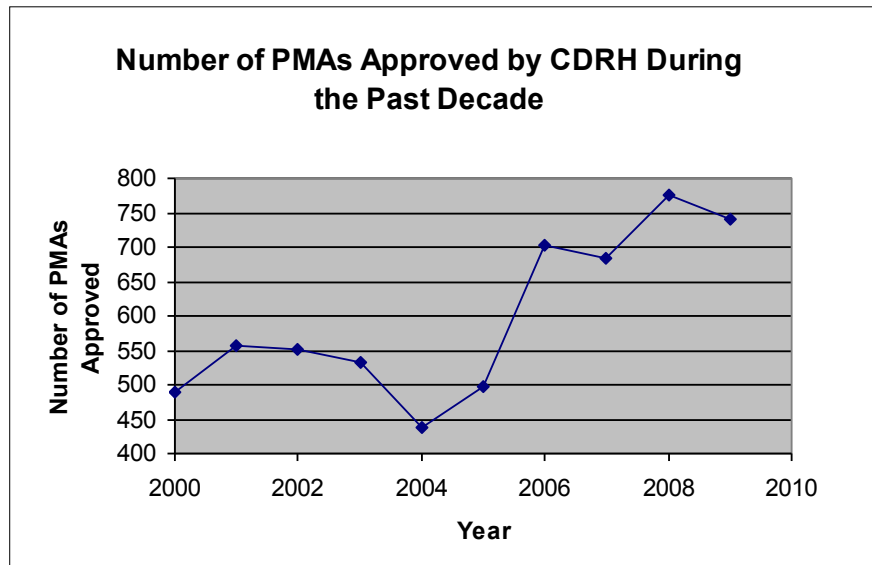


Figure 1

Therefore devices are important due to their benefit to the healthcare industry and increased approval of products by the FDA.

Regulatory

Medical devices are approved by two branches at the FDA – CDRH (Center for Devices and Radiologic Health) and CBER (Center for Biologics Evaluation and Research). CDRH handles all device submissions except for HIV devices and blood screening devices which are handled by CBER.

CDRH

Devices are classified as I, II or III based “on the intended use of the device and also upon indications for use” (<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/ClassifyYourDevice/default.htm>, November 25, 2009).

Class I, II and III devices (<http://www.devicewatch.org/reg/reg.shtml>, November 25, 2009) are defined as:

- Class I - Generally, these are simple devices with minimal risk to the user.
 - Examples: enemas, crutches, elastic bandages, bedpans
- Class II - These devices pose a moderate level of risk to the user.
 - Examples: condoms, intravenous administration sets, sutures, inflatable blood pressure cuffs

- Class III - These devices pose a serious level of risk to the user, mostly because they are implants or sustain life.
 - Examples: implantable pacemakers, blood vessel stents, breast implants

Devices at CDRH are approved through either the 510K, PMA or IDE process. In general, class I and II devices can be approved by a 510K submission, while a class III device requires a PMA submission. IDE approval allows a device to be used in support of a 510K or PMA submission. 510(k) submissions usually compare a new device with a predicate device (a predicate device is defined as a legally marketed device) to demonstrate that the new device is substantially equivalent to a predicate device. PMA (Pre-Market Approval) submissions are used to demonstrate to the FDA that a new or modified device is safe and effective. The standard for PMAs is higher than the requirements for 510(k) submissions.

CBER

Devices at CBER are also approved by either the 510K or PMA process as described above. In addition, some devices may require a Biologics License Application (BLA).

More detailed information about regulatory requirements for devices has been published elsewhere (Smoak, 2010).

CDISC

Representation

In May 2006 an SDTM Device sub-team was formed to begin work on reviewing SDTM domains and developing new domains (Smoak, 2007). In February 2009, at the CDISC Intrade meeting, the Device sub-team met with representatives from a medical device organization called AdvaMed (www.advamed.org), CDASH team members and representatives from CBER and CDRH. At this Intrade meeting a strategy was forged to co-develop CDASH and SDTM domains concurrently for devices. This is the first time that a CDISC team has co-developed CDASH and SDTM domains concurrently.

Currently, the Device sub-team is composed of device industry experts, representatives from CDRH and CBER and members of the CDASH and SDS teams. Areas of industry expertise include diagnostics, imaging, implantable devices and orthopedics.

Scope

Originally, the Device sub-team had a focus on SDTM. The scope has now been expanded to include:

- reviewing and modifying existing CDASH/SDTM domains as needed
- developing new CDASH/SDTM domains to handle data which are unique to devices

CRF-Analysis

To facilitate the CDASH review, 138 Case Report Forms (CRFs) were collected from more than 40 device companies. A frequency analysis was performed on these collected CRFs (Shiralkar P et al, 2010). The purpose of the frequency analysis is to find out where devices differ from the current CDASH domains,

to modify the CDASH domains as needed for devices where necessary and develop new domains for devices as needed. The general conclusion of this CRF review is that most basic device data can be addressed by the current CDASH structures.

Goal

The main goals of the Device sub-team are:

- To make it easier for sites and sponsors to conduct device trials
- To decrease some of the variety seen in CRFs
- To collect data once for multiple purposes
- To improve data quality and patient safety
- To provide mappings so users can easily go from the CDASH domains to the SDTM datasets
- To make it easier for regulatory agencies (like CDRH and CBER) to receive, view and assess submissions

Possible new domains under consideration include:

- Device Properties (DP)
- Device in Use (DU)
- Device Exposure (DX)
- Device Events (DE)
- Device Tracking and Disposition (DT)
- Device Subject Relationships (DR)

The team has identified the need for device related terminology development. The CDISC Controlled Terminology has been approached for assistance in the development of the needed Device terms.

The Device sub-team is working on developing a draft standard and SDTM and CDASH implementation guides for devices. This draft standard and implementation guide would become the Initial Consensus Version and then go through the CDISC consensus process which includes both an internal and public review prior to becoming a CDISC approved Standard. This standard process is shown below in Figure 2:

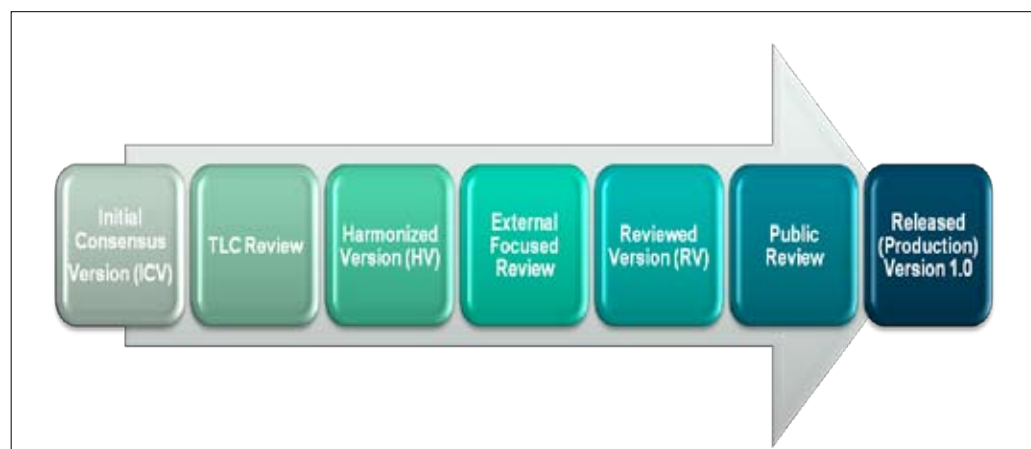


Figure 2

Conclusion

Medical devices and diagnostics are important to the health care industry in terms of the number of products currently under development. The number of device approvals (PMAs) by the FDA has increased by 52% in the past decade. A CDISC Device sub-team is working on reviewing and enhancing existing CDASH/SDTM domains and developing new domains to capture and format device related data to meet this growing need. The Device sub-team is a cooperative effort between industry experts, members of the CDASH/SDS teams and CDRH and CBER (FDA). These standards would then be used by medical device companies in submissions to regulatory authorities (CDRH and CBER).

References

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