IMDRF International Medical Device Regulators Forum

January 24, 2019

The Regulated Product Submission (RPS) proposal was endorsed as a New Work Item (NWI) by IMDRF at its inaugural meeting in Singapore in March 2012. The proposal, as endorsed, included the objective of establishing a comprehensive harmonized structure for premarket medical device submissions. The harmonized structure was established as the Table of Contents (ToC) which was first introduced in February 2013 for both IVD and non-IVD devices and has undergone revisions as recently as March 2018.

In order to evaluate the benefits and challenges of utilizing the ToC structure, an IMDRF pilot program involving Australia, Brazil, Canada, China, the European Union, and the United States was initiated October 1, 2015, in addition to regional pilots that were initiated about the same time. The pilot program ended December 2017 with 17 devices accepted into the pilot. To date, 15 applications have been approved from those submitted. The following conclusions were drawn from the pilot:

- The consistent structure of well-defined ToC sections and numbering, along with the regional classification matrix, allowed for better navigation through the applications and easier access to the data.
- Reviewers generally like the ToC format.
- The structure is adequate for manufacturers to utilize, but additional guidance would be helpful and a stronger commitment for implementation by regulators is essential for manufacturers to begin investing resources.
- Issues encountered to date are provided in the below table.

In addition to the ToC pilot, two rounds of RPS test cases were conducted to evaluate a "fit for purpose" of the Health Level Seven (HL7) RPS Standard to allow electronic exchange of information related for premarket medical device applications. Both reports have been published on the IMDRF website.

Members of the IMDRF RPS WG continue to support the concept of utilizing a harmonized ToC application format and see value in the establishment of subsequent harmonized electronic submissions of regulated health products. We do acknowledge that it may be a long-term effort to implement harmonized electronic submissions as common practice.

In the interim, we confirm that the ToC structure is an agreeable format capable of supporting the regulatory submission requirements for all member countries. Some members have already announced their intention to adopt the ToC while others are reviewing how the ToC structure may be introduced as an alternative submission format within their current regulatory environments.

The following feedback was received from pilot participants:

Benefits of the ToC	• The consistent structure of well-defined ToC sections and numbering along with the regional classification matrix allowed for better navigation through the applications and easier access to the data. The ToC format was generally preferred to the STED format.
Reviewers' feedback	• The ToC was less searchable compared to a dossier in single pdf file. • The ToC format is more useful for applications containing large amounts of data. While the ToC is considered less advantageous for minor amendments, it could still work well with exclusion of irrelevant headings. • It is important to follow the recommended headings for efficiency.
Manufacturers' feedback from those involved in the pilot.	• There were some technical limitations due to the hybrid nature of using the ToC structure in a non-RPS environment (e.g. file name limitations). • A positive experience from the pilot is leading some industry members to likely use the ToC as a global template for some types of submissions. • More guidance has been requested as well as an expressed concern about longer review times.