



**IMDRF** International Medical  
Device Regulators Forum

## **FINAL DOCUMENT**

### **International Medical Device Regulators Forum**

**Title:** IMDRF Table of Contents (ToC) Pilot Plan

**Authoring Group:** Regulated Product Submissions, Table of Contents Working Group

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A handwritten signature in black ink, appearing to read 'T. Tomiyama', is written above the printed name.

Toshiyoshi Tomiyama, IMDRF Chair

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## 1 Executive Summary

The Regulated Product Submission (RPS) proposal was endorsed as a New Work Item (NWI) by IMDRF at its inaugural meeting in Singapore (March 2012). The working group to this point has accomplished the following:

1. Established that the Health Level Seven (HL7) RPS Standard is "fit for purpose" for the electronic exchange of information related to premarket medical device applications.
2. Established a comprehensive Table of Contents (ToC) for the following premarket applications
  - a. Non-IVD Market Authorisation
  - b. IVD Market Authorisation

The ToC Working Group<sup>1</sup> has previously conducted pilots for both of the ToC structures, using historical submissions. Regional pilots are also currently being undertaken by some IMDRF members. Further IMDRF piloting is to be conducted with the following general objectives:

- To evaluate the adaptability of the ToC structure from an industry perspective when applying to more than one jurisdiction (simultaneously or sequentially) using real regulatory submissions

The proposed timeline for this pilot is described below.

Development of supporting documents	Jan-Jun 2015
Initiation of pilot	Sep 2015
Close of pilot (minimum of 12 months duration)	Sep 2016

The IMDRF ToC Pilot Implementation will undergo the following study phases: recruitment, enrollment and study results analysis. If the success criteria is met within the timelines set forth, the pilot will be concluded and all findings will be posted on the IMDRF website.

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<sup>1</sup> The IMDRF Table of Content Working Group is composed of the regulatory authorities from the agencies represented by the IMDRF Management Committee.

## 2 Background

The International Medical Device Regulators Forum (IMDRF) was conceived in February 2011 as a forum to discuss future directions in medical device regulatory harmonization. It is a voluntary group of medical device regulators from around the world who have come together to build on the strong foundational work of the Global Harmonization Task Force (GHTF). The Forum will accelerate international medical device regulatory harmonization and convergence. The Regulated Product Submission (RPS) proposal was endorsed as a New Work Item (NWI) by IMDRF at its inaugural meeting in Singapore (March 2012). The working group to this point has accomplished the following:

1. Established that the Health Level Seven (HL7) RPS Standard is "fit for purpose" for the electronic exchange of information related to premarket medical device applications.
2. Established a comprehensive Table of Contents (ToC) for the following premarket applications
  - a. **Non-IVD (nIVD) Market Authorisation**
  - b. **IVD Market Authorisation**

The ToC Working Group<sup>2</sup> has previously conducted pilots for both of the ToC structures, using historical submissions. These pilots provided valuable feedback regarding the ToC structure and completeness, however there were obvious limitations to using historical submissions and there were limited samples involving more than one jurisdiction. Furthermore, there was no specific guidelines regarding the means of building a submission in a pre-RPS implementation. Additional IMDRF piloting is considered necessary to evaluate the adaptability of the ToC structure from an industry perspective when applying to more than one jurisdiction (simultaneously or sequentially), and to test the ToC structures using real, live, electronic, regulatory submissions.

Regional pilots have also been or are being undertaken by some IMDRF members, guidance for regional piloting is provided in Section 4 of this document.

## 3 ToC Pilot Implementation Design

The design for the IMDRF ToC Pilot Implementation includes both administrative and technical components. In the sections below, there is an administrative overview of the pilot; and a description of the pilot study phases.

### 3.1 Pilot Overview

The ToC Pilot Implementation seeks to work across regulatory jurisdictions to receive premarket submissions from the medical device regulated industry using the IMDRF ToC and Regional Classification Matrices. Samples are to be real regulatory submissions that will result in regulatory decisions and may be submitted sequentially or simultaneously to multiple

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<sup>2</sup> The IMDRF Table of Content Working Group is composed of the regulatory authorities from the agencies represented by the IMDRF Management Committee.

participating IMDRF jurisdictions. The sections below will outline the administrative components of the pilot.

### 3.1.1 Pilot Objectives

The IMDRF Pilot ToC Implementation will be driven by the following objectives:

- To develop and validate documentation supporting the use of the IMDRF ToCs using feedback from industry participants. This includes validating the use of the regional classification matrices.
- To identify potential challenges in the industry process and develop proposals (which may include change requests and/or implementation solutions) on how these can be addressed moving forward.
- To provide industry and regulators with experience using the ToCs with real submissions in a controlled setting.
- To evaluate the proper usage of the ToC headings including the appropriate placement of documents within the headings and submission of complete and relevant content.
- To identify additional ToC harmonization opportunities.
- To establish and ensure ToC pilot technical guidelines are fit for purpose and to the extent possible, harmonized amongst jurisdictions.

Any regional piloting undertaken should aim to align with the objectives outlined in this document in addition to any region-specific objectives.

### 3.1.2 Pilot Scope

The scope of regulatory submissions accepted during the pilot should be:

- real regulatory submissions
- intended for more than one participating jurisdiction over the pilot period
- accepted regionally for regulatory review

The submission of combination products will not be considered within scope for this pilot.

**NOTE:** Some jurisdictions may also be conducting a regional pilot, refer to Section 4 for regional piloting recommendations for additional information. Participation in the IMDRF ToC Pilot may or may not indicate qualification for the regional pilots.

The following submissions type are consider within the scope of the pilot:

**Table 1: Submission Types by Region**

<b>Jurisdiction</b>	<b>Submission Types</b>	
ANVISA	<b>IVD</b>	<ul style="list-style-type: none"> <li>• New IVD registration (Anvisa-IVD-Reg-NEW)</li> </ul>
	<b>nIVD</b>	<ul style="list-style-type: none"> <li>• New non-IVD registration (Anvisa-NIVD-Reg-NEW)</li> </ul>
CHINA	<b>IVD</b>	<ul style="list-style-type: none"> <li>• Initial registration</li> <li>• Registration of alteration</li> </ul>
	<b>nIVD</b>	<ul style="list-style-type: none"> <li>• Initial registration</li> <li>• Registration of alteration</li> </ul>
EU	<b>IVD</b>	<ul style="list-style-type: none"> <li>• List A &amp; B Applications</li> </ul>
	<b>nIVD</b>	<ul style="list-style-type: none"> <li>• Class III Design Dossiers</li> </ul>
Health Canada	<b>IVD</b>	<ul style="list-style-type: none"> <li>• Class III New</li> <li>• Class III Amendment</li> <li>• Class IV New</li> <li>• Class IV Amendment</li> </ul>
	<b>nIVD</b>	<ul style="list-style-type: none"> <li>• Class III New</li> <li>• Class III Amendment</li> <li>• Class IV New</li> <li>• Class IV Amendment</li> </ul>

Jurisdiction	Submission Types	
TGA	<b>IVD</b>	<ul style="list-style-type: none"> <li>All new or change applications for conformity assessments</li> </ul>
	<b>nIVD</b>	<ul style="list-style-type: none"> <li>All new or change applications for conformity assessments</li> </ul>
USFDA	<b>IVD</b>	<b>PMA</b> <sup>3</sup> Original (initial and amendments), Supplement <sup>4</sup> (initial and amendments) <b>510(k)Traditional</b> <sup>5</sup> (initial, supplements and amendments <sup>6</sup> )
	<b>nIVD</b>	<b>PMA</b> <sup>7</sup> Original (initial and amendments), Supplement <sup>8</sup> (initial and amendments) <b>510(k)Traditional</b> <sup>9</sup> (initial, supplements and amendments <sup>10</sup> )

<sup>3</sup> Excludes Combination Products

<sup>4</sup> Excludes Bundled Submissions

<sup>5</sup> Excludes Third-Party, Combination Products and Bundled Submissions

<sup>6</sup> Only includes amendments before final decision

<sup>7</sup> Excludes Combination Products

<sup>8</sup> Excludes Bundled Submissions

<sup>9</sup> Excludes Third-Party, Combination Products and Bundled Submissions

<sup>10</sup> Only includes amendments before final decision

### 3.1.3 Stakeholders

The stakeholders in the IMDRF ToC Pilot Implementation activities are outlined in the table below. Each stakeholder has specific roles and responsibilities in the pilot activities.

**Table 2: Stakeholder Roles and Responsibilities**

<b>Stakeholder</b>	<b>Role</b>	<b>Responsibilities</b>
Regulators	Region/Jurisdiction	The Regulators will work within the bounds of each jurisdiction’s administrative and legal requirements. The Regulators agree to maintain confidentiality of commercial in confidential information that arises out of the negotiation, testing or feedback processes. The Regulators agree to act within the agreed timeframes, to raise issues as they arise, and to give and receive feedback as required.
	Regional Pilot Coordinator	Responsible for liaising with manufacturers participating in the pilot in their jurisdiction and for collecting feedback for discussion with the IMDRF group. Responsible for coordinating with reviewers to collect feedback and findings. Responsible for keeping records relating to the pilot submissions including, the manufacturer, submission type, and the ToC Pilot materials used to assemble it (e.g.version of classification matrix, IMDRF and regional instructions and FAQ documents). Manage version control of all regional pilot documents.
Regulated Industry	Applicants/Manufacturers	Manufacturers and their agents agree to act in good faith to maximise the short and long term benefits of the testing process. Manufacturers and their agents agree to respect the confidentiality of any information disclosed in the negotiation, testing or feedback processes. Manufacturers and their agents agree to act within agreed timeframes, to raise issues as they arise, and to give and



<b>Stakeholder</b>	<b>Role</b>	<b>Responsibilities</b>
		receive feedback as required.
IMDRF WG Members	Pilot Coordinator	Act within agreed timeframes and minimise delays in the piloting process Maintain and respect confidentiality of any commercial in confidence information arising as part of the negotiation, testing or feedback processes Track general information samples submitted by Industry with the expressed knowledge of its use in the pilot for the purpose of establishing the characteristics of the devices, submissions types, and manufacturers to be shared with IMDRF Regulators <sup>11</sup> . Collate feedback provided by industry and the ToC Pilot Regional Contacts and provide reports in a timely manner. Manage version control of IMDRF documents during the pilot.
	Working Group members	Participated in the evaluation of feedback from the pilot. Participating the revision process for any documentation used for the pilot, including the currently published IMDRF ToC documents.

### 3.1.4 Timelines and Targets

A minimum of 20 cross-jurisdictional samples are the target.

- The number of samples per jurisdiction will be evaluated by each region when considering the pilot success criteria.
- Representation of IVD and nIVD submissions should be similar.

The pilot is expected to remain open for 12 months.

The completion date and target number of samples may be modified based on the extent of industry volunteers and experience/feedback from pilot submissions.

The following table describes major milestones/deliverables and the targeted completion date.

**Table 3: Milestones and Timelines**

<b>Milestone</b>	<b>Timeline</b>
Initial version of IMDRF ToC Pilot Implementation package <b>for public consultation</b>	Feb 2015

<sup>11</sup> As allowed by each Regulator

**IMDRF/RPS WG/N26FINAL:2015 (Edition2)**

<b>Milestone</b>	<b>Timeline</b>
Background information/Request for participation published	May 2015
Initial version of Regional Instructions and FAQ document to describe the regional technical guidelines for submissions as well as other regional ToC Pilot guidance	May 2015
Regional classification matrices finalized for ToC Pilot to include all submission types within pilot scope	June 2015
Create harmonized folder structure(s) and ToC granularity document	June 2015
Initiate pilot	September 2015
Evaluate feedback and adapt ToC Pilot supporting documentation and/or the ToC structure or content as necessary	September 2015 – September 2016
Finalize ToC pilot findings	November 2016
Request endorsement of ToC Pilot documentation and revised ToC if necessary*	January 2017
Publish ToC Pilot documentation and revised ToC if necessary.	After MC endorsement

### 3.1.5 Success Criteria

The success of the ToC pilot will be measured by the following objective and subjective criteria:

#### Objective

- Each submission type within scope should be tested
- Inclusion of submissions that are sent to more than one region – i.e., the same/similar device submission content is sent to more than one region based on regional regulatory requirements
- Meeting required submission content – administratively

#### Subjective

- Conduct surveys for industry stakeholders
  - Ability to manage content under the proposed ToC headings and classification matrices
  - Ease of adapting submission content for multiple jurisdictions
  - Collect any unsolicited feedback regardless of level of satisfaction
- Conduct surveys for regulator
  - Review of submission content for completeness
  - Identification of any ToC heading or granularity issues (as evidenced by the number of changes to the ToC structure and organization and reasons for the change)
  - Recommendations for improvements whether it affects the regional classifications matrices or the IMDRF ToC

Many of the endpoints of this pilot are subjective in nature. Feedback should be requested from each regulator indicating their support for the ToC requirements defined and used in the pilot. Industry feedback will be considered in the context of the anticipated burden of ToC implementation and extent and nature of issues encountered and the ability of IMDRF to rectify these issues.

**Note:** Any issues with transmission or submission format should not be considered as they maybe specific to the pilot and do not affect the ToC or the classification matrices.

### 3.1.6 Confidentiality

The Regulators participating in this pilot undertake to use submissions only for the requested regulatory activity and objectives of this pilot. Any submissions generated in relation to this testing will not be distributed to other manufacturers or other regulators. Industry participants should share any submission content directly with the appropriate regulators through the official regulatory processes in place – i.e., submission content will be shared across regulators directly by regulated industry.

### 3.1.7 Information Sharing

Feedback provided on the ToC structure, experience developing regulatory submissions or suggestions for additional ToC headings may be shared and made public, excluding any confidential content.

Basic applicant and submission identifying information (e.g., Applicant/Correspondent/Manufacturer Name, Device Name, Device Type, Submission Type)

will be shared amongst IMDRF Regulators for the purpose of conducting the pilot. The invitation to participants will provide the specific details of the information to be shared amongst the Regulators as it is a condition for pilot participation.

Any information provided in the resulting pilot findings should only disclose information explicitly stated as releaseable.

### **3.1.8 Outreach**

Depending on the responsiveness to the expression of interest, open information webinars and industry conference attendance may be considered in order to increase awareness and understanding of the IMDRF ToC pilot.

### **3.1.9 Publication of Pilot Documents**

Final versions of the ToC Pilot documentation and any future revisions of the ToC will be posted to imdrf.org at the conclusion of the pilot, when the success criteria are met.

## **3.2 Pilot Study Phases**

The following section outlines each of the phases required to conduct the IMDRF ToC Pilot implementation. The phases include the following:

- Recruitment
- Participant Enrollment
- Study Results/Analysis

The study phases will be monitored and controlled to ensure the pilot objectives are met, and if any revisions need to be made they will be addressed immediately. If changes to the pilot study phases, the information will be updated and distributed to all relevant stakeholders.

### **3.2.1 Recruitment**

The IMDRF RPS WG will develop a general call for expression of interest for participation in this pilot. The information provided will include a general description of the objectives, timelines, and qualification criteria. This will be posted on imdrf.org and interested parties will communicate directly with the ToC Pilot Coordinator.

There will not be a stated closing date indicated on this open invitation; and it will remain posted on imdrf.org until the pilot is determined to be complete.

The call for expression of interest should include a listing of jurisdictions and submission types currently within scope of the pilot, along with acknowledgment that the list may change and to contact the ToC Pilot Coordinator for the most up to date information.

The call for expression of interest will include specification of the information that will be shared amongst regulators for the purpose of conducting the pilot.

In addition to posting on imdrf.org, the call for expression of interest will be distributed to major medical device industry organizations to maximize exposure.

### 3.2.2 Pilot Enrollment

The enrollment of participants in the pilot will be determined by achieving the general objectives of the ToC Pilot implementation. The following section outlines the acceptance criteria and enrollment activities.

#### 3.2.2.1 Acceptance/Selection Criteria

The ability to submit premarket submissions to more than one region or jurisdiction is essential to evaluating the ToC usage in a real-world regulatory environment. The following minimum criteria should be met:

- Manufacturers are to provide agreed upon submission according to the IMDRF ToC Structure and regional classification matrices.
- Manufacturers are to provide feedback on (a) the adaptability of ToC based submissions for use in multiple jurisdictions and (b) the Assembly and Technical Guide for IMDRF Table of Content (ToC) Submissions<sup>12</sup>.

Participants may be selected based on the following considerations:

- **Sample Size:** The number of samples accepted into the pilot may be limited to maintain manageability of the overall pilot and should meet the Pilot's objectives.
- **Submission Types:** Representation from both IVD and nIVD submissions is considered important to the objectives of the pilot, however, the distribution does not need to be equivalent.
- **Special Considerations:** Regulatory processes are not always the same across regions – i.e., the risk class and regulatory submission requirements may differ and thus reduce the comparative quality of submissions. In addition, efforts will be made to ensure the pilot will include submissions to multiple regions.
- Regional requirements may also need to be satisfied.

In addition, manufacturers and IMDRF WG members should expect that Regulators will also provide feedback on (a) the reviewability of submissions and completeness of submissions and (b) the Assembly and Technical Guide for IMDRF Table of Content (ToC) Submissions.

#### 3.2.2.2 Enrollment

Upon acceptance into the pilot, the regulated industry pilot participant will be provided with an information package containing the most up to date guidance on the ToC pilot. Teleconferences may be offered to help address industry questions prior to and/or during submission creation. This information package<sup>13</sup> will consist of:

- ToC Pilot Plan
- IMDRF Assembly and Technical Guide for IMDRF Table of Contents (ToC) Submissions
- Applicable current Regional classification matrices (to be provided by the applicable region)

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<sup>12</sup> This does not include the transmission method or submission format.

<sup>13</sup> Information package will include multiple documents, and/or referenced resources.

- Regional Assembly and Technical Guide for IMDRF Table of Contents (ToC) Submissions (address any additional regional electronic filing requirements and submission format requirements beyond those addressed by the IMDRF document)
- FAQs for using the ToC structure
- IMDRF and Regional ToC Pilot contact details

Additional materials may be provided regionally.

### 3.2.3 Study Results/Analysis

Pilot submissions will be reviewed in accordance with standard regional protocols and performance targets.

**Note:** Depending on the type of regulatory submission, the submission life cycle may continue after the assessment of the pilot objectives.

Feedback from reviewers will be provided on the reviewability of the submission and any observations regarding issues in the submission content elements of the ToC pilot. The scope of reviewer feedback should generally be limited to appropriate use of the ToC, ease of navigating the submission (based on proposed headings and not the technical submission format), general ease of review and should not include feedback relating to the quality of the evidence within the submission.

Feedback from industry will be accepted throughout the submission building process. Any issues identified through the pilot will be directed to the relevant jurisdiction's IMDRF ToC Pilot Regional Contact. The IMDRF ToC Pilot Regional Contact will establish if the issue is regional or specific to IMDRF. All IMDRF issues will be brought forward to the IMDRF ToC Pilot Coordinator for resolution.

## 4 Regional Piloting

Regions may choose to conduct regional pilots in addition to the IMDRF pilot described in this document. Any regional piloting undertaken should aim to align with the objectives outlined in this document in addition to any region-specific objectives.

Jurisdictions planning to conduct simultaneous regional piloting should ensure plans are in place to provide open communication with IMDRF members to facilitate the harmonization of ToC Pilot technical guidelines as well as share feedback regarding the ToC content and/or structure.