



**IMDRF** International Medical  
Device Regulators Forum

## **PROPOSED DOCUMENT**

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

**Title:** Assembly and Technical Guide for IMDRF Table of Contents (ToC) Submissions (ToC-based submissions)

**Authoring Group:** Regulated Product Submissions Table of Contents WG

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16 **Preface**

17

18 The document herein was produced by the International Medical Device Regulators Forum  
19 (IMDRF), a voluntary group of medical device regulators from around the world. The document  
20 has been subject to consultation throughout its development.

21

22 There are no restrictions on the reproduction, distribution or use of this document; however,  
23 incorporation of this document, in part or in whole, into any other document, or its translation  
24 into languages other than English, does not convey or represent an endorsement of any kind by  
25 the International Medical Device Regulators Forum.

## 26 **1.0 Introduction**

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

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

41 The ToC Working Group<sup>1</sup> has previously conducted pilots for both the nIVD and IVD Market  
42 Authorization ToC structures, using historical submissions. These pilots provided valuable  
43 feedback regarding the ToC structure and completeness, however there were obvious limitations  
44 to using historical submissions and there were limited samples involving more than one region.  
45 Furthermore, there were no specific guidelines regarding the means of building a submission in a  
46 pre-RPS implementation.

47 This document is intended to supplement the IMDRF ToC Pilot Plan and describe additional  
48 harmonized guidelines for the acceptable folder structure and file format(s) for ToC-based  
49 submissions.

## 50 **2.0 Scope**

51 This guide is intended for use in the assembly of IMDRF Table of Contents (ToC) based medical  
52 device regulatory submissions currently within the scope of submission types accepted by each  
53 IMDRF region.

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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.

54 **3.0 GUIDE TO BUILDING A TOC-BASED SUBMISSION**

55 There are a number of reference documents and guides that need to be consulted when creating a  
 56 ToC-based medical device submission. This section provides information about these reference  
 57 documents as well as information about how to use these documents to generate a ToC-based  
 58 submission.

59 **3.1 Pilot Documents**

60 The table below lists the documents required to assemble an IMDRF ToC-based regulatory  
 61 submission during the IMDRF TOC Pilot.

62 Table 1 - List of pilot documents

Document	Description	Location
<a href="#">IMDRF In Vitro Diagnostic Medical Device Market Authorization Table of Contents (IVD MA ToC)</a> <b>or</b> <a href="#">IMDRF Non-In Vitro Diagnostic Medical Device Market Authorization Table of Contents (nIVD MA ToC)</a>	These documents define the heading names and hierarchy of the ToC structure. They also include detailed information about the content that belongs under each heading.	<a href="http://www.imdrf.org">www.imdrf.org</a>
<a href="#">IMDRF Assembly and Technical Guide for IMDRF Table of Content (ToC) Submissions [THIS DOCUMENT]</a>	This document provides information about the reference documents available relating to the IMDRF ToC and harmonized technical specifications for ToC-based submissions.	<a href="http://www.imdrf.org">www.imdrf.org</a> (when finalized)
<a href="#">IMDRF Frequently asked Questions Document</a>	Additional reference document that provides responses to commonly asked questions.	<a href="http://www.imdrf.org">www.imdrf.org</a> (when available)
<a href="#">IMDRF Standard ToC Folder Structure (presented as a zip file)</a>	This is a folder structure provided by IMDRF to replicate the hierarchy and headings of the ToC. Note: some headings have been modified from the full names defined in the nIVD and IVD MA ToC documents to reduce path lengths.	<a href="http://www.imdrf.org">www.imdrf.org</a>

Document	Description	Location
<u>REGIONAL</u> Classification Matrix	As the IMDRF ToC documents are comprehensive in nature, not all headings are required for all submission types and/or regions. The classification matrix defines whether for the given submissions type a heading is required, not required, optional, conditionally required, etc.	Various - contact region* of interest for details
<u>REGIONAL</u> Assembly and Technical Guide for IMDRF Table of Content (ToC) Submissions	Similar to this document, regions may have additional requirements or regional specific guidance relating to the building and submission of a ToC-based submission that will be included in a regional Assembly and Technical Guide (e.g. transmission methods or special instructions for file transfer media).	Various - contact region* of interest for details
<u>REGIONAL</u> Frequently asked Questions Document	Additional reference document that provides responses to commonly asked questions.	Various - contact region* of interest for details

\*The regions involved in the pilot are ANVISA, EU, Health Canada, TGA, USFDA and CFDA.

### 63 3.2 Sample general process for building a ToC-based submission

64 This section describes one example of how the pilot documents could be used to manually  
65 compile an IMDRF ToC pilot submission. It is important to note that this is intended to provide  
66 further context to the pilot documents. Other approaches may be acceptable, including using  
67 commercially available submission publishing software to generate a submission meeting the  
68 requirements defined in the pilot documents.

69 **Step 1:** Download<sup>2</sup> the required IMDRF Standard ToC Folder Structure for the applicable ToC  
70 structure (e.g. IVD or nIVD)

#### 71 **Step 2:**

- 72 · **Step 2a:** Begin building the submission consulting the relevant IMDRF Market  
73 Authorization Table of Contents (IVD MA ToC or nIVD MA ToC) for content related  
74 guidance. Consult the regional classification matrix to establish the headings that require  
75 content based on the submission type. **See Implementation Considerations below for  
76 important considerations in this process.**  
77

<sup>2</sup> See IMDRF Standard ToC Folder Structure file

78       ·   **Step 2b:** Consult this document as well as the IMDRF FAQ documents and regional  
79       equivalents for the region of interest for technical requirements relating to the  
80       files/folders that must be populated.

81   **Step 3:** Consult the regional classification matrix of interest to establish which folders can be  
82   deleted from the comprehensive structure based on the submission type – **see Section 4.1 below**  
83   **for further guidance.**

84   Implementation Considerations:

- 85       1. Implementers should consider the potential for maintaining content that will be submitted  
86       to multiple regions. Although certain regions may have additional content requirements  
87       for certain headings<sup>3</sup>, it may be prudent to build a non region-specific version of the  
88       submission using the complete IMDRF Standard ToC Folder Structure<sup>4</sup>. Make copies of  
89       this complete version for each region that you are intending to submit before deleting any  
90       folders not required for the intended region. Future regional adaptations can then be more  
91       easily produced from this baseline submission structure and content. This reduces the risk  
92       of:
- 93           ○ Inclusion of regional content that is not required for the submission.
  - 94           ○ Missing required elements due to folders that were deleted but are required for  
95           other regions.
- 96       2. Conversely, if the approach described above is not possible and a submission is being  
97       built from a folder structure previously submitted to another region, take care to:
- 98           ○ Consider those heading that are regional or require regional focus and to ensure  
99           that regional content that is not relevant to the subject regulator is removed.
  - 100          ○ Ensure that any folders that may have been deleted for the original submission are  
101          reconsidered for inclusion in the new submission.
  - 102          ○ Ensure that content is current (e.g. market history is up to date).

---

<sup>3</sup> For a complete description of common and regional content requirements for each heading refer to: [IMDRF In Vitro Diagnostic Medical Device Market Authorization Table of Contents \(IVD MA ToC\)](#) or [IMDRF Non-In Vitro Diagnostic Device Market Authorization Table of Contents \(nIVD MA ToC\)](#)

<sup>4</sup> Note that the use of PDFs and folders is an interim format designed to test a standardised Table of Contents and future implementations may be more user friendly. It is time consuming for multiple reviewers to open chains of folders every time to find that they are empty and to ensure there is no evaluable content. It is not normal practice for regulators to alter submissions, e.g. by deleting unneeded documents or folders, as the regulators need to maintain the integrity of the original submission. The IMDRF ToC Working Group appreciates your efforts to delete empty folders and provide content as per the regional guidance documents before submission.

## 105 **4.0 TECHNICAL GUIDELINES**

106 The IMDRF ToC Pilot will rely on technical guidelines to provide consistency across the  
107 regions. The following sections include basic guidelines for submitting a ToC based submission.

### 108 **4.1 Folder Structure**

109 The IMDRF documents, In Vitro Diagnostic Medical Device Market Authorization Table of  
110 Contents (IVD MA ToC) and Non-In Vitro Diagnostic Device Market Authorization Table of  
111 Contents (nIVD MA ToC) define the content for each folder. The folder structure is to be built as  
112 prescribed by IMDRF. Refer to the IMDRF Standard ToC Folder Structure file, which is a  
113 physical folder structure template provided by IMDRF to help facilitate the preparation of  
114 applications in the required ToC format.

115 Regional Classification Matrices describe which elements of the ToC are required for each  
116 regulatory submission within scope. There are factors influencing the inclusion/exclusion of  
117 submission contents, these considerations are detailed below.

118 Each folder within the submission has been established as either **Required** or **Not Required** for  
119 the particular submission. This is explicitly defined by the classification matrix (e.g. *Required* or  
120 *Not Required* classification) or through interpretation of the classification (e.g. through  
121 assessment of conditions<sup>5</sup> for those that are classified as *Conditionally Required* or a decision by  
122 the applicant for those that are classified as *Optional*). With this in mind, Figure 1 below depicts  
123 many of the classifications that can result in a folder being **Required** or **Not Required** within  
124 the submission.

125 Any folder that is established as **Required** should not be deleted. Content must be submitted in  
126 this folder.

127 Any folder that is established as **Not Required** should be deleted to ensure the submission  
128 content package does not contain empty folders. If any parent folder contains no content, then  
129 that parent folder should also be deleted.

130 Any folder that is established as **Conditionally Required** requires a determination against the  
131 conditions by the applicant. A folder should be retained if content is required or should be  
132 deleted if content is not required.

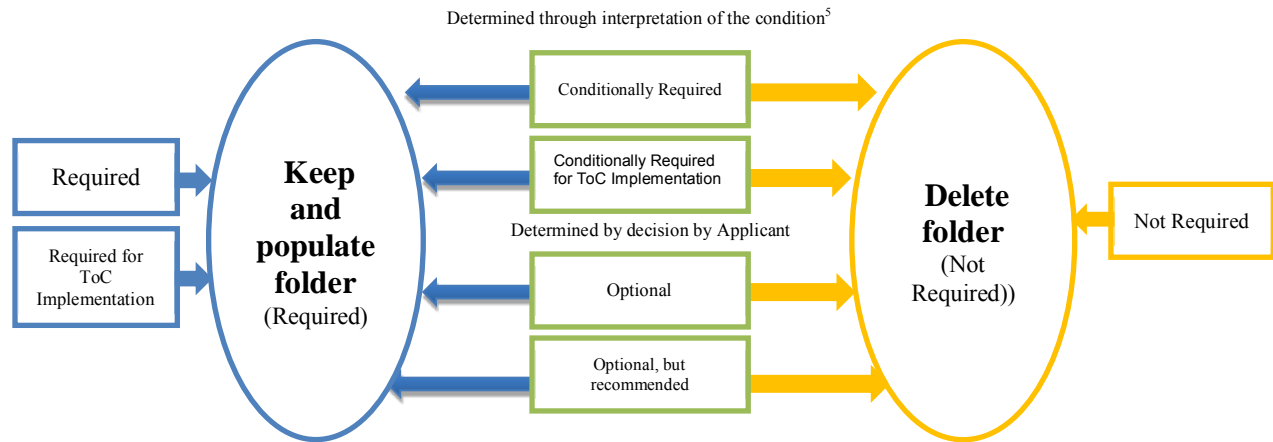
133  
134 Any folder that is established as **Optional** requires a decision by the applicant then should be  
135 deleted if not populated.

136 It should be noted that some regions may require a statement describing why a section is not  
137 provided. Refer to regional pilot instructions for additional details.

---

<sup>5</sup> Conditions for *Conditionally Required* headings are outlined in the Classification Matrices





138 Figure 1 - Those classifications defined in the classification matrix (rectangles) that can lead to content being  
 139 Required or Not Required in for a particular submission (ovals).

140 **4.2 Folder Naming Convention**

141 The folders in the provided templates will be numbered and named per the ToC requirements,  
 142 with the exception of the custom headings which are to be numbered and named as defined in the  
 143 IMDRF ToC (e.g. [Study description, study identifier, date of initiation] indicating the  
 144 information the sender should include as the folder name of the custom folder. In the IMDRF  
 145 Standard Folder Structure file – these folders appear with “[Custom]” in the folder name). The  
 146 final digit of the heading number should be revised as appropriate to ensure appropriate  
 147 sequential presentation of the custom folders when more than one study is being included.  
 148 For example, for the Physical and Mechanical Characterization heading, the first custom study  
 149 folder should be named “3.5.01.1[Study description, study identifier, date of initiation]” and the  
 150 second custom study folder should be named “3.5.01.2[Study description, study identifier, date  
 151 of initiation]”. If there are more than 10 studies, the sequence numbering should use 2 digits  
 152 (e.g. 3.5.01.01... 3.5.01.10 for the example above).

153  
 154 The character count for the [Custom] or [Trial Details] folder names should be no more than 50  
 155 characters (including the section number). Abbreviations in their names are expected and  
 156 acceptable

157  
 158 **NOTE:** Restrictions in file and folder names exist to ensure maximum allowable system file path  
 159 lengths are not exceeded.

160  
 161 “Overview” folders have been created in the folder template where the IMDRF guidance  
 162 indicates a requirement for content at a parent folder. This folder structure was created to ensure  
 163 the sequence of information presented is maintained in a Windows environment. For example, in

164 | [the nIVD structure, Section 3.5.06 Biocompatibility & Toxicology Evaluation, there is a sub-](#)  
165 | [folder named “3.5.06.0-Overview” in the template. The content prescribed by the IMDRF](#)  
166 | [guidance for Section 3.5.06 should be placed in this folder.](#)

### 167 4.3 File Format and Naming

168 Portable document format (PDF) files are the preferred file format although other formats such  
169 as Microsoft Office (.doc, .ppt, .xls) are also acceptable in some regions. Refer to regional pilot  
170 instructions for specific file format and versions.

171 The applicant should create all PDF files directly from the source documents whenever feasible  
172 rather than creating them by scanning. **PDF documents produced by scanning paper**  
173 **documents are far inferior to those produced directly from the source document, such as**  
174 **Word document, and, thus, should be avoided if at all possible.** Scanned documents,  
175 particularly tables and graphs, are more difficult to read and do not allow the reviewers to copy  
176 and paste text.

177 For any scanned document, you should perform optical character recognition (OCR) so that the  
178 text is searchable. Check to see that the content has been correctly converted by: (1) highlighting  
179 an area of text and (2) searching for a word or phrase. If the word or phrase is not returned in the  
180 search, then the OCR did not recognize the text. We recognize that OCR may not be feasible in  
181 some cases for documents with figures and images.

182 Most file names are user defined, with a limitation of 50 characters (including the file extension  
183 and section number). File names should be meaningful and provide some indication of their  
184 content. When more than one file is presented in a folder, suffix number should be used to ensure  
185 the intended sequence of presentation is maintained.

186 File names are prescribed under the user defined [Custom] folders and must be:

- 187 • 1-Summary
- 188 • 2-Full Report
- 189 • 3-Statistical Data

190  
191 File names are prescribed under the user defined [Trial details] folder and must be:

192

nIVD	IVD
1-Clinical Trial Synopsis	1-Clinical Study Synopsis
2-Clinical Trial Report	2-Clinical Study Report
3-Clinical Trial Data	3-Clinical Study Data

193

194 **NOTE:** Restrictions in file and folder naming exist to ensure maximum allowable system file  
195 path lengths are not exceeded. Applicants should be aware that computer operating systems have  
196 limitations and are requested to **keep filenames and pathnames in submissions as short as**  
197 **possible.**

198  
199 The IMDRF folder templates and file naming specifications have been established in an effort to  
200 ensure submissions can be received and stored by regulators without reaching the operating  
201 system limits. It is recommended that applicants examine the length of the entire pathname (i.e.  
202 all nested folders and file name and file extension) prior to transmission to verify the path length  
203 is 200 characters or less.

#### 204 **4.4 File and Submission Size Limitations**

205 No individual PDF file in the submission shall exceed 100 MB.

206 The entire submission should not exceed 4GB to ensure acceptance by all participating regions.

#### 207 **4.5 Document Security**

208 Files should not have any security settings, specifically:

- 209
- 210 ● Files must not have password protection preventing the file from opening.
- 211 ● Files should be set to allow printing, selecting text and graphics, and adding or changing
- 212 notes and form fields.
- 213

Applicants should use secure upload facilities or reputable couriers to protect the transmission to the regulators.

#### 214 **4.6 Bookmarking in PDF Files**

215 It is also important that PDF files be properly structured, with a properly bookmarked internal  
216 table of contents. The following are recommended as good structuring practices:

- 217 ● Documents of ten pages or more should have their own internal table of contents.
- 218 ● When creating bookmarks, the magnification setting should be set to Inherit Zoom so that  
219 the destination page displays at the same magnification level that the reviewer is using for  
220 the rest of the document.
- 221 ● Sections, subsections, tables, figures and appendices should all be bookmarked.
- 222 ● Attachments to PDF files should be avoided.
- 223 ● Too many levels of bookmarks are inefficient. In most instances, three levels of  
224 bookmarks should be sufficient:
  - 225 1 Heading
  - 226 1.1 Subheading
  - 227 1.1.1 Sub-subheading.

228 It is recognized that bookmarks are generated automatically from document headings;  
229 nevertheless, it is recommended that they be kept concise.

230 Set the Navigation Tab to open to “Bookmarks Panel and Page.” This sets the initial document  
231 view when the file is opened. If there are no bookmarks, set the Navigation Tab to “Page Only.”  
232 Page Layout and Magnification should be set to “Default.”

## 233 4.7 Hyperlinking in PDF files

234 Hyperlinks are used to improve navigation through individual PDF documents and are  
235 encouraged. Hyperlinks can be designated by rectangles using thin lines or by blue text or you  
236 can use invisible rectangles for hypertext links in a table of contents to avoid obscuring text.  
237 Hyperlinks throughout the body of the document to supporting annotations, related sections,  
238 references, appendices, tables, or figures that are not located on the same page are helpful and  
239 improve navigation efficiency.

240 Hyperlinks between documents are acceptable but care must be taken in creating the links  
241 between different documents so that they will function once the application is received by the  
242 regulator (the use of relative linking is recommended). It is the applicant's responsibility to  
243 ensure that hyperlinks are functioning. Links must also include references to the specific section  
244 or page in the event the link is broken.

## 245 4.8 Granularity Rules

246 There are no limitations on the number of files per heading within the submission, however, the  
247 following guidelines should be considered.

248 1) Efforts should be made to draft documents that concisely communicate the content  
249 described in the IMDRF [In Vitro Diagnostic Medical Device Market Authorization Table](#)  
250 [of Contents \(IVD MA ToC\)](#) or [Non-In Vitro Diagnostic Medical Device Market](#)  
251 [Authorization Table of Contents \(nlVD MA ToC\)](#), rather than simply including existing  
252 documentation that contains superfluous information not required for the particular  
253 heading. For example:

254 · Including a number of Material Safety Data Sheets within “*2.4.1 - Comprehensive*  
255 *Device Description and Principle of Operation*” is less helpful than summarizing  
256 the specific details of relevance to this heading.

257 2) When multiple files are considered necessary, file naming methods should ensure that the  
258 files are presented in their intended sequence, for example in folder named “*2.4.1-*  
259 *Comprehensive Device Description & Principle of Operation*” the files would appear as:  
260 2.4.1.0-Comprehensive Device Description and Principle of Operation.pdf  
261 2.4.1.1-Engineering drawings.pdf

## 262 4.9 Pagination

263 Pages of the submission should be numbered in such a manner that information can be easily  
264 referenced by page number. Pagination should be applied to each document (i.e., the physical  
265 file). This may be done by numbering the pages within a section or chapter (e.g., CH2.4.1-1,  
266 CH2.4.1-2).