



**IMDRF** International Medical  
Device Regulators Forum

## **FINAL DOCUMENT**

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

**Title: Strategic Assessment of Electronic Submission Messaging Formats**

**Authoring Group: IMDRF RPS WG**

**Date: 2 October 2015**

A handwritten signature in black ink, appearing to read 'T. Tominaga'.

Toshiyoshi Tominaga, IMDRF Chair

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## **Preface**

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

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## 1 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 on Medical Devices (GHTF), and to accelerate international medical device regulatory harmonization and convergence. The IMDRF Management Committee (MC) sponsors and approves work through the formation of Working Groups.

The IMDRF RPS Working Group (RPS WG) was convened by the IMDRF MC in 2012 to evaluate the HL7 RPS standard under development, and to determine whether it was fit for use to support medical device submissions. The group was also asked to define a common ‘Table of Contents’ (TOC) for medical device regulatory submissions as a first step in defining a common data set capable of supporting a harmonized electronic submission format.

The HL7 RPS standard was approved as a normative standard in the fall of 2014. Based on work done by the RPS WG, additional requirements were included in the final standard to support medical device submissions. The IMDRF TOC was approved as a final guidance document and pilots of the guidance are currently underway in some regions, and planned in others.

## 2 Scope

This document provides a strategic analysis of alternative electronic information exchange formats against medical device business objectives from both regulators and industry. Implementation of the IMDRF TOC is assumed for all options analyzed. As a result, benefits and challenges discussed in this document pertain only to the electronic information exchange format, not the IMDRF TOC.

The scope of this document is limited to premarket medical device submissions and secondary uses of regulatory submission data. The following topics are out of scope: Pharmaceutical and combination product submissions; and software solutions used to implement the exchange standard.

Full implementation of any electronic submission messaging format will take time, and will involve multiple key milestones and decision points. This document provides a recommended strategic direction. It does not include analysis of cost for any solution. Cost analysis requires implementation planning for the alternative formats, and engagement from software vendors that is considered pre-mature without strategic alignment on a messaging format.

Although software solutions and combination products are out of scope, the recommendation still includes:

- Discussion of requirements to ensure software solutions that support the recommendation are accessible to all stakeholders regardless of their means or capability.
- Comment on the benefits or risks of the recommendation may have on future combination product submissions.

### 3 Definitions

**HL7** – Health Level 7; an accredited standard development organization focused on electronic messaging standards that support healthcare.

**ICH** – International Conference on Harmonisation

**IMDRF** – International Medical Device Regulators Forum

**IMDRF TOC** – a harmonized table of contents structure that may be used for pre-market medical device submissions.

**RPS** – Regulated Product Submissions, an HL7 messaging standard that supports submission of information for regulated products.

**SmartForm** – a PDF fillable form to collect information about the submission, to supplement the structured data that is found in an electronic exchange message.

### 4 Executive Summary

The RPS WG recommends that the IMDRF MC endorse implementation of the RPS standard for medical devices. Implementation of RPS is a multi-year effort, and there are concerns around cost and burden within a large segment of industry. As a result, we further recommend that incremental steps be taken to implement the HL7 RPS Message Standard that help address industry concerns.

This recommendation is based on an evaluation of three possible electronic submission format options: a harmonized folder structure, a custom IMDRF messaging standard, and the HL7 RPS standard.

Each of these options was evaluated by multiple industry and regulator stakeholders. Scoring was based on how well the options met defined business objectives compared to current submission formats (i.e. paper, eCopy, etc.). Final scores were weighted to ensure perspectives from regulators and industry were given equal consideration. Industry scores were weighted to reflect industry composition. Regulatory scores were weighted to reflect the RPS WG regulator membership. Higher scores reflect the more desirable option.

Final scores for each option are shown below.

Option 1 Status Quo (Baseline)	Option 2 Harmonized Folder structure	Option 3 Custom IMDRF Message Standard	Option 4 HL7 RPS Message Standard
45.0	<u>48.9</u>	<u>51.5</u>	<u>52.3</u>

If the recommendation is accepted, the RPS WG recommends creation of a publicly available strategy that details milestones to RPS implementation, including incremental steps to achieve a full implementation. The strategy should include a high level sequence of events to provide stakeholders a rough idea of when key changes will occur, and may require regions to conduct economic impact assessments prior to the implementation of the recommendation.

## 5 Business Drivers & Requirements

Table 1 outlines the business challenges, and objectives related to the message exchange format used for submissions. The table also shows high level benefits if each business objective is fully met.

Because each area may impact different stakeholders, stakeholders impacted by each objective are also noted. Each of the resulting objectives will be used as a basis for the evaluation, and were scored by each of the stakeholders.

**Table 1 - Challenges, Business Objectives & Potential Benefits**

<b>Problem Area</b>	<b>Problem Description</b>	<b>Resulting Objective(s)</b>	<b>Projected Benefits</b>	<b>Stakeholder Impact</b>
No harmonized common message exchange format for submissions	The format required for submissions currently varies across different regions. Some markets accept only paper. Others require a collection of PDF files in a specific folder structure. Some require upload of submission documents to a website. These differences require manufacturers to manage multiple technical tools and processes to support submissions.	Efficiently produce submissions for multiple regions without managing multiple submission creation processes, and software tools	Reduce effort / cost to support multiple technical exchange formats across different regulators	Industry

<b>Problem Area</b>	<b>Problem Description</b>	<b>Resulting Objective(s)</b>	<b>Projected Benefits</b>	<b>Stakeholder Impact</b>
	<p>Effective exchange of information among world regulators is currently limited due to the variety of required submission formats.</p> <p>In some cases, the lack of a harmonized message exchange format for submissions may result in an inability to effectively exchange information with intra-regional regulators</p>	<p>Enable efficient exchange of information amongst regulators.</p>	<p>Provide a means for more efficient exchange of information among regulators worldwide.</p>	<p>Regulators</p>

<b>Problem Area</b>	<b>Problem Description</b>	<b>Resulting Objective(s)</b>	<b>Projected Benefits</b>	<b>Stakeholder Impact</b>
Managing Submission & Content Lifecycle	<p>Inability to connect submission content over time. During the lifecycle of a product, many submissions are made to a regulator. In addition to the initial submission to gain product approval, more information is supplied in response to review questions. Over time changes are made to the product that require additional submissions. Currently, there is not a way to show how the documents provided to support product approval change over time; or to easily see the current set of documents that support marketing of the product.</p>	<p>Enable a clear view to the lifecycle of Application content over time, as well as the ability to quickly see the most current version of an Application.</p>	<p>Provide a means for more efficient traceability of submission content over the course of the product lifecycle</p>	<p>Regulators and Industry</p>



Problem Area	Problem Description	Resulting Objective(s)	Projected Benefits	Stakeholder Impact
	Inability to access data from premarket submissions during post market surveillance within a single regulatory agency (harvesting information from premarket forms and documents - e.g., device descriptions, risk assessment, other documents submitted premarket).	Include additional metadata on submission content for better discovery in the future (i.e., TOC headings and keywords).	Allow for more information in support of post market surveillance	Regulators
	Inability to transfer submission ownership and history between regulators (if an applicant changes notified bodies), or to another applicant (if a company is acquired or product line divested).	Provide a mechanism through which the full submission lifecycle for a product can be easily transferred between stakeholders	Improves efficiency, compliance and accuracy when transferring submissions	Industry and Regulators

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<b>Problem Area</b>	<b>Problem Description</b>	<b>Resulting Objective(s)</b>	<b>Projected Benefits</b>	<b>Stakeholder Impact</b>
	Submissions for the same product may be made to various regulators at different points in the product lifecycle. Future changes to the product may require submissions in some countries and not others. This results in each country having a different set of documentation that is considered current for the same product. In planning future submissions, industry needs to research / understand the set of documentation that is considered “current” in each market.	When product changes result in changes to submitted documentation, facilitate more efficient analysis of which submissions and which regions would be impacted by the change.	Improve efficiency in review of product changes to determine regulatory impact	Industry

Problem Area	Problem Description	Resulting Objective(s)	Projected Benefits	Stakeholder Impact
	Some current systems (if available) require manual effort to determine how a current market application (i.e. submission) relates to a previous marketing application(s). For example, a submission for a manufacturing process change may cover multiple applications. The applications impacted are currently described in document content. This requires regulators and industry to locate those relationships and manually enter them into tracking systems.	Enable regulators and industry to consistently and clearly identify / communicate how a submission relates to previous applications	Allow a better understanding of application history.  Enables more efficient resource utilization.	Regulators and Industry
Use of Paper by some stakeholders as a preferred format in management of submissions	Locating information provided in paper is time consuming and prone to error. Other industries have moved to electronic information. The medical device industry needs to move in that direction as well.	Enable efficient access (for appropriate parties) to information provided electronically in submissions	Provide a more efficient means of accessing regulated submission content.  Enable more efficient resource utilization	Regulators and Industry

<b>Problem Area</b>	<b>Problem Description</b>	<b>Resulting Objective(s)</b>	<b>Projected Benefits</b>	<b>Stakeholder Impact</b>
	Storage of paper submissions is expensive. Although few industry stakeholders still retain paper, some regulators do.	Enable a solution for electronic storage of product submissions	Significant reduction in storage costs	Regulators and Industry
	It is difficult to distribute paper to multiple reviewers. Access / review by remote workers requires availability of electronic documents	Enable efficient simultaneous access to information (for reviewers) provided electronically in submissions	Provide a more efficient means of review by multiple resources. Enable more efficient resource utilization.	Regulators
Submission log-in / Acknowledgements	Some regions require manual log-in to receive and acknowledge of submissions (including data entry and upload/routing of content)	Enable reduction of resources / time required for manual login (data entry, record creation) of submissions Note: This objective would require the collection of structured data values from industry	Enables more efficient resource utilization	Regulators

Problem Area	Problem Description	Resulting Objective(s)	Projected Benefits	Stakeholder Impact
	Inconsistent manual acknowledgement of successful receipt and validation of technical and regulatory status of submission contents. In some cases industry finds it challenging to obtain a clear status for submissions under review.	Provide a way to automatically identify the current review status of a submission.	Status of submission is clear	Industry
Regulatory Requirement Changes and Submission Lifecycle	Regulation changes result in changes to required submission content. A single application may include submissions made at different points in time – each of which may include different submission content based on the requirements that applied at the time of submission. It is difficult track the lifecycle of submission content within an Application if the structure (TOC) of all submissions within that application is not consistent.	Provide a way to maintain the lifecycle of an Application over time when the regulation changes result in TOC variance between submissions.		Regulators and Industry

Lastly, in addition to the objectives stated above, the cost to maintain the solution and standard are included as qualitative evaluation criteria. With respect to the solution, the cost includes consideration of resources to manage day to day submission activity, and effort to provide governance over time. There are also costs to maintain the standard, and they include the governance and maintenance to manage the change over time. It is important to note these criteria cannot enumerate the overall cost across the various industry and regulatory stakeholders. Therefore, these evaluation criteria should be considered a qualitative measure of the costs.

If all objectives can be met, the following key business benefits are anticipated:

1. Reduced industry effort / cost to support multiple technical exchange formats for different regulators. Note: this benefit will be limited to IMDRF regions initially. It is hoped that with broader regional adoption of a common message exchange format, the benefit will increase.
2. More efficient exchange of information among regulators worldwide.
3. Efficient traceability of submission content over the course of the product lifecycle for both regulators and industry.
4. More information for regulators in support of post market surveillance.
5. Improved efficiency, compliance and accuracy for both regulators and industry when transferring submission ownership.
6. Improved efficiency for industry in review of product changes to determine regulatory impact.
7. Better understanding of application history will enable more efficient resource utilization for all stakeholders.
8. A more efficient means of accessing regulated submission content for all stakeholders.
9. Significant reduction in submission storage costs for stakeholders who still retain paper copies.
10. A more efficient means for regulators to support review by multiple resources.
11. More efficient resource utilization for submission management and review by Regulators.

## 6 Stakeholders

At a high level, the medical device industry and regulators are the primary stakeholder segments in the pre-market submission process. These broad groupings are referenced in Table 1 to indicate if the business objectives have an impact on the stakeholder. However there is significant diversity and differing points of view within those high level segments. These differences mean that some in industry may perceive significant benefit from a potential solution, while other industry stakeholders see no benefit. To fully represent this diversity, subgroups of stakeholders have been defined and used in analysis of possible solutions to insure the analysis accurately reflects the full range of perspectives.

Each group of stakeholders is summarized in Table 2 below. Appendix B of this document details how these stakeholder groups were weighted in the analysis and final recommendation.

Table 2 - Stakeholder Groups

<b>INDUSTRY</b>	
Companies that currently support eCTD or have publishing software in-house	A company in this category has already made an investment in software and staff to support electronic submissions. The implementation learning curve may not be as steep. They may also be able to leverage money & time already invested.
Companies that support multiple complex submissions	A complex submission is one that requires many supporting studies (i.e. clinical, bench testing). The same product may have a complex submission for one or two products in multiple regions, or the company may have many products with complex submissions in only one region.  For these companies, there is a different level of value in tracking versions of documents and where they are submitted.
Companies that have primarily simple submissions	Companies in this group work with simple submissions (the submission has only one or two supporting studies), and generally have lower risk products.

<b>REGULATORS</b>	
Regulators with electronic review tools and experience reviewing structured content in submissions	Regulators in this group have software tools that are used in submission review today. They may also have experience within their organization reviewing eCTD or other similar submission formats.
Regulators who don't currently have review tools	Regulators in this group review in paper or a common electronic file format – like Word or PDF. They do not currently review submissions in eCTD or similar formats

## 7 Technology Analysis and Recommendation

### 7.1 Technology Options

Four approaches were considered as potential technical exchange format options for premarket submissions. As discussed in the Scope section of this document, all options assume implementation of the IMDRF TOC. Each of the four options are summarized in Table 3 below. Note that the first option is to maintain current practice, and not implement a harmonized technical exchange format. This option is included in the analysis as a baseline to compare other alternatives. The RPS WG does not feel that Option 1 is a viable solution.

Table 3 - Submission Exchange Options

<b>Option Name</b>	<b>Description</b>	<b>Notes</b>
Option 1 Status Quo (Baseline)	No Change to Current Practice (Status Quo)	Each region would implement the IMDRF TOC, but would continue to operate as they do today with respect to the submission exchange format. Regions may develop a different submission exchange formats over time. Some regions may opt to stay with paper. This represents the current state today (no harmonized technical exchange format) and is a baseline for the analysis of possible alternatives.
Option 2 Harmonized Folder structure	A harmonized hierarchical folder structure housing e-files, and a harmonized SmartForm that captures some metadata about the submission.	Assumes all regions would accept a single folder structure and guidelines for file format that can be provided in the structure. Electronic forms could be leveraged to provide key information about the submission in format that can be automatically loaded into a system.
Option 3 Custom IMDRF Message Standard	An IMDRF developed Messaging Standard	IMDRF would develop a harmonized messaging format that specifically meets device needs. This option assumes a greater technical complexity than Option 2, and assumes the standard developed would have



Option Name	Description	Notes
		the ability to manage submission content lifecycle and meta-data.
Option 4 HL7 RPS Message Standard	HL7 RPS XML Messaging Standard	An IMDRF implementation of the HL7 RPS messaging standard for devices.

## 7.2 Evaluation Methodology

Each technology option will be scored in categories correlating to the Business Objectives from Table 1, and an additional category of cost to maintain the solution over time. The maintenance category considers costs and time to provide governance for the technology option over time, and to manage day to day submission activity using the solution.

Each option is given a score of 1 – 5 (1 is worst, 5 is best) in each of the categories. Since Option 1 is to do nothing, this has been given a score of 3 in all categories, and represents a baseline against which the other solutions can be compared. Other possible technology solutions are scored comparatively against Option 1 (status quo). If a solution is no better or worse than the current state in one area, it will receive a 3 – to match the 3 given to Option 1. If a solution makes the problem area better or worse than maintaining Status Quo a score is assigned a value higher (4 or 5) or lower (1 or 2) to status quo score of 3, respectively.

Scoring is done from the perspective of each stakeholder subgroup (see Table 2). As a result each business objective will have multiple scores in each category for each option.

Scores for each stakeholder group are then weighted to achieve the following:

- An equal weight to both industry and regulator input
- Proportional weighting within the regulator scores to reflect the percentage of each regulator stakeholder group on the RPS WG
- Industry scores are weighted to approximate the composition of overall industry. Stakeholders with primarily simple submissions: 85%; stakeholders with complex submissions 10%; stakeholders with eCTD experience and/or publishing tools 5%

Detailed weighting formulas can be found in Appendix B.

After weighting is applied, the scores are then added together to create a total score for each option. This total score provides an objective way to compare the options to each other.

It should be noted that this analysis is not intended to be statistically rigorous. Instead it is an effort to obtain consensus, subjective scores across stakeholder groups; and to build that feedback into an objective analysis that can be used to set strategic direction.

### 7.3 Evaluation of Technology Options

This assessment shows the total score for each option across each of the stakeholder sub-groups. It also provides the overall score with weighting applied for each option. Detailed scoring for each detailed category can be found in Appendix A

Stakeholder Sub-Group	Option 1 Status Quo (Baseline)	Option 2 Harmonized Folder structure	Option 3 Custom IMDRF Message Standard	Option 4 HL7 RPS Message Standard
<b>INDUSTRY</b> - Companies that currently support eCTD or have publishing software in-house	45.0	<u>50</u>	<u>48.5</u>	<u>54.3</u>
<b>INDUSTRY</b> - Companies that support multiple complex submissions	45.0	<u>48.9</u>	<u>50.4</u>	<u>50.3</u>
<b>INDUSTRY</b> - Companies that have primarily simple submissions	45.0	<u>50.6</u>	<u>49.4</u>	<u>48.5</u>
<b>REGULATORS</b> – jurisdictions with electronic review tools or experience reviewing structured content in submissions	45.0	<u>44.1</u>	<u>53.2</u>	<u>56.5</u>
<b>REGULATORS</b> - jurisdictions that don't currently have review tools	45.0	<u>50.5</u>	<u>53.8</u>	<u>54.6</u>
<b>TOTAL SCORE (Weighting Applied)</b>	45.0	<u>48.9</u>	<u>51.5</u>	<u>52.3</u>

#### 7.3.1 Industry Scoring Feedback

Industry discussions are summarized below according to each business objective. The overall scores are the result of consensus discussions within multiple industry groups, and represent the average of the scores received. It should be noted that industry scoring discussions revealed very different perspectives based a combination of factors:

- The region(s) represented in the discussions
- Stakeholder group – (variance between stakeholder groups was present in some regional discussions, but not all)
- The organizational structure of the company as centralized or de-centralized

The summary below includes views expressed during all discussions for full transparency and an accurate view of the diverse perspectives. As a result the final scores are based the weighted average and do not represent individual stakeholder viewpoints.

The main concern within industry remains the cost to implement and maintain software tools that may be required for any option. Many companies with simple submissions in particular do not see any benefit to the additional costs they feel would be incurred for all options.

Since consideration of options 3 and 4 are currently in an early exploratory stage, it was understood throughout industry discussions that a robust cost-benefit analysis is not possible at this time. For industry stakeholder adoption this is a significant consideration, and will need to be assessed once sufficient implementation planning has been done to support such an analysis. Industry views this cost-benefit analysis as a critical step.

***Efficiently produce submissions for multiple regions without managing multiple submission creation processes, and software tools***

Although some companies could see the potential benefit of meeting this objective, there were some that did not view this as a priority. Companies who operate in a de-centralized fashion today manage multiple processes and tools as a result of the way they are structured. Introduction of a harmonized submission format is not likely to change that. Among those companies, some viewed all options as adding unnecessary complexity.

There were many companies who felt the move to a harmonized format is worthwhile. Although there was concern that even with use of a messaging standard like RPS, each region may impose unique implementation requirements that would undermine this objective. Regional differences in eCTD implementation were cited as an example.

Some felt that Option 4 would only be the best choice if regional variance could be eliminated, and tools used to create the RPS format also could produce PDF and other paper format submissions to meet requirements in countries that do not recognize the format chosen by IMDRF.

Generally, companies with simple submissions preferred use of the folder structure.

***Enable a clear view to the lifecycle of Application content over time, as well as the ability to quickly see the most current version of an Application.***

Companies with complex submissions who currently manage submissions with many supplements or change submissions that occur over time saw the benefit of content lifecycle tracking. This clearly resonated with those who manage multiple PMAs in the US, and with European companies who manage design dossiers.

Some companies noted that the ability to fully take advantage of lifecycle tracking will depend on the tools available to industry, and on the cost of those tools.

Some did not see that Option 2 provided any ability to manage lifecycle of submission content. Others noted that since RPS is being adopted by ICH as eCTD v4.0, it clearly meets requirements for submission lifecycle tracking.

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In the US, companies with primarily 510(k)s did not see the need for, or benefit in lifecycle tracking. Each 510(k) is its own application. Submission of a new 510(k) for a line extension or change results in a new application, rather than a change to an existing application.

***Provide a mechanism through which the full submission lifecycle for a product can be easily transferred between stakeholders***

Some companies did not see the value in this objective. They did not feel transfer of existing submissions during an acquisition was a problem today, and so did not see the relevance of the submission exchange format to this objective.

For those companies who saw value in the objective, there was not a clear consensus as to which of the options could best enable this.

***When product changes result in changes to submitted documentation, facilitate more efficient analysis of which submissions and which regions would be impacted by the change.***

A large number of companies felt that the ability to meet this objective exists today if companies are willing to invest in the tools and processes to do so. Although a future electronic messaging format may contain information that could aid in this analysis, a sponsor's ability to take advantage of that would still depend greatly on the type of tool implemented within the company. As a result, many felt that all proposed options would not provide a significant improvement over the current state (Option 1).

***Enable regulators and industry to consistently and clearly identify / communicate how a submission relates to previous applications***

There was general consensus among most companies participating in the scoring process that Options 3 and 4 would be better able to provide the submission to application(s) relationships in a structured way. The folder structure as currently proposed for the TOC pilot does not embed this information, so development of a harmonized SmartForm would be required to meet the objective with Option 2.

Some companies did not see the value in this objective. They felt that these relationships are currently communicated in the body of cover letters and other documentation that accompanies submissions; and did not see the value of communicating the information in a more structured way.

***Enable efficient access (for appropriate parties) to information provided electronically in submissions***

This objective directly relates to the challenges of still managing paper submissions. In many industry discussions, this objective was viewed as enabling efficient access to submissions within each company (including to functions outside of Regulatory Affairs).

Some companies currently have an electronic archive of submissions made that is broadly available within their organizations. For those that do not, all three options were viewed as providing a consistent structure around which such access could be built. However Options 3 and 4 would require additional software to view the submission, which Option 2 does not. For that reason, many felt that Option 2 would best meet this objective.

***Enable a solution for electronic storage of product submissions***

This objective relates specifically to elimination of paper storage. Most companies who participated in the scoring process currently store submissions they have made electronically. As a result many did not feel any of the options would improve the current state. A few companies who currently still manage paper expressed concerns about the part 11 compliance burden that may result from the change to electronic submission storage.

Part 11 compliance was also a concern for the tools that might be required to produce any of the proposed formats; including the potential use of a SmartForm for Option 2.

***Provide a way to automatically identify the current review status of a submission.***

Within the US, industry identified two components to this objective: 1) automatically push submission status changes to industry as they occur; 2) provide a mechanism for industry to query the status of a submission in “real-time”.

Many felt that the XML solutions have potential to improve meet these requirements. The RPS standard has a status value for a Submission – and can store acceptable values based on controlled vocabulary lists. However the ability of any option to meet industry requirements depends very much on how the submission format is implemented within each regulatory agency.

***Provide a way to maintain the lifecycle of an Application over time when the regulation changes result in TOC variance between submissions.***

Many companies agreed that Options 3 and 4 have a better ability to track changes in the TOC and still maintain the Application lifecycle. US stakeholders with primarily 510(k)s noted that this was not a concern for 510(k)s since there is no lifecycle to manage.

There were concerns brought forward around how changes to the TOC would be managed / implemented. Some companies expressed concern that additional submissions might be required to bring older Applications in-line with TOC changes. In countries where approvals expire, there was concern that products might need to comply with new TOC requirements upon renewal – and that the documentation might not exist for older products. There were questions around how much notice industry would be given before changes to the TOC and classification matrices would take effect.

Some companies noted that while Options 3 and 4 would clearly be better at dealing with TOC changes over time, it may require that companies invest in software tools to take advantage of that ability. There is concern that those tools may not be affordable for all companies.

Within Europe, there was a suggestion that the TOC implementation should be timed to align with the MDD changes, since the MDD changes might require TOC changes.

***Cost to maintain the solution. This includes consideration of resources to manage day to day submission activity, and effort to provide governance over time***

Most industry stakeholders felt that any of the proposed options would be more complex and require some technology investment and maintenance vs what is done today.

A few companies felt the structure and consistency would over time enable more efficient use of internal resources within companies, and as a result the maintenance cost would over time go down.

Companies that current maintain eCTDs, felt that Option 4 (RPS) would allow them to take advantage of costs they already need to incur to maintain their current tools. Options 2 or 3 would instead require an investment in maintenance of additional tools.

Most expressed concern about IMDRF effort that might be required to maintain / govern a custom format over time.

### **7.3.2 Regulator Scoring Feedback**

Regulator comments are summarized below according to business objectives. The scores for electronic submission options for both regulator groups were relatively consistent, giving Option 2 the lowest overall score, and Option 4 the highest. Although the scores were consistent, the regulator groups had comments to be noted about the business objectives, which have been summarized below:

***Enable efficient exchange of information amongst regulators.***

This objective assumes that work-sharing will occur beyond Notified Bodies.

Regulators also were in consensus that although this objective states that an “exchange” of information will take place, two way communication is out of scope for the assessment of the IMDRF message standard as well as the HL7 RPS message standard, Options 3 and 4. The exchange would be instead defined as one way transfer of information amongst regulators.

This concern for a lack of two way communication prevented regulators from ranking the proposed solutions significantly higher than the status quo.

***Provide a mechanism through which the full submission lifecycle for a product can be easily transferred.***

Regulators also assumed that this objective referred to one way communication amongst regulator groups, and so, regulators were in consensus that the scores for the proposed options should not differ significantly from the status quo.

***Enable a solution for electronic storage of product submissions.***

Regulators under the subgroup “Regulators With Tools” gave the options for this objective relatively neutral scores, as these regulators already have access to the electronic review and/or submission tools. All information regarding product submissions is assumed to be currently stored electronically. The only additional benefit would be any reuse of submission documents as the files will be retrievable from the electronic storage by its meta-data (e.g., unique identifier).

Regulators Without Tools, however, gave higher scores than the status quo, as these regulators do not currently have access to the tools that allow for electronic storage of submissions. The regulators without tools were in agreement that Option 3 and 4 are more effective solutions in electronically storing and reusing submission content.

***Enable reduction of resources/time required for manual login (data entry, record creation) of submissions.***

Most regulators agreed that the proposed solution of creating a harmonized folder structure was not pertinent to addressing this objective, and therefore was given a score relatively close the status quo.

Regulators scored Option 3 highest under the assumption that structured data, which fully meets all information requirements, enables the automation of data entry and record creation.

It was also discussed among regulators that Option 4 had limits to what is provided in the RPS standard message, and could possibly lead to the exclusion and/or removal of certain product information (i.e., Common Data Elements (CDE) as a starting point).

***Provide a way to maintain the lifecycle of an application over time when the regulation changes results in TOC variance between submissions.***

For this objective, regulators agreed that Options 3 and 4 should be given significantly higher scores, as controlled vocabularies (i.e., pre-defined value sets) are present for both options.

Both the IMDRF and RPS Message standards would provide a greater flexibility in submissions and are therefore scored accordingly.

***Cost to maintain the solution. This includes consideration of resources to manage day to day submission activity, and effort to provide governance over time.***

Most regulators felt that the proposed options raised several concerns in regards to this objective. This is due to the complexity of the costs involved in the implementation and maintenance of the solution, and certain concerns include:

- What is the total cost of ownership?
- Will the business as usual and change management costs split?
- Focus on supporting one submission format

For regulators that have eCTD software, the creation of an IMDRF message (Option 3), would require additional investment to maintain an exchange message that would have the same functionality as the RPS message. It was also noted that there are existing commercial software vendors that will be updating their software to meet the new ICH requirements. By creating a separate IMDRF message, the medical device regulators and industry would not fully benefit from investment made by the software vendors to meet the ICH requirements.

For the remaining objectives, all regulators were in consensus and the scores were consistent.

**7.3.3 Overall Scoring Analysis**

For all stakeholder groups, more than one of the evaluated options scored higher than the status quo. Based on this, there is value for stakeholders in pursuing a harmonized electronic submission format. The cumulative scoring results show that RPS has the highest score of all the options evaluated.

Scoring showed a lack of consensus across industry stakeholders. Prior to weighting, each of the three industry stakeholder groups had higher scores for a different option. In addition, industry stakeholders

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in the simple submissions category scored RPS lower than Options 2 and 3. This is notable because the simple submissions stakeholder group is estimated to represent 85% of industry.

All Regulators scored the HL7 RPS Message Standard, Option 4, as the best option, with Option 3 also rating better than the Option 2. Therefore, Regulators did not think the move from status quo to a harmonized folder structure will lead to any significant benefit, whereas moving to a standard message based option would yield the most benefit because it would provide additional functionality (e.g., life cycle of submission content and structured data) and with Option 4 there would be the opportunity to share resources available in the pharmaceutical and biologic domain.

## 8 Final Recommendation

Based on the scoring and subsequent analysis, it is recommended that the IMDRF MC endorse RPS as the future electronic information exchange format to be used for medical device submissions; and that the MC charter additional efforts within the RPS WG to develop a harmonized, device specific implementation of the RPS standard. The RPS WG feels this is strategically the best option given the scoring outcome, and the planned use of RPS by ICH for pharmaceutical submissions. Submission messaging format alignment between the drug and device industries could benefit combination product submissions in the future.

It should be noted that implementation of RPS is a long term undertaking, and efforts will most likely take several years. The medical device industry structure differs from pharmaceuticals in that it is primarily composed of small and medium size enterprises (80 – 95% / jurisdiction), and generally has a lower revenue per product. These differences should be taken into consideration when planning RPS implementation.

To address these concerns, the RPS WG recommends that gradual steps be taken to implement the HL7 RPS Message Standard (e.g. use of a harmonized folder structure as a transition format, etc.). In addition, the full implementation of RPS that will require establishment of an ongoing governance model to maintain harmonization and address proposed changes.

### 8.1 Next Steps

If the recommendation of the strategic direction is accepted, the RPS WG will develop and post a strategic plan that details milestones for a future RPS implementation including incremental steps towards the full implementation and key stakeholder implementation requirements. The strategy should include the necessary sequence of events to provide stakeholders with a roadmap of the key changes that may occur during the transition to a standardized messaging format, and timing for those changes, and key decision points. Examples of roadmap milestones may include, but are not limited to:

- Developing an IMDRF RPS implementation guide (and regional guidance)
- Identification / implementation of a transitional format to begin accepting submissions using the IMDRF TOC.
- Identification of regulatory requirements (e.g., rulemaking and legislation) necessary for implementation and resulting timelines
- Consolidation of stakeholder-specific cost analysis (e.g., region-specific economic impact assessment and/or industry-based cost assessments) based on implementation plans and vendor inputs
- Creation of a governance structure and process



The strategic plan will provide a clear path for all parties – specifically industry and software vendors. It may also be used as an action plan within the RPS WG to support any future implementation activities;

## 9 Appendix A: Detailed Scoring of Technology Options

The information in this appendix provides the raw scores for each of the stakeholder groups defined in Section 6. The business objectives that did not affect the stakeholder are defaulted to a score of 3.0, and therefore are grayed out in the tables presented below. In addition, Option 1, Status Quo as a baseline was also defaulted to a score of 3.0, and is therefore also grayed out for each objective.

### 9.1 Regulators With Tools

<b>Problem Area / Objective</b>	<b>Option 1 Status Quo (Baseline)</b>	<b>Option 2 Harmonized Folder Structure</b>	<b>Option 3 Custom IMDRF Message Standard</b>	<b>Option 4 HL7 RPS Message Standard</b>
Efficiently produce submissions for multiple regions without managing multiple submission creation processes, and software tools	3.0	3.0	3.0	3.0
Enable efficient exchange of information amongst regulators	3.0	3.6	3.6	3.6
Enable a clear view to the lifecycle of Application content over time, as well as the ability to quickly see the most current version of an Application.	3.0	4.1	4.6	4.6
Include additional metadata on submission content for better discovery in the future (i.e., TOC headings and keywords).	3.0	3.0	3.5	3.5
Provide a mechanism through which the full submission lifecycle for a product can be easily transferred between stakeholders	3.0	3.0	3.0	3.0
When product changes result in changes to submitted documentation, facilitate more efficient analysis of which submissions and which regions would be impacted by the change.	3.0	3.0	3.0	3.0
Enable regulators and industry to consistently and clearly identify / communicate how a submission relates to previous applications	3.0	3.0	4.6	5.0

<b>Problem Area / Objective</b>	<b>Option 1 Status Quo (Baseline)</b>	<b>Option 2 Harmonized Folder Structure</b>	<b>Option 3 Custom IMDRF Message Standard</b>	<b>Option 4 HL7 RPS Message Standard</b>
Enable efficient access (for appropriate parties) to information provided electronically in submissions	3.0	3.8	4.5	4.9
Enable a solution for electronic storage of product submissions	3.0	3.0	3.0	3.0
Enable efficient simultaneous access to information (for reviewers) provided electronically in submissions	3.0	3.0	3.0	3.0
Enable reduction of resources / time required for manual login (data entry, record creation) of submissions Note: This objective would require the collection of structured data values from industry	3.0	3.0	4.5	4.1
Provide a way to automatically identify the current review status of a submission.	3.0	3.0	3.0	3.0
Provide a way to maintain the lifecycle of an Application over time when the regulation changes result in TOC variance between submissions.	3.0	1.6	5.0	5.0
Cost to maintain the solution. This includes consideration of resources to manage day to day submission activity, and effort to provide governance over time	3.0	2.0	3.4	4.0
Cost to maintain the standard	3.0	2.0	1.5	3.8
<b>TOTAL SCORE</b>	45.0	44.1	53.2	56.5
<b>AVERAGE SCORE</b>	3.0	2.9	3.5	3.8

## 9.2 Regulators Without Tools

<b>Problem Area / Objective</b>	<b>Option 1 Status Quo (Baseline)</b>	<b>Option 2 Harmonized Folder Structure</b>	<b>Option 3 Custom IMDRF Message Standard</b>	<b>Option 4 HL7 RPS Message Standard</b>
Efficiently produce submissions for multiple regions without managing multiple submission creation processes, and software tools	3.0	3.0	3.0	3.0
Enable efficient exchange of information amongst regulators	3.0	4.1	4.0	3.8
Enable a clear view to the lifecycle of Application content over time, as well as the ability to quickly see the most current version of an Application.	3.0	3.3	3.9	4.1
Include additional metadata on submission content for better discovery in the future (i.e., TOC headings and keywords).	3.0	3.5	4.1	4.3
Provide a mechanism through which the full submission lifecycle for a product can be easily transferred between stakeholders	3.0	3.1	3.1	3.4
When product changes result in changes to submitted documentation, facilitate more efficient analysis of which submissions and which regions would be impacted by the change.	3.0	3.0	3.0	3.0
Enable regulators and industry to consistently and clearly identify / communicate how a submission relates to previous applications	3.0	3.3	4.0	4.0
Enable efficient access (for appropriate parties) to information provided electronically in submissions	3.0	3.9	4.5	4.5
Enable a solution for electronic storage of product submissions	3.0	3.9	4.5	4.5

<b>Problem Area / Objective</b>	<b>Option 1 Status Quo (Baseline)</b>	<b>Option 2 Harmonized Folder Structure</b>	<b>Option 3 Custom IMDRF Message Standard</b>	<b>Option 4 HL7 RPS Message Standard</b>
Enable efficient simultaneous access to information (for reviewers) provided electronically in submissions	3.0	4.0	4.1	4.1
Enable reduction of resources / time required for manual login (data entry, record creation) of submissions Note: This objective would require the collection of structured data values from industry	3.0	3.3	4.1	4.1
Provide a way to automatically identify the current review status of a submission.	3.0	3.0	3.0	3.0
Provide a way to maintain the lifecycle of an Application over time when the regulation changes result in TOC variance between submissions.	3.0	3.1	4.1	4.1
Cost to maintain the solution. This includes consideration of resources to manage day to day submission activity, and effort to provide governance over time	3.0	3.0	2.5	2.5
Cost to maintain the standard	3.0	3.1	1.8	2.3
<b>TOTAL SCORE</b>	45.0	50.5	53.8	54.6
<b>AVERAGE SCORE</b>	3.0	3.4	3.6	3.6

### 9.3 Industry with Tools or eCTD Support

<b>Problem Area / Objective</b>	<b>Option 1 Status Quo (Baseline)</b>	<b>Option 2 Harmonized Folder Structure</b>	<b>Option 3 Custom IMDRF Message Standard</b>	<b>Option 4 HL7 RPS Message Standard</b>
Efficiently produce submissions for multiple regions without managing multiple submission creation processes, and software tools	3.0	4.0	4.0	4.8
Enable efficient exchange of information amongst regulators	3.0	3.0	3.0	3.0
Enable a clear view to the lifecycle of Application content over time, as well as the ability to quickly see the most current version of an Application.	3.0	3.5	4.3	4.8
Include additional metadata on submission content for better discovery in the future (i.e., TOC headings and keywords).	3.0	3.0	3.0	3.0
Provide a mechanism through which the full submission lifecycle for a product can be easily transferred between stakeholders	3.0	3.5	3.5	4.0
When product changes result in changes to submitted documentation, facilitate more efficient analysis of which submissions and which regions would be impacted by the change.	3.0	3.5	3.5	3.5
Enable regulators and industry to consistently and clearly identify / communicate how a submission relates to previous applications	3.0	3.5	4.3	4.5
Enable efficient access (for appropriate parties) to information provided electronically in submissions	3.0	4.0	4.0	4.0
Enable a solution for electronic storage of product submissions	3.0	3.5	3.5	3.5

<b>Problem Area / Objective</b>	<b>Option 1 Status Quo (Baseline)</b>	<b>Option 2 Harmonized Folder Structure</b>	<b>Option 3 Custom IMDRF Message Standard</b>	<b>Option 4 HL7 RPS Message Standard</b>
Enable efficient simultaneous access to information (for reviewers) provided electronically in submissions	3.0	3.0	3.0	3.0
Enable reduction of resources / time required for manual login (data entry, record creation) of submissions Note: This objective would require the collection of structured data values from industry	3.0	3.0	3.0	3.0
Provide a way to automatically identify the current review status of a submission.	3.0	3.0	3.5	3.5
Provide a way to maintain the lifecycle of an Application over time when the regulation changes result in TOC variance between submissions.	3.0	3.5	4.0	3.8
Cost to maintain the solution. This includes consideration of resources to manage day to day submission activity, and effort to provide governance over time	3.0	3.0	1.0	3.0
Cost to maintain the standard	3.0	3.0	1.0	3.0
<b>TOTAL SCORE</b>	45.0	50.0	48.5	54.3
<b>AVERAGE SCORE</b>	3.0	3.3	3.2	3.6

## 9.4 Industry – Complex Submissions

<b>Problem Area / Objective</b>	<b>Option 1 Status Quo (Baseline)</b>	<b>Option 2 Harmonized Folder Structure</b>	<b>Option 3 Custom IMDRF Message Standard</b>	<b>Option 4 HL7 RPS Message Standard</b>
Efficiently produce submissions for multiple regions without managing multiple submission creation processes, and software tools	3.0	3.9	3.9	4.1
Enable efficient exchange of information amongst regulators	3.0	3.0	3.0	3.0
Enable a clear view to the lifecycle of Application content over time, as well as the ability to quickly see the most current version of an Application.	3.0	3.0	3.8	4.1
Include additional metadata on submission content for better discovery in the future (i.e., TOC headings and keywords).	3.0	3.0	3.0	3.0
Provide a mechanism through which the full submission lifecycle for a product can be easily transferred between stakeholders	3.0	3.2	3.6	3.6
When product changes result in changes to submitted documentation, facilitate more efficient analysis of which submissions and which regions would be impacted by the change.	3.0	3.3	3.2	3.3
Enable regulators and industry to consistently and clearly identify / communicate how a submission relates to previous applications	3.0	3.4	4.1	4.2
Enable efficient access (for appropriate parties) to information provided electronically in submissions	3.0	3.8	3.5	3.1
Enable a solution for electronic storage of product submissions	3.0	3.2	3.2	3.0



<b>Problem Area / Objective</b>	<b>Option 1 Status Quo (Baseline)</b>	<b>Option 2 Harmonized Folder Structure</b>	<b>Option 3 Custom IMDRF Message Standard</b>	<b>Option 4 HL7 RPS Message Standard</b>
Enable efficient simultaneous access to information (for reviewers) provided electronically in submissions	3.0	3.0	3.0	3.0
Enable reduction of resources / time required for manual login (data entry, record creation) of submissions Note: This objective would require the collection of structured data values from industry	3.0	3.0	3.0	3.0
Provide a way to automatically identify the current review status of a submission.	3.0	3.5	4.3	4.0
Provide a way to maintain the lifecycle of an Application over time when the regulation changes result in TOC variance between submissions.	3.0	3.7	4.2	3.8
Cost to maintain the solution. This includes consideration of resources to manage day to day submission activity, and effort to provide governance over time	3.0	3.0	2.2	2.6
Cost to maintain the standard	3.0	3.0	2.2	2.6
<b>TOTAL SCORE</b>	45.0	48.9	50.4	50.3
<b>AVERAGE SCORE</b>	3.0	3.3	3.4	3.4

## 9.5 Industry – Simple Submissions

<b>Problem Area / Objective</b>	<b>Option 1 Status Quo (Baseline)</b>	<b>Option 2 Harmonized Folder Structure</b>	<b>Option 3 Custom IMDRF Message Standard</b>	<b>Option 4 HL7 RPS Message Standard</b>
Efficiently produce submissions for multiple regions without managing multiple submission creation processes, and software tools	3.0	4.1	3.9	3.8
Enable efficient exchange of information amongst regulators	3.0	3.0	3.0	3.0
Enable a clear view to the lifecycle of Application content over time, as well as the ability to quickly see the most current version of an Application.	3.0	3.3	4.2	4.1
Include additional metadata on submission content for better discovery in the future (i.e., TOC headings and keywords).	3.0	3.0	3.0	3.0
Provide a mechanism through which the full submission lifecycle for a product can be easily transferred between stakeholders	3.0	3.3	3.5	3.5
When product changes result in changes to submitted documentation, facilitate more efficient analysis of which submissions and which regions would be impacted by the change.	3.0	3.5	3.4	3.3
Enable regulators and industry to consistently and clearly identify / communicate how a submission relates to previous applications	3.0	3.8	3.8	3.6
Enable efficient access (for appropriate parties) to information provided electronically in submissions	3.0	4.0	3.5	3.2
Enable a solution for electronic storage of product submissions	3.0	3.5	3.1	3.0

<b>Problem Area / Objective</b>	<b>Option 1 Status Quo (Baseline)</b>	<b>Option 2 Harmonized Folder Structure</b>	<b>Option 3 Custom IMDRF Message Standard</b>	<b>Option 4 HL7 RPS Message Standard</b>
Enable efficient simultaneous access to information (for reviewers) provided electronically in submissions	3.0	3.0	3.0	3.0
Enable reduction of resources / time required for manual login (data entry, record creation) of submissions Note: This objective would require the collection of structured data values from industry	3.0	3.0	3.0	3.0
Provide a way to automatically identify the current review status of a submission.	3.0	3.8	3.9	3.9
Provide a way to maintain the lifecycle of an Application over time when the regulation changes result in TOC variance between submissions.	3.0	3.4	3.5	3.3
Cost to maintain the solution. This includes consideration of resources to manage day to day submission activity, and effort to provide governance over time	3.0	3.0	2.3	2.5
Cost to maintain the standard	3.0	3.0	2.3	2.5
<b>TOTAL SCORE</b>	45.0	50.6	49.4	48.5
<b>AVERAGE SCORE</b>	3.0	3.4	3.3	3.2

## 10 Appendix B: Breakdown of Stakeholder Group and Subgroup Weighting Formulas

In order to obtain an accurate global representation of Industry and Regulators' scoring evaluations, each stakeholder subgroup was weighted respective to their overall impact on either Regulator or Industry stakeholder group as a whole, which were then equally weighted in the Grand Total. The weights for each of the stakeholder subgroups, as well as the groups as a whole, are as follows:

<b>Regulators</b>	<b>Weighting</b>
Regulators with electronic review tools and experience reviewing structured content in submissions	50% (Weight on Regulators Total)
Regulators who don't currently have review tools	50% (Weight on Regulators Total)
<b>Regulators (Total)</b>	<b>50% (Weight on Grand Total)</b>

<b>Industry</b>	<b>Weighting</b>
Companies that currently support eCTD or have publishing software in-house	5% (Weight on Industry Total)
Companies that support multiple complex submissions	10% (Weight on Industry Total)
Companies that have primarily simple submissions	85% (Weight on Industry Total)
<b>Industry (Total)</b>	<b>50% (Weight on Grand Total)</b>

Overall Totals were calculated as:

- 25% Regulators with electronic review tools and experience reviewing structured content in submissions
- 25% Regulators who don't currently have review tools
- 2.5% Companies that currently support eCTD or have publishing software in-house
- 7.5% Companies that support multiple complex submissions
- 40% Companies that have primarily simple submissions

Calculations for these weightings are included in the accompanying excel file which recorded the scores for each of the stakeholder groups.