IMDRF International Medical Device Regulators Forum

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Marketing Review Report Work Instruction

AUTHORING GROUP

Good Regulatory Review Practices

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Preface

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

Contents

1. Introduction

This is one document in a collection of documents produced by the International Medical Device Regulators Forum (IMDRF) intended to improve the efficiency and effectiveness of the review process for marketing of medical devices.

Two documents, IMDRF GRRP WG/N40 – *Competence, Training, and Conduct Requirements for Regulatory Reviewers* and IMDRF GRRP WG/N59 – *Requirements for Medical Device Conformity Assessment Bodies for Regulatory Authority Recognition*, are complementary documents. These two documents N40 and N59 are focused on requirements for Conformity Assessment Bodies (CABs) conducting marketing review(s) of medical devices and IVD medical devices and individuals performing regulatory reviews and other related functions under their respective medical device legislation, regulations, and procedures required in their regulatory jurisdiction.

Three additional documents, IMDRF GRRP WG/N61 – *Regulatory Authority Assessment Method for Recognition and Surveillance of Conformity Assessment Bodies Conducting Medical Device Regulatory Reviews*, IMDRF GRRP WG/N63 - *Competence and Training Requirements for Regulatory Authority Assessors of Conformity Assessment Bodies Conducting Medical Device Regulatory Reviews*, and IMDRF GRRP WG/N66 - *Assessment and Decision Process for the Recognition of a Conformity Assessment Body Conducting Medical Device Regulatory Reviews* are complementary documents. These three documents N61, N63, and N66 are focused on how Regulatory Authorities will evaluate or “assess” a CAB’s compliance to the requirements in the IMDRF GRRP WG/N59 and N40 documents.

In addition, IMDRF GRRP WG/N47 *Essential Principles of Safety and Performance of Medical Devices and IVD Medical Devices* and IMDRF GRRP WG/N52 *Principles of Labeling for Medical Devices and IVD Medical Devices* are complementary documents. These two documents N47 and N52 are focused on the fundamental design, manufacturing, and labeling requirements for medical devices that, when met, provide assurance the device is safe and performs as intended, offers significant benefits to, among others, manufacturers, users, patients/consumers, and Regulatory Authorities.

This document IMDRF/GRRP WG/NXX provides instructions regarding creation of a medical device marketing review report. The marketing review report serves as a written record of the CAB's determination of the extent of fulfillment of specified requirements. It enables the CAB to capture in a consistent manner the evidence of a manufacturer's conformity with the criteria for the marketing review and will facilitate the exchange of information between Regulatory Authorities. This document expands upon section 7.5.2 of IMDRF/GRRP WG/N59 by articulating exactly the type of information that a "marketing review report" should include to address the requirements of section 7.7 of N59.

This collection of IMDRF GRRP documents will provide the fundamental building blocks by providing a common set of requirements to be utilized by the Regulatory Authorities for the recognition and monitoring of entities that perform regulatory reviews and other related functions. It should be noted that in some jurisdictions the recognition process is called designation, notification, registration, or accreditation.

IMDRF developed these GRRP documents to encourage and support global convergence of regulatory systems, where possible, seeking to strike a balance between the responsibilities of Regulatory Authorities to safeguard the health of their citizens as well as their obligations to avoid placing unnecessary burdens upon medical device CABs or the regulated industry. 0 IMDRF Regulatory Authorities may add additional requirements beyond this document when their legislation requires such additions.

To prevent confusion between marketing review activities performed by a CAB and the activities performed by medical device Regulatory Authority Assessors for CAB recognition and surveillance, in this document, the latter are designated as "assessments."

2. Scope

The scope of this guidance document is limited to the information that participating IMDRF Regulatory Authorities require in medical device marketing review reports, the format of reports, and the information necessary for participating IMDRF Regulatory Authorities to effectively use the marketing review reports in accordance with their legislation and regulations.

This document applies to all medical devices except IVD medical devices and is intended to identify the type of information a CAB would be expected to review during evaluation of a marketing submission. Depending on the particular medical device, some of the headings and content do not apply. In those cases, justifications should be provided for their exclusion. For example, Essential Principle 6.5.1 describes an essential principle of safety and performance "where a medical device incorporates, as an integral part, a substance which, if used separately may be considered to be a medicinal product/drug as defined in the relevant legislation that applies in that RA and which is liable to act upon the body with action ancillary to that of the medical device." Given variability in definitions and review practices across jurisdictions, this document does not establish a regulatory pathway or describe exactly what information should be reviewed for these types of products. In addition, the following are out of scope for this document; refer to each specific regulator for guidance regarding the below.

- Submissions requesting approval to conduct clinical trials.
- Surveillance activities (e.g., periodic sampling and/or reports to ensure continued safety and performance).

3. References

- IMDRF GRRP WG/N40:2017 *Competence, Training, and Conduct Requirements for Regulatory Reviewers*
- IMDRF GRRP WG/N47:2018 *Essential Principles of Safety and Performance of Medical Devices and IVD Medical Devices*
- IMDRF Standards WG/N51:2018 *Optimizing Standards for Regulatory Use*
- IMDRF GRRP WG/N52:2019 *Principles of Labeling for Medical Devices and IVD Medical Devices*
- IMDRF GRRP WG/N59: 2020 *Requirements for Medical Device Conformity Assessment Bodies for Regulatory Authority Recognition*
- IMDRF GRRP WG/N61: 2020 *Regulatory Authority Assessment Method for Recognition and Surveillance of Conformity Assessment Bodies Conducting Medical Device Regulatory Reviews*
- IMDRF GRRP WG/N63: 2020 *Competence and Training Requirements for Regulatory Authority Assessors of Conformity Assessment Bodies Conducting Medical Device Regulatory Reviews*
- IMDRF GRRP WG/N66: 2021 *Assessment and Decision Process for the Recognition of a Conformity Assessment Body Conducting Medical Device Regulatory Reviews*
- IMDRF/RPS WG/N9 FINAL:2019 (Edition 3) *Non-In Vitro Diagnostic Device Market Authorization Table of Contents (nIVDMAToC)*
- ISO/IEC 17065:2012 *Conformity assessment — Requirements for bodies certifying products, processes, and services*
- GHTF/SG1/N055:2009 *Definition of the Terms Manufacturer, Authorized Representative, Distributor, and Importer*

4. Definitions

All definitions from referenced IMDRF documents apply to this document, plus the following (the underlined terms are previously defined):

Marketing Review Report: the record of a regulatory review of a marketing submission for a medical device or IVD medical device.

5. Medical Device Marketing Review Report Work Instruction

Instructions for completing each section of the Medical Device Marketing Review Report are provided below. The section headings mirror those of IMDRF/RPS WG/N9 for consistency between information included in the marketing submission and documentation of the CAB's review of that submission. The heading "Chapter 0" has been added for information not included in Chapters 1-6 of N9; that is, for information relevant to the medical device marketing review report, but not expected to be included in the marketing submission itself. Please note the following, which apply to all sections of the report:

- Documenting the CAB's Assessment

  In many sections, the marketing review report should include not only a summary of the information provided by the manufacturer regarding the section topic, but also an assessment by the CAB of the acceptability of this information.

  This assessment should:

  - Document the CAB's final opinion on all information provided by the manufacturer related to the given section topic. That is, any information provided by the manufacturer either within the initial submission or in response to interactions with the CAB should be included in the assessment.
  - Provide a rationale for why the totality of information provided is or is not acceptable with respect to the following questions.
    - Did the provided information demonstrate conformity with the applicable Essential Principles?
    - Were conclusions supported by the results/information presented?
    - Are all issues (e.g., questions/concerns identified during the review that required interaction/communication with the manufacturer) addressed?
    - Is there any discrepancy within the manufacturer's conclusions?
  - Describe any nonconformities remaining at the end of review that prevent a positive recommendation from the CAB.
  - Note any follow up items that the manufacturer has committed to conduct (e.g., product stability studies).

This assessment should **not** include a detailed listing and history of all interactions with the manufacturer on a specific topic. Questions sent to the manufacturer by the CAB and responses (including data and corrective action plan(s)) provided by the manufacturer to address the CAB's concerns should be provided either within the body of the report or as an appendix.

- Determining Review Expectations

Review expectations for marketing submissions depend on a number of factors including:

  - Risk classification of device type;
  - Risks identified for the specific device;
  - Novelty and complexity of the specific device;
  - Conformity assessment procedure applied by the manufacturer; and
  - IMDRF jurisdiction for which marketing authorization is sought.

For example, a CAB may be expected to review the labeling components of a higher risk device in more detail compared to the review of a lower risk device. As another example, one regulatory authority may expect a review of all general Quality System procedures for high risk devices, while another may accept a specific type of certificate to indicate sufficient Quality System procedures.

This document is comprehensive in scope in that, consistent with IMDRF/RPS WG/N9, it includes both common (IMDRF) and regional content. As a consequence, not all headings are relevant or reviewed to the same extent for all submission types, all device types, and/or all IMDRF jurisdictions. The relevance of each section and the extent of review depends on the jurisdiction for which marketing authorization is sought. CABs are required to review materials published by individual RAs regarding review expectations (e.g., recognized standards and guidance) specific to submission types and/or device types as well as to contact an RA if there are questions about review expectations during the review.

- Use of "N/A"

"N/A" should not be used in the marketing review report without an accompanying rationale. For example, a given section may be "N/A" based on the type of device (e.g., a device that does not include software) or based on the jurisdictions for which marketing authorization is sought (e.g., detailed quality management procedures may not be required for 510(k) submissions to the U.S. FDA). In these cases, "N/A" may be included in a section, but a rationale should also be provided as to why the section is not applicable.

- Screening Review

Section 7.3 of IMDRF/GRRP WG/N59 indicates that a CAB performs a screening review prior to evaluating the marketing submission. This report does not differentiate between a screening review and an evaluation. Instead, this report includes all information that a regulatory authority would expect to see from a CAB after a complete assessment of the marketing submission (including both screening and evaluation).

Chapter 0 Regulatory Review

0.1 Information about the Conformity Assessment Body

The report should include the name, full address, contact information, and any identification numbers relevant to the CAB performing the regulatory review. The report should also indicate the aspects of the CAB's scope of recognition that are relevant to the review conducted. The report should specifically confirm that the CAB's scope of recognition at the time of the regulatory review was consistent with the scope of the review conducted.

0.2 Scope of Regulatory Review

The report should include a summary statement that specifically indicates the scope of regulatory review consistent with section 7.7.3(a) of IMDRF/GRRP WG/N59. At a minimum, the summary should include the device name, device type, manufacturer name, and jurisdictions for which marketing authorization is sought as well as indication of whether the submission is an initial submission or includes changes to a model of the device already authorized for marketing. If the marketing submission includes many different models or configurations, the report should include a discussion as to whether the submission and its review outcome are representative of all of the devices included in the submission. For example, a clinical monitoring system might include a variety of features and configurations with differing levels of complexity and risk. The report should indicate with supporting rationale, which features and configurations are within the scope of the regulatory review.

Information relevant to this section of the report may be found in the following sections of IMDRF/RPS WG/N9:

- 1.01 ("Cover Letter")
- 1.04 ("Application Form/Administrative Information")
- 1.05 ("Listing of Device(s)")
- 2.02 ("General Summary of Submission")

0.3 Relevant Dates

The report should include the dates the submission was received by the CAB and the date the CAB completed their review.

0.4 Recommendation

The report should include a certification and/or recommendation as to whether, based on the review of provided documentation, the device conforms or does not conform to all applicable Essential Principles and other regulatory requirements. Per section 7.7.3(a) of IMDRF/GRRP WG/N59, the certification and/or recommendation should include clear identification of the subject medical device and its use (scope of certification).

0.5 Summary of Review

The report should include a high-level summary of the review including device name, indications for use, and highlights of the review. A detailed listing of history of interactions with the manufacturer should be included (as an appendix or within the body of the document) with the report. The report should also include, per section 7.7.3(a) of IMDRF/GRRP WGN59, a discussion of the review criteria used to assess the regulatory submission.

Comment should be provided regarding whether the Summary and Certifications for Premarket Submissions provided by the manufacturer are accurate and acceptable based on the requirements in IMDRF/RPS WG/N9 section 2.03.

0.6 Review Team

The report should include a listing of the names, titles, and roles of each individual who assessed the file or provided signatory authority.

0.7 External Consultations

The report should identify any consultations obtained during regulatory review from external resources, as defined in Section 6.2 of IMDRF/GRRP WG/N59 and Section 6.2.4 of IMDRF/GRRP WG/N61. The report should clearly indicate the rationale for obtaining external consultation, the expertise of the external consultant, the information provided to and received from the external consultant, and how the external consultation impacted the overall regulatory review. For example, in the course of reviewing a product that incorporates both medical device component(s) and a medicinal/drug substance, a CAB may choose to obtain external consultation regarding the drug/medicinal substance in order to inform their review of the medical device component(s).

Chapter 1 Regional Administrative

1.01 Cover Letter

(A) Submission Type and Number

The report should include the type of submission submitted by the manufacturer. Refer to each specific regulator for applicable submission types.

If available, the report should also include the submission number for each identifying jurisdiction. This information may not be available at the time of the CAB review given that, in some jurisdictions, the CAB review precedes the review by the regulatory authority and, therefore, assignment of a submission number by the regulatory authority. In these cases, the identifying number, if any, assigned by the CAB itself for tracking purposes should be provided for reference.

Information relevant to this section of the report may also be found in IMDRF/RPS WG/N9 section 1.04 (“Application Form/Administrative Information”).

(B) Device Classification and Identification Information

The report should include the device classification and any associated identifiers required for the applicable jurisdictions. Comment should be provided regarding the degree to which the information provided supports the proposed classification per section 7.4.2 of IMDRF/GRRP WG/N59.

Information relevant to this section of the report may also be found in section 1.04 (“Application Form/Administrative Information”).

(C) Applicable Jurisdictions

The report should include the jurisdictions for which marketing authorization is sought.

1.02 Submission Table of Contents

N/A- the report does not need to include the Table of Contents provided in the marketing submission.

1.03 List of Terms/Acronyms

N/A- the report does not need to include the list of terms/acronyms provided in the marketing submission. However, the first time an acronym or term is used in the report, the definition should be provided.

1.04 Application Form/Administrative Information

The report should include the name, full address, any identification numbers, and primary contact information for the applicant, manufacturer, authorized representative, etc. as required by the jurisdictions for which marketing authorization is sought.

1.05 Listing of Devices

The report should list all devices for which marketing authorization is sought.

1.06 Quality Management System, Full Quality System or Other Regulatory Certificates

The report should indicate whether the applicable quality management system, full quality system, or other regulatory certificates were provided and acceptable based on the jurisdictions for which marketing authorization is sought.

This section of the report should also list the name(s), location(s), and scope(s)/role(s) of each manufacturing facility and/or supplier for the medical device, using the relevant information provided in Chapter 6A of the marketing submission. The report should also include a description of any relationship between facilities when there is more than one involved in the manufacturing process. Note that (per GHTF/SG1/N055:2009, *Definition of the Terms Manufacturer, Authorized Representative, Distributor, and Importer*) a manufacturing facility includes locations with responsibility for design and/or manufacture.

1.07 Free Sale Certificate/Certificate of Marketing Authorization

The report should indicate whether and what free sale certificates/certificates of marketing authorization are available and from which regulatory jurisdiction(s).

1.08 Expedited Review Documentation

The report should indicate whether expedited review has been requested and/or granted by the CAB (see section 4.2.6 of IMDRF/GRRP WG/N59) and/or a regulatory authority and what associated supporting documentation was included.

1.09 User Fees

N/A- User fee documentation review per this section is conducted by the regulatory authority, not by the CAB.

1.10 Pre-Submission Correspondence and Previous Regulator Interactions

The report should include how previous regulator interactions informed the review of the submission. This includes both a summary of previous interactions as well as the impact on review considerations (e.g., if specific testing is expected for a particular jurisdiction based on feedback previously provided by that regulatory authority).

1.11 Acceptance for Review Checklist

The report should indicate what acceptance for review checklist information was provided in the marketing submission, whether the information was acceptable, and how the information impacted the review conducted.

1.12 Statements/Certifications/Declarations of Conformity

The report should indicate what statements/certifications/declarations of conformity were provided in the marketing submission, whether the information was acceptable, and how the information impacted the review conducted.

1.13 Letters of Reference

The report should include reference to any applications related to the subject submission (e.g., regional document references (e.g., Master Files) or predicate device applications). Any assessment in the remainder of the report should clearly indicate if comments and information are provided relative to the marketing submission or a referenced application and, if so, which referenced application. In addition, review of any referenced application is limited to the scope of the letter of reference provided by the manufacturer.

1.14 Letters of Authorization

The report should indicate whether the applicable letters of authorization were provided based on the jurisdictions for which marketing authorization is sought.

1.15 Other Regional Administrative Information

The report should include an assessment of any other non-clinical evidence provided in the marketing submission.

Chapter 2 Submission Context

2.01 Chapter Table of Contents

N/A- the report does not need to include the Chapter Table of Contents provided in the marketing submission.

2.02 General Summary of Submission

N/A- information from this section, along with analysis of its acceptability and review conclusions, should be incorporated into the Scope and Summary of Regulatory Review sections in Chapter 0.

2.03 Summary and Certifications for Premarket Submissions

The report should indicate whether the applicable summary and certifications for premarket submissions were provided and acceptable based on the jurisdictions for which marketing authorization is sought.

2.04 Device Description

The report should include a summary description of the device, its principles of operation, packaging, history of development, and reference and comparison to similar and/or previous generations of device.

2.05 Indications for Use and/or Intended Use, and Contraindications

The report should include the indications for use, intended use, intended use environment, intended patient population, intended users, and any contraindications for use. Per section 7.4.3 of IMDRF/GRRP WG/N59, the CAB should ensure that the marketing submission supports the proposed intended use of the medical device.

2.06 Global Market History

The report should include the global market history of the device including where the device is currently authorized to be marketed and the experience in those region(s) (e.g., any incidents and/or recalls). Distinction should be made between information provided by the manufacturer and obtained by CAB reviewer(s) during research of relevant regulator databases. Relevant regulatory databases should be consulted based on the jurisdiction for which marketing authorization is sought.

Comment should be provided regarding whether the global marketing history raises any specific concerns for the regulatory review (e.g., previous recalls may result in need to ascertain whether specific failure modes have been mitigated).

2.07 Other Submission Context Information

The report should include an assessment of any other submission context information provided in the marketing submission.

Chapter 3 Non-Clinical Evidence

3.01 Chapter Table of Contents

N/A- the report does not need to include the Chapter Table of Contents provided in the marketing submission.

3.02 Risk Management

The report should include an assessment of the acceptability of the manufacturer's risk management approach including an assessment of whether the risk management plan was appropriate, whether all expected risks were appropriately identified and mitigated, and whether the approach is consistent with relevant Essential Principles (see Appendix A) and regulatory requirements. Per section 7.4.4 of IMDRF/GRRP WG/N59, the results of an audit conducted as part of a marketing certification scheme should be considered when the CAB conducts its review of the marketing submission.

Comment should be provided regarding whether the review of the risk management activities raises any specific concerns for the regulatory review (e.g., risks mitigated with non-clinical studies require assessment of the specific methods and results of those studies).

3.03 Essential Principles (EP) Checklist

Per section 7.7.2 of IMDRF/GRRP WG/N59, the CAB should review the marketing submission with respect to the requirements of the relevant regulatory authority. To document this review, the report should include an assessment of the acceptability of the manufacturer's identification of applicable Essential Principles and regulatory requirements as well as the methods used to demonstrate conformity to each. Specific attention should be paid to any Essential Principle or regulatory requirement deemed not applicable by the manufacturer.

Comment should be provided as to whether the review of the Essential Principles and regulatory requirements raises any specific concerns for the regulatory review (e.g., methods used to demonstrate conformity for each Essential Principle may indicate need for particular review in other sections of the submission).

3.04 Standards

The report should indicate the key standards and guidance documents used by the manufacturer to support their marketing submission. The report should also include the CAB's assessment of whether all appropriate standards and guidance documents were identified and used by the manufacturer in order to address the applicable regulatory requirements.

3.05 Non-clinical Studies

Standards and state of the art guidance are valuable resources in determining whether appropriate non-clinical studies have been conducted and whether or not the evidence provided demonstrates conformity to the relevant Essential Principles and regulatory requirements. Regulatory authorities may provide information on the standards recognized and state of the art guidance issued by jurisdiction. If available, this information should be consulted and considered during review of information regarding non-clinical studies.

In some jurisdictions, the accreditation of the testing laboratory conducting the non-clinical study impacts the review of the study methods and results. Testing laboratory accreditation should be considered as appropriate for each jurisdiction.

3.05.01 Physical and Mechanical Characterization

The report should include an assessment of the evidence to support physical and mechanical characterization including whether or not the information provided demonstrates conformity with the relevant Essential Principles (see Appendix A) and regulatory requirements.

3.05.02 Chemical/Material Characterization

The report should include an assessment of the evidence to support chemical/material characterization including whether or not the information provided demonstrates conformity with the relevant Essential Principles (see Appendix A) and regulatory requirements.

3.05.03 Electrical Systems: Safety, Mechanical, and Environmental Protection and Electromagnetic Compatibility

The report should include an assessment of the evidence to support electrical systems including whether or not the information provided demonstrates conformity with the relevant Essential Principles (see Appendix A) and regulatory requirements.

Note that review of testing to support Magnetic Resonance (MR) conditional labeling and safety during anticipated conditions of use should be included in this section of the report. This includes assessment of

- Magnetically induced displacement force
- Magnetically induced torque
- Extent of imaging artifacts
- Radiofrequency (RF)-induced heating or heating induced by time-varying magnetic field gradients
- Gradient-induced vibration
- Gradient-induced extrinsic electrical potential
- Rectification of RF pulses from MR exams

3.05.04 Radiation Safety

The report should include an assessment of the studies to support radiation safety including whether or not the information provided demonstrates conformity with the relevant Essential Principles (see Appendix A) and regulatory requirements.

3.05.05 Software/Firmware

The report should include an assessment of the information provided to support the use of any software/firmware including whether or not the information demonstrates conformity with the relevant Essential Principles (see Appendix A) and regulatory requirements. Note that this section includes review and assessment of

- Section 3.05.05.01 (software/firmware description),
- Section 3.05.05.02 (hazard analysis),
- Section 3.05.05.03 (software requirement specification),
- Section 3.05.05.04 (architecture design chart),
- Section 3.05.05.05 (software design specification),
- Section 3.05.05.06 (traceability analysis),
- Section 3.05.05.07 (software development environment description),
- Section 3.05.05.08 (software verification and validation),
- Section 3.05.05.09 (revision level history),
- Section 3.05.05.10 (unresolved anomalies (bugs or defects)),
- Section 3.05.05.11 (cybersecurity), and
- Section 3.05.05.12 (interoperability).

3.05.06 Biocompatibility and Toxicology Evaluation

The report should include an assessment of the evidence to support biocompatibility and assess toxicology including whether or not the information provided demonstrates conformity with the relevant Essential Principles (see Appendix A) and regulatory requirements.

3.05.07 Non-Material-Mediated Pyrogenicity

The report should include an assessment of the evidence to support pyrogenicity evaluation, such as endotoxin levels, including whether or not the information provided demonstrates conformity with the relevant Essential Principles (see Appendix A) and regulatory requirements.

3.05.08 Safety of Materials of Biological Origin

The report should include an assessment of the evaluations performed to demonstrate the safety of materials of biological origin. This includes assessment of whether or not the information provided demonstrates conformity with the relevant Essential Principles (see Appendix A) and regulatory requirements.

3.05.09 Sterilization Validation

The report should include an assessment of the evidence supporting sterility of the device including whether or not the information provided demonstrates conformity with the relevant Essential Principles (see Appendix A) and regulatory requirements. Note that this section includes review and assessment of

- Section 3.05.09.01 (end-user sterilization),
- Section 3.05.09.02 (manufacturer sterilization validation),
- Section 3.05.09.03 (residual toxicity),
- Section 3.05.09.04 (cleaning and disinfection validation), and
- Section 3.05.09.05 (reprocessing of single use devices, validation data).

3.05.10 Animal Testing

The report should include an assessment of the animal testing including whether or not the studies demonstrate conformity with the relevant Essential Principles (see Appendix A) and regulatory requirements.

3.05.11 Usability/Human Factors

The report should include an assessment of the studies assessing the instructions and/or device design relevant to the intended user in terms of impact of human behavior, abilities, limitations, and other characteristics on the ability of the device to perform as intended including whether or not the information provided demonstrates conformity with the relevant Essential Principles (see Appendix A) and regulatory requirements.

3.06 Non-clinical Bibliography

The report should include a summary of the sources included in the non-clinical bibliography. This includes an assessment of whether or not the sources provide information that demonstrates conformity with the relevant Essential Principles (see Appendix A) and regulatory requirements.

3.07 Expiration Period and Packaging Validation

The report should include an assessment of the expiration period/shelf life and packaging validation studies including whether or not the results demonstrate conformity with the relevant Essential Principles (see Appendix A) and regulatory requirements. Note that this section includes review and assessment of

- Section 3.07.01 (product stability), and
- Section 3.07.02 (packaging validation).

3.08 Other Non-clinical Evidence

The report should include an assessment of any other non-clinical evidence provided in the marketing submission.

Chapter 4 Clinical Evidence

4.01 Chapter Table of Contents

N/A- the report does not need to include the Chapter Table of Contents provided in the marketing submission.

4.02 Overall Clinical Evidence Summary

The report should include a summary and assessment of the clinical evidence provided to demonstrate conformity with the relevant Essential Principles (see Appendix A) and regulatory requirements. This includes any clinical studies (pre- and/or post-market) conducted by the manufacturer and/or results of a literature review.

Comment should be provided on whether the clinical evidence provided is representative of the device and indications for use subject in the submission as well as the qualifications of any persons involved in clinical evidence evaluation.

4.03 Informed Consent Information

The report should indicate whether informed consent forms or any other information related to informed consent of patients was provided and acceptable based on the requirements for marketing authorization in the jurisdiction for which marketing authorization is sought.

4.04 Investigators Sites and IRB Contact Information

The report should indicate whether investigator sites and IRB contact information were provided and acceptable based on the requirements for marketing authorization in the jurisdiction for which marketing authorization is sought.

4.05 Other Clinical Evidence

The report should include an assessment of any other clinical evidence provided in the marketing submission.

Chapter 5 Labeling and Promotional Material

In addition to the regulatory requirements of a given jurisdiction, information regarding expectations for labeling may be found not only in IMDRF/GRRP WG/N47, but also the separate *Principles of Labelling for Medical Devices and IVD Medical Devices* IMDRF document (IMDRF/GRRP WG/N52). Specific attention should be paid to whether all product labeling (packaging, IFU, etc) is consistent with information (e.g., the methods and results from the non-clinical and clinical evidence) submitted in the marketing submission. Note that advertising and promotional materials may be considered elements of labeling in some jurisdictions, but they are outside the scope of this document. Individual jurisdictions may have their own regulations or requirements regarding other labeling elements or advertising and promotional materials. If necessary, this section can also be used to discuss any observations related to jurisdiction-specific regulations or requirements involving other labeling elements or advertising and promotional materials.

5.01 Chapter Table of Contents

N/A- the report does not need to include the Chapter Table of Contents provided in the marketing submission.

5.02 Product/Package Labels

The report should include a description of the product/package labels materials provided by the manufacturer and an assessment of whether they are in conformance with the relevant Essential Principles (see Appendix A) and regulatory requirements.

5.03 Package Insert/Instructions for Use

The report should include a description of the package insert/instructions for use provided by the manufacturer and an assessment of whether they are in conformance with the relevant Essential Principles (see Appendix A) and regulatory requirements.

5.04 E-Labeling

The report should include a description of the e-labeling provided by the manufacturer and an assessment of whether its format, availability, and change management are in conformance with regulatory requirements.

5.05 Physician Labeling

The report should include a description of the physician labeling provided by the manufacturer and an assessment of whether it is in conformance with the relevant Essential Principles (see Appendix A) and regulatory requirements.

5.06 Patient Labeling

The report should include a description of the patient labeling provided by the manufacturer and an assessment of whether it is in conformance with the relevant Essential Principles (see Appendix A) and regulatory requirements. Specific attention should be paid to whether the materials can be easily comprehended and correctly used by the user (see Section 3.05.11), particularly for devices intended to be used by lay users and not physicians.

5.07 Technical and/or Operators Manual

The report should include a description of the technical and/or operators manual provided by the manufacturer and an assessment of whether it is in conformance with the relevant Essential Principles (see Appendix A) and regulatory requirements.

5.08 Patient File Stickers/Cards and Implant Registration Cards

The report should include a description of the patient file stickers/cards and implant registration cards provided by the manufacturer and an assessment of whether they are in conformance with the relevant Essential Principles (see Appendix A) and regulatory requirements.

5.09 Product Brochures

The report should include a description of the product brochures provided by the manufacturer and an assessment of whether they are in conformance with the relevant Essential Principles (see Appendix A) and regulatory requirements. Specific attention should be paid to whether the materials can be easily comprehended and correctly used by the user (see Section 3.05.11), particularly for devices intended to be used by lay users and not physicians, and as to whether the claims are consistent with the indications for use and information provided in the marketing submission.

5.10 Other Labeling

The report should include an assessment of any other labeling provided in the marketing submission.

Chapter 6A Quality Management System Procedures and Chapter 6B Quality Management System Device Specific Information

The report should include a summary and assessment of quality management system procedures and device specific information provided in the marketing submission including whether the procedures and information conform to relevant Essential Principles (see Appendix A) and regulatory requirements. At a minimum, the report should include a summary of overall manufacturing methods as well as a listing of the addresses and contact information as well as roles of all sites where the device or its components are manufactured. The report should include an assessment of whether the information provided is acceptable or raises any concerns regarding other aspects of the regulatory review.

Note that per IMDRF/GRRP WG/N59:

- Section 7.4.4: “If the CAB conducted an audit or receives the results of an audit as part of the marketing certification scheme, the CAB shall ensure that the audit results support the marketing submission.”
- Section 7.5.1: “If the relevant Regulatory Authority requires QMS/GMP certification prior to marketing and an audit was not part of the CAB’s evaluation, the CAB shall ensure that the manufacturer holds appropriate QMS/GMP certification relevant to the medical device under review.”

Appendix A

Mapping of CAB Marketing Review Report Sections to the Essential Principles of Safety and Performance

The below table indicates which Essential Principles of Safety and Performance as established in IMDRF/GRRP WG/N47 are primarily reviewed in which sections of the CAB marketing review report.

This list is not all inclusive in that Essential Principles may be evaluated in more than one section. For brevity, only the primary Essential Principles are listed. For example, a discussion of whether or not conformity has been demonstrated relative to Essential Principle 5.1.5 regarding elimination or reduction of risks related to use may be reviewed and discussed within any or all of the below CAB marketing review report sections:

- 4.7 (“Information about Essential Principles and Regulatory Requirements”)
- 4.8 (“Information about Risk Management”)
- 4.9 (J) (“Animal Testing”)
- 4.9 (K) (“Usability/Human Factors”)
- 4.10 (“Information about Clinical Evidence”)
- 4.11 (“Information about Labeling”)

The table, however, only lists Essential Principle 5.1.5 as being primarily reviewed within section 4.8 of the CAB marketing review report. Where no primary section could be identified for review of an Essential Principles, the Essential Principle is listed as being reviewed in all sections (i.e., by reviewing the totality of data provided by the manufacturer).

CAB Marketing Review Report Section	Essential Principle
All - Totality of Review	5.1.1
	5.1.6
	5.1.9
	5.5.1
	5.5.2
	5.5.5
	5.5.8
	5.9.1

CAB Marketing Review Report Section		Essential Principle
		6.1.2 6.5.1
Chapter 0 Regulatory Review		None
Chapter 1 Regional Administrative		None
Chapter 2 Submission Context		None
Chapter 3 Non-Clinical Evidence		
	3.01 Chapter Table of Contents	None
	3.02 Risk Management	5.1.2 5.1.3 5.1.4 5.1.5 5.5.4 5.5.6 5.7.1 6.3.1
	3.03 Essential Principles (EP) Checklist	All
	3.04 Standards	All
	3.05 Non-clinical Studies	Refer to specific subsection
	3.05.01 Physical and Mechanical Characterization	5.3.1 5.3.4
	3.05.02 Chemical/Material Characterization	5.3.1
	3.05.03 Electrical Systems: Safety, Mechanical, and Environmental Protection and Electromagnetic Compatibility	5.3.1 5.5.3 5.6.1 5.6.2 5.6.3

CAB Marketing Review Report Section	Essential Principle
	5.6.4
	5.6.5
	5.7.2
	5.7.3
	5.7.4
	5.7.5
	5.7.6
	5.7.7
3.05.04 Radiation Safety	5.11.1
	5.11.2
	5.11.3
	5.11.4
	5.11.5
	5.11.6
	6.2.1
	6.2.2
3.05.05 Software/Firmware	5.8.1
	5.8.2
	5.8.3
	5.8.4
	5.8.5
3.05.06 Biocompatibility and Toxicology Evaluation	5.3.1
	5.3.2
	5.3.3
	6.1.1
	6.1.3
3.05.07 Non-Material-Mediated Pyrogenicity	5.3.1
	5.3.2
	5.3.3
3.05.08 Safety of Materials of Biological Origin	5.13.1
	5.13.2
	5.13.3
3.05.09 Sterilization Validation	5.1.7

CAB Marketing Review Report Section		Essential Principle
		5.4.1 5.4.2 5.4.3 5.4.4 5.4.5 5.4.6
	3.05.10 Animal Testing	Depends upon objectives of animal testing
	3.05.11 Usability/Human Factors	5.3.5 5.5.7 5.12.1 5.12.2 5.12.3 6.3.2 6.4.1 6.4.2
	3.06 Non-clinical Bibliography	Depends upon contents of sources
	3.07 Expiration Period and Package Validation	5.1.7 5.1.8 5.4.2 5.4.3 5.4.4 5.4.5 5.4.6
	3.08 Other Non-clinical Evidence	Depends upon information provided
Chapter 4 Clinical Evidence		
	4.01 Chapter Table of Contents	None

CAB Marketing Review Report Section		Essential Principle
	4.02 Overall Clinical Evidence	5.2.1 5.2.2
	4.03 Informed Consent Information	5.2.1 5.2.2
	4.04 Investigator Sites and IRB Contact Information	5.2.1 5.2.2
	4.05 Other Clinical Evidence	Depends upon information provided
Chapter 5 Labeling and Promotional Material		
	5.01 Chapter Table of Contents	None
	5.02 Product/Package Labels	5.4.7 5.10.1
	5.03 Package Insert/Instructions for Use	5.1.4 5.4.7 5.10.1
	5.04 E-Labeling	5.1.4 5.4.7 5.10.1
	5.05 Physician Labeling	5.1.4 5.4.7 5.10.1
	5.06 Patient Labeling	5.1.4 5.4.7 5.10.1
	5.07 Technical/Operator Manual	5.1.4 5.4.7 5.10.1
	5.08 Patient File Stickers/Cards and Implant Registration Cards	5.4.7 5.10.1

CAB Marketing Review Report Section		Essential Principle
	5.09 Product Brochures	5.4.7 5.10.1
	5.10 Other Labeling	Depends upon information provided
Chapter 6A Quality Management System Procedures and Chapter 6B Quality Management System Device Specific Information	All	4.0

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