



**Global Harmonization Working Party**

Towards Medical Device Harmonization

**PROPOSED FINAL DOCUMENT**

**Title:** Change Management to Registered Medical Devices

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66 **Preface**

67 This document is produced by the Global Harmonization Working Party, based on change  
68 management guidances worldwide. The document is intended to provide non-binding guidance for  
69 use in the regulatory system of medical devices, including in vitro diagnostic (IVD) medical devices  
70 and software as medical device, and has been subject to consultation throughout its development.

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72 However, incorporation of this document, in part or in whole, into any other document does not  
73 convey or represent an endorsement of any kind by the Global Harmonization Working Party.

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## 75 **1.0 Introduction**

76 The objective of the Global Harmonization Working Party (GHWP) is to encourage  
77 convergence at the worldwide level in the evolution of regulatory systems of medical devices,  
78 including in vitro diagnostic (IVD) medical devices and software as a medical device in order to  
79 protect the public health by those regulatory means considered the most suitable.

80 This document has been developed to encourage and support global convergence of regulatory  
81 systems. It is intended for use by Regulatory Authorities (RAs), Conformity Assessment Bodies  
82 (CABs) and industry, and will provide benefits in establishing, in a consistent way, an economic  
83 and effective approach to the control of medical devices in the interest of public health. It seeks to  
84 strike a balance between the responsibilities of RAs to safeguard the health of their citizens and  
85 their obligations to avoid placing unnecessary burdens upon the industry.

86 During the life-cycle of a medical device, changes may take place from time to time. Changes  
87 made to a registered medical device must be linked to the principles of safety and/or performance  
88 (Essential Principles) and the ability of a risk based regulatory system to control the risk of the  
89 medical device placed in the market.

90 To ensure continued safety and/or performance/effectiveness of the medical device, a  
91 manufacturer must assess the effect of the change on the patient, practitioner and/or user of the  
92 medical device, and decide whether the change is expected to affect the safety and/or  
93 performance/effectiveness of the medical device, and/or the arrangements implemented to achieve  
94 continued compliance of the quality system with the relevant standards (e.g. design verification,  
95 design validation, human factors, organizational structure, addition or deletion or move of a facility)  
96 and/or the requirements of the applicable regulations.

97 According to the nature of the change, the Regulatory Authority (RA) will determine whether  
98 evidence of safety and/or performance/effectiveness has been appropriately collected and reviewed  
99 by the manufacturer based on the report made by the manufacturer.

100 Working Group 1, 2 and 3 of the GHWP have prepared this guidance document. Comments or  
101 questions should be directed to the Chair of GHWP Work Group 2 whose contact details may be  
102 found on the GHWP web page (<http://www.ghwp.info/>).

103 **Note:** The term “Registered medical device” refers to a medical device that can be legally  
104 marketed in the relevant jurisdiction.

105

## 106 **2.0 Rationale, Purpose and Scope**

### 107 **2.1 Rationale**

108 Risk based and harmonised worldwide requirements for managing changes to registered  
109 medical devices would offer significant benefits to the manufacturer, the users, the patients and the  
110 RAs. Eliminating or reducing differences between jurisdictions can decrease the cost of regulatory  
111 compliance activities, increases regulatory resource efficiencies for RAs and allows patients earlier  
112 access to new technologies and treatments.

113

### 114 **2.2 Purpose**

115 This document assists RAs and manufacturers in assessing and managing changes during the  
116 life cycle of medical devices. The document provides guidance on general principles,  
117 categorization, reporting, and alternative pathways for managing changes using a risk based  
118 approach with examples.

119

### 120 **2.3 Scope**

121 This document applies to all products that fall within the definitions of Medical Device, In  
122 Vitro Diagnostic (IVD) Medical Device and Software as a Medical Device that appear within the  
123 AHWP document *Definition of the Terms 'Medical Device' and 'In Vitro Diagnostic (IVD) Medical*  
124 *Device'*.

125

## 126 **3.0 References**

127 AHWP/WG2-WG1/F001:2016 *Definition of the Terms 'Medical Device' and 'In Vitro Diagnostic*  
128 *(IVD) Medical Device'*.

129 AHWP/WG1a/F002:2013 *Essential Principles of Safety and Performance of IVD Medical Devices.*

130 AHWP/WG3/F001:2015 *Guidance Document on Medical Device Software - Qualification and*  
131 *Classification*

132 AHWP/WG2 /F001:2021 *AHWP Reagent Replacement and Instrument Family Policy*

133 US - Guidance for Industry and Food and Drug Administration Staff, Deciding When to Submit a  
134 510(k) for a Change to an Existing Device - October 25, 2017

135 US - Guidance for Industry and Food and Drug Administration Staff, Deciding When to Submit a  
136 510(k) for a Software Change to an Existing Device - October 25, 2017

137 US - Guidance for Industry and Food and Drug Administration Staff, Replacement Reagent and  
138 Instrument Family Policy - December 11, 2003

139 US - Guidance for Industry and Food and Drug Administration Staff - Modifications to Devices  
140 Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process -  
141 December 11, 2008

- 142 US - Guidance for Industry and Food and Drug Administration Staff -Changes to an Approved  
143 Application: Biological Products - July, 1997
- 144 US - Draft Guidance for Industry and Food and Drug Administration Staff – Marketing Submission  
145 Recommendations for a Predetermined Change Control Plan for Artificial Intelligence/Machine  
146 Learning (AI/ML)-Enabled Device Software Functions - April 2023
- 147 US - Guidance for Industry and Food and Drug Administration Staff - Replacement Reagent and  
148 Instrument Family Policy for In Vitro Diagnostic Devices - August 17, 2022
- 149 US - Guidance for Industry and Food and Drug Administration Staff - Assay Migration Studies for  
150 In Vitro Diagnostic Devices - April 2013
- 151 Canada - Draft guidance on how to interpret ‘significant change’ of a medical device - February 7,  
152 2024
- 153 Japan - (PFSB/MDRMPED Notification No. 1120-1) Points to Consider When Applying for  
154 Marketing Approval for Medical Device - Nov. 25, 2014
- 155 Singapore - Medical Device Guidance - GN-21 - Guidance on Change Notification on Registered  
156 Medical Devices, Revision 5 - March 2023
- 157 Singapore - GL-04-R3 Regulatory Guidelines for Software Medical Devices - A Life Cycle  
158 Approach, Revision 2 - April 2022
- 159 Singapore - Medical Device Guidance- GN-12-1-R2.1 - Guidance on Grouping of Medical Devices  
160 for Product Registration - General Grouping Criteria, Revision 2.1 - November 2017
- 161 Singapore - Medical Device Guidance- GN-12-2- Guidance on Grouping of Medical Devices for  
162 Product Registration - Device Specific Grouping Criteria
- 163 Kingdom of Saudi Arabia - MDS-G-012-V1/230322 - Guidance on MDMA Significant and Non-  
164 Significant Changes
- 165 Malaysia - MDA/GD/0020 - Change Notification for Registered Medical Device, Fourth Edition -  
166 21 November 2022
- 167 Australia - Changes affecting TGA - issued conformity assessment certificates - Guidelines for  
168 notifying the TGA about ‘substantial changes’ to, or transfers of, conformity assessment  
169 certificates, Version 2.0 - August 2021
- 170 EU - MDCG 2020-3 Rev 1. Guidance on significant changes regarding the transitional provision  
171 under Article 120 of the MDR with regard to devices covered by certificates according to MDD or  
172 AIMDD - May 2023
- 173 EU - MDCG 2022-20 - Substantial modification of performance study under the In Vitro Diagnostic  
174 Medical Devices Regulation (EU) 2017/746 - December 2022
- 175 South Korea - Guidance for Review and Approval of Artificial Intelligence-based Medical Devices  
176 - May 2022
- 177 South Korea - “Guidance for Approval and Evaluation of Reagent of the Family *In Vitro* Diagnostic  
178 Devices” - August, 2015
- 179 South Korea - Case examples of Medical Electrical Equipment with significant changes, 2018

- 180 South Korea - Guidance for Change Management of IVD Medical Device, 5<sup>th</sup> version - March 2019
- 181 South Korea - Act on Nurturing Medical Devices Industry and Supporting Innovative Medical  
182 Devices - August, 2021
- 183 South Korea - Guidance for Precertification of Innovative Medical Devices - October-2021
- 184 WHO - Reportable Changes to a WHO Prequalified in vitro diagnostic Medical Device, 2016
- 185 WHO - Reportable Changes to a WHO Prequalified Male Circumcision Device, 2019
- 186 WHO - Annex 3- WHO Global Model Regulatory Framework for medical devices including in  
187 vitro diagnostic medical devices, WHO Medical device technical series, Replacement of Annex 4  
188 of WHO Technical Report Series, No. 1003

189

## 190 **4.0 Definitions**

191 **Medical Device** - The term is as defined in AHWP/WG2-WG1/F001:2016 “Definition of the Terms  
192 ‘Medical Device’ and ‘In Vitro Diagnostic (IVD) Medical Device’.

193 **IVD Medical Device** - The term is as defined in AHWP/WG2-WG1/F001:2016 “Definition of the  
194 Terms ‘Medical Device’ and ‘In Vitro Diagnostic (IVD) Medical Device’.

195 **Software in a Medical Device (SiMD)** - The term is as defined in AHWP/WG3/F001:2015  
196 Guidance Document on Qualification of Medical Device Software.

197 **Software as a Medical Device (SaMD)** - The term is as defined in AHWP/WG3/F001:2015  
198 Guidance Document on Qualification of Medical Device Software.

199 **AI/ML** - The term is as defined in IMDRF/AIMD WG/N67 Machine Learning-enabled Medical  
200 Devices- Key Terms and Definitions as Machine Learning-enabled Medical Device (MLMD) A  
201 medical device that uses machine learning, in part or in whole, to achieve its intended medical  
202 purpose.

203 **Manufacturer** - For the purpose of this document, the term "manufacturer" must be understood to  
204 include the manufacturer, its authorized representative or any other person who is responsible for  
205 placing the device on the market.

206 **Intended use/intended purpose** - The term is as defined in IMDRF/IVD WG/N64FINAL:2021.

207 **Non-significant change**<sup>1</sup> - A non-significant change is any change that has little or no potential to  
208 affect the safety and/or performance/effectiveness of the medical device.

209 **Quality Control (QC)** - It is part of quality management focused on fulfilling quality requirements.  
210 (ISO 9000)

211 **Quality Management System (QMS)** - For the purpose of this guidance document, the term means  
212 the claimed compliance with ISO 13485 or its equivalent of the part the management system with  
213 regard to quality.

---

<sup>1</sup> The terms non-significant change and minor change are used in different jurisdictions but generally they can be used interchangeably.



214 **Regulatory Authority (RA)** - It is a government agency or other entity that exercises a legal right  
215 to control the use or sale of medical devices within its jurisdiction, and may take enforcement action  
216 to ensure that medical devices marketed within its jurisdiction comply with legal requirements.  
217 (AHWP/-WG2-WG8/F002:2014)

218 **Risk Management** - is a systematic application of management policies, procedures and practices  
219 to the tasks of analysing, evaluating, controlling and monitoring risk. (ISO 14971:2019 Medical  
220 devices - Application of risk management to medical devices)

221 **Facility** - means a site that is substantially involved in the manufacture or design and storage of a  
222 medical device.

223 **Recognition** - The acceptance of the regulatory decision of another regulator or other trusted  
224 institution. Recognition should be based on evidence of conformity that the regulatory requirements  
225 of the reference health authority is sufficient to meet the regulatory requirements of the relying  
226 authority. Recognition may be unilateral or mutual and may, in the latter case, be the subject of a  
227 mutual recognition agreement.

228 **Reliance** - The act whereby the National Regulatory Authority (NRA) (defined as Regulatory  
229 Authority in this document) in one jurisdiction may take into account and give significant weight  
230 to assessments performed by another NRA or trusted institution, or to any other authoritative  
231 information in reaching its own decision. The relying authority remains independent, responsible  
232 and accountable regarding the decisions taken, even when it relies on the decisions and information  
233 of others. (WHO definition - Good reliance practices in regulatory decision-making: high-level  
234 principles and recommendations)

235 **Reference Agency /Reference regulatory authority** - A supranational, national or regional authority  
236 or a trusted authority such as WHO prequalification (WHO PQ) whose regulatory decisions and/or  
237 regulatory work products are relied upon by another regulatory authority to inform its own  
238 regulatory decisions. (WHO definition - Good reliance practices in regulatory decision-making:  
239 high-level principles and recommendations)

240 **Significant Change<sup>2</sup>** - Means any change that could reasonably be expected to affect the safety  
241 and/or performance/effectiveness of a medical device or its conformity with the essential  
242 principles.

243 **System** - A medical device system comprises of a number of medical devices and/or accessories  
244 that are: from the same product owner/manufacture, intended to be used in combination to achieve  
245 a common intended purpose, compatible when used as a system and sold under a single system  
246 name or the labelling, IFU, brochures or catalogues for each constituent component indicates that  
247 the constituent component is intended to be used together or for use with the system. (Singapore -  
248 Medical Device Guidance - GN-12-1-R2.1 - Guidance on Grouping of Medical Devices for Product  
249 Registration - General Grouping Criteria, Medical Device Guidance- GN-12-2- Guidance on  
250 Grouping of Medical Devices for Product Registration - Device Specific Grouping Criteria)

251

## 252 **5.0 General Principles**

253 For any change made to a registered Medical Device, In Vitro Diagnostic (IVD) Medical  
254 Device and Software as a Medical Device, the manufacturer must consider

---

<sup>2</sup> The terms significant change and major change are used in different jurisdictions but generally they can be used interchangeably

- 255 • the device in question,  
256 • the impact of the change on the patient, practitioner and/or user of the device, and  
257 • the impact of the change on the intended use/indication for use, risk classification, and  
258 • the specifications of the device,

259 and decide whether the change could reasonably be expected to affect the safety and/or  
260 performance/effectiveness of a device or its conformity with the essential principles and the risk-  
261 benefit profile associated throughout its lifecycle.

262 In the case of multiple simultaneous changes, this guidance document should be utilized to aid  
263 in the assessment of each change individually, as well as to evaluate the cumulative impact of all  
264 changes collectively. Concurrently, a risk assessment should be conducted to ensure a  
265 comprehensive review and implementation of mitigation means.

266 There may be instances where the standard regulatory framework is inadequate for addressing  
267 unique characteristics of emerging technologies, therefore effective risk analysis approach should  
268 be considered by RAs to address these novel challenges.

269 The following sections give guidelines on assessment and categorisation, reporting and  
270 innovative pathways for changes.

271

## 272 **6.0 Categorisation and Assessment of Changes**

### 273 **6.1 Categorisation of Changes**

274 Changes to a registered medical device are categorised as significant (or major in some  
275 jurisdictions) and non-significant (or minor) change according to the impact on the safety  
276 and/or performance/effectiveness of the medical device.

277 A **significant change** (refer to definition of “significant change”) means any change that could  
278 reasonably be expected to affect the safety and/or performance/effectiveness of a medical device or  
279 its conformity with the essential principles.

280 Significant changes can include changes to any of the following:

- 281 (a) the manufacturing process, facility or equipment;  
282 (b) the manufacturing quality control procedures, including the methods, tests, reference or  
283 procedures used to control the quality, purity and sterility of the device or of the materials used  
284 in its manufacture;  
285 (c) the design of the device, including its performance characteristics, principles of operation and  
286 specifications of materials, energy source, software or accessories; and  
287 (d) the intended use/indication for use of the device, including any new or extended use, any  
288 addition or deletion of a contra-indication for the device, and any change to the period used to  
289 establish its expiry date

290 A significant change typically may:

- 291 • Result in risks to the patient not previously identified  
292 • Increase the probability of existing hazards occurring

- 293
- Alter the presentation of existing or new risks to the user (this can involve
- 294 labelling changes or new indications for use)

295 A **non-significant change** is any change that has little or no potential to affect the safety and/or

296 performance/effectiveness of the medical device.

297

## 298 6.2 Tools to Assess Changes and the Way of Reporting

299 The following section presents flowcharts to assist manufacturers when assessing whether a

300 change is considered a “significant change” which may need to be reported to the RA.

301 The **main flowchart** is a generalized discussion of the broad principles that can be used to

302 determine if a change would affect the safety and/or performance/effectiveness of a Medical

303 Device, In Vitro Diagnostic (IVD) Medical Device and Software as a Medical Device.

304 **Flowchart A to F** details specific questions and answers to assist in determining if a change is

305 considered significant or non-significant. The accompanying discussions and flowcharts are

306 intended to define the processes used to categorise the change.

307

308 The following flowcharts are given in Appendix 1.

- 309 • **Main Flowchart:** General Changes made to Medical Devices and In Vitro Diagnostic
- 310 (IVD) Medical Devices
- 311 • **Flowchart A:** Changes in Manufacturing Processes, Facility and/or Quality
- 312 Management System (including QC) for Medical Devices and In
- 313 Vitro Diagnostic (IVD) Medical Devices
- 314 • **Flowchart B:** Changes in Design for Medical Devices and In Vitro Diagnostic
- 315 (IVD) Medical Devices
- 316 • **Flowchart C:** Changes to Sterilisation Facility and its Process and/or Quality
- 317 Management System
- 318 • **Flowchart D:** Changes to Software for Medical Devices
- 319 • **Flowchart E1:** Changes in Materials for General Medical Devices
- 320 • **Flowchart E2:** Changes in Materials for In Vitro Diagnostic (IVD) Medical
- 321 Devices
- 322 • **Flowchart F:** Changes to Labelling of Medical Devices and In Vitro Diagnostic
- 323 (IVD) Medical Devices

324

## 325 7.0 Reporting of Changes

326 According to the nature of the change, it is the RA that determines whether evidence of safety  
327 and/or performance/effectiveness have been appropriately collected and reviewed based on the  
328 reporting procedure made by the manufacturer.

329 It is recommended that the RA takes a **risk-based approach in change management**  
330 **reporting** and prioritize resources to focus on **higher risk products with significant changes** that  
331 raise the highest risk to patients to ensure optimal efficiency of regulatory resources.

332 “Significant changes” should be reported to the RA prior to implementation of the change with  
333 supporting documentation to show the device is still safe and performing as intended.

334 “Non-Significant changes” are not normally reported to the RA prior to implementation of the  
335 change, however the assessment and supporting documentation to show the device is still safe and  
336 performing as intended has to be recorded in QMS and/or technical documentation.

337 **Table 1** depicts the recommended risk-based approach in reporting of changes.

338

339 **Table 1: Recommended Risk-Based Approach in Reporting of Changes**

Product Risk Classification	Non-Significant Changes	Significant Changes
Low risk	No submission required. Change to be recorded in QMS and/or technical documentation of the medical device.	No submission required. Change to be recorded in QMS and/or technical documentation of the medical device.
Medium risk		Change registration or change notification required. (change notification with immediate implementation is recommended)
Medium/High Risk		License amendment or change registration required. (change submission with RA approval recommended)
High risk		
<p><b>Note 1:</b> In some jurisdictions, all changes whether significant or non-significant may need to be reported, hence it is recommended to consult local jurisdiction and guidance on the reporting requirements</p> <p><b>Note 2:</b> QMS requirement: Manufacturer should</p> <ul style="list-style-type: none"> <li>• assess the change,</li> <li>• perform risk assessment of the product,</li> <li>• document the change and if applicable update the technical documentation.</li> </ul>		

340

341 A manufacturer is required to submit a license amendment or change registration to RA for  
342 review and approval once they have determined that the proposed change to a medium/high risk or

343 high risk medical device is a significant change. Only upon receipt of approval of changes by the  
344 RA, manufacturers may sell and/or import the modified medical device in the market.

345 **Note:** The need to report changes prior to implementation vs reporting post-implementation  
346 can depend on factors such as the type of change and regional requirements.

347

## 348 **7.1 Bundling of Changes**

### 349 **7.1.1 Multiple changes on a device at the same time**

350 It is recommended if multiple changes are made on a device around the same time; the  
351 assessment of each change should be made according to the flowcharts outlined in this guideline.  
352 If the changes are significant, the manufacturer may summarize all significant changes in one report  
353 and describe how the modified medical device differs from the previously registered device.

354 A significant change is only one type of change that may require a manufacturer to obtain an  
355 amended medical device license or change registration approval. When several successive or  
356 simultaneous changes are being considered in the evolution of a registered device, this guidance  
357 document should be used to assess each change separately, as well as the collective impact of the  
358 changes. A side-by-side comparison of the proposed changes to the currently registered device may  
359 be useful.

360 Hence, it is recommended that RAs allow the submission of multiple changes to the same  
361 product in a single submission to enable assessment of the collective impact of the changes.

362

### 363 **7.1.2 Single/same change to multiple products**

364 If the same general simple change such as legal entity name change, legal manufacturer's  
365 address and other changes happen to multiple products of a manufacturer, the change across the  
366 products may be bundled to register or report in a single submission.

367 Additionally in cases where the medical device is registered as a system, changes may be  
368 proposed to one or more of the component parts. This document should be used to assess each  
369 change separately, as well as the collective impact of the changes.

370

## 371 **7.2 Supplementary Submission**

372 It is recommended that RAs allow the submission of multiple changes to the same product or  
373 product group, which is under RA review for a prior change or license renewal. RAs should either

- 374 • review one change to a given device while other changes to that same device are under  
375 consideration; or
- 376 • review all submitted changes together.

377 Manufacturers should be aware that newly submitted changes should be compared with other  
378 changes, because regulatory acceptance of the earlier change cannot be assumed and the  
379 manufacturer should keep good communication with RAs.

380

381 **7.3 Transition Measures and Time Period for Change Implementation**

382 It is recommended for RAs to allow a reasonable transition period for manufacturers to  
383 transition from an unchanged medical device to the version/lot/model that has incorporated the  
384 change. During such a transition period, **import and/or sales/distribution of both versions should**  
385 **be allowed** to facilitate smooth transition as well as ensure supply continuity. Both versions of the  
386 medical device have to conform to the Essential Requirements for Safety and Performance for  
387 medical devices as stipulated in the *Regulations*.

388 When there are multiple versions of a device legally available, perhaps due to marketing both  
389 or because one is going through such a transition period, it should be clear how patients/users will  
390 be informed of the version of the device they are using/have access to and any necessary information  
391 about the differences.

392 Hence, the manufacturer shall ensure that appropriate mechanisms are in place to differentiate  
393 and identify the changed device from the original version based on device or manufacturing  
394 attributes (e.g., through batch/lot/serial number and manufacturing date), and maintain relevant  
395 inventory records on file to ensure traceability of both versions as part of their QMS requirements.  
396 All relevant records on file shall be made available to the RA upon request.

397

## 398 **8.0 Innovative Pathways for Changes**

399 As the technologies evolve, so do the regulatory science, RA may consider innovative  
400 pathways for changes where appropriate on a risk-based approach.

401

### 402 **8.1 Reliance/Recognition**

403 As indicated in the WHO Guidance for Good Reliance Practice, reliance models are  
404 recommended for RAs to handle both pre-market and post market responsibilities related to the  
405 device full life cycle, including product changes.

406 Hence, it is recommended that RAs could recognize change approvals from **a reference**  
407 **agency** in order to facilitate local access to more rapid innovation. This may require Mutual  
408 Recognition Agreements. Where some RAs may not directly recognize approvals by **a reference**  
409 **agency**, they could still rely on evidence used in a device change previously registered by another  
410 regulator in order to reduce duplicative efforts, as well as the time and resources needed for review.

411

### 412 **8.2 Replacement Reagent and Instrument Family Policy**

413 Additional innovative review pathways are also encouraged to expedite device availability for  
414 patients. For example, the ***GHWP Replacement Reagent and Instrument Family Policy*** expedites  
415 availability of medium risk assays onto instruments within the same family. Assay Migration  
416 provides a more efficient pathway to migrate an assay to a new, already cleared instrument by  
417 leveraging a limited dataset.

418 The Reagent Replacement Policy is a risk-based approach that relies on the manufacturer's  
419 Quality Management System (QMS), including risk-based assessments, and criteria, testing, and  
420 internal documentation for each reagent application, to allow a portfolio or "menu" of low or  
421 medium risk reagents to be moved to a previously registered instrument or an instrument in the  
422 instrument family.

423 In the Instrument Family Policy an instrument can be added to an already existing Instrument  
424 Family. In turn, the Instrument Family allows the Replacement Reagent Policy to take effect.

425 For adding either a registered test kit/assay to a previously registered instrument (Replacement  
426 Reagent Policy), or a new instrument family member to a previously registered instrument family  
427 (Instrument Family Policy), please refer to the GHWP guidance document on ***The Replacement***  
428 ***Reagent and Instrument Family Policy***.

429

### 430 **8.3 Simplified Change Management of SaMD/ SiMD**

431 Given the need to frequently update and localise software, a simplified change management  
432 framework can enable agile modifications while maintaining a high-level of safety. Changes to  
433 SaMD/SiMD can be managed by restricting the scope that needs regulatory review, limiting it to  
434 changes that relate to major functions, such as analysis algorithms (analysis methods), development  
435 language, operating environment, or communication functions. Other changes can be reasonably  
436 reported after the modifications have been implemented. (South Korea - Regulations on Approval,  
437 Notification, Review of Medical Devices, June-2023)

438 **Note:** In case of SiMD, the effect of the change to the whole medical device should be  
439 considered.

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#### 441 **8.4 Predetermined Change Control Plan (PCCP) of SaMD**

442 Predetermined Change Control Plan (PCCP) allows regulators to review a list of proposed  
443 changes, a change protocol (how the change will be implemented) and related acceptance criteria  
444 during the initial premarket review, essentially pre-approving the change as long as the protocol  
445 and criteria are followed. PCCP serves as an “agreement” between a manufacturer and regulator  
446 that, if the manufacturer follows the protocol for changes within its scope and meets the agreed  
447 upon criteria, the manufacturer can implement the modification without further regulatory review.

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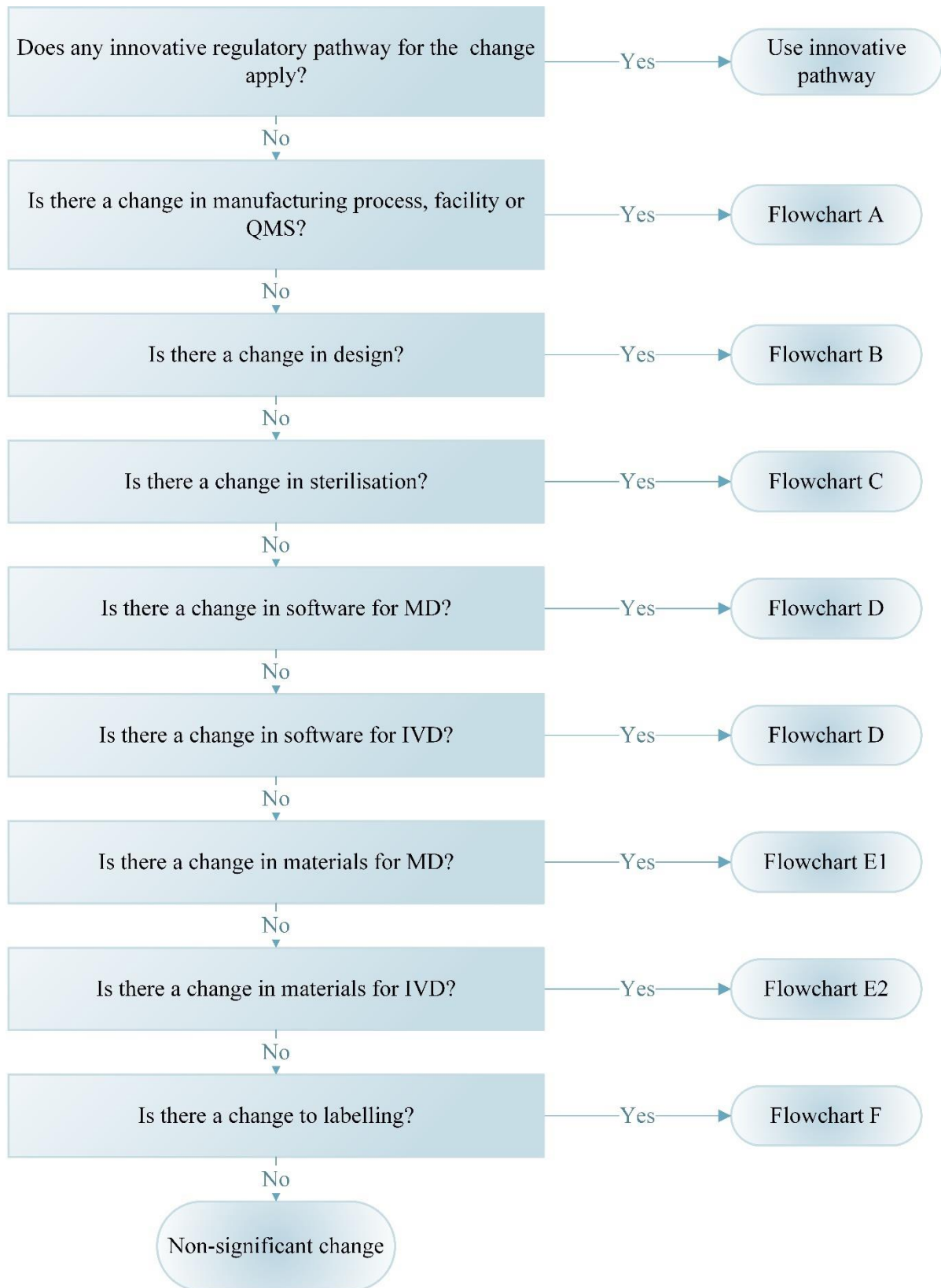
#### 449 **8.5 (Pre)certification Program for Innovative Medical Device Manufacturer**

450 Innovative Medical Devices refer to medical devices that meet an unmet clinical need or meet  
451 a need in a way that is superior to existing methods in terms of safety and effectiveness. Innovative  
452 Medical Devices can be designated by RAs to encourage and assist their development in a number  
453 of ways. Additionally, manufacturers that can demonstrate excellence in consistently developing  
454 devices to a high-standard of safety may also be recognised and given further flexibility.



455 **9.0 APPENDIX 1 - Flowcharts**

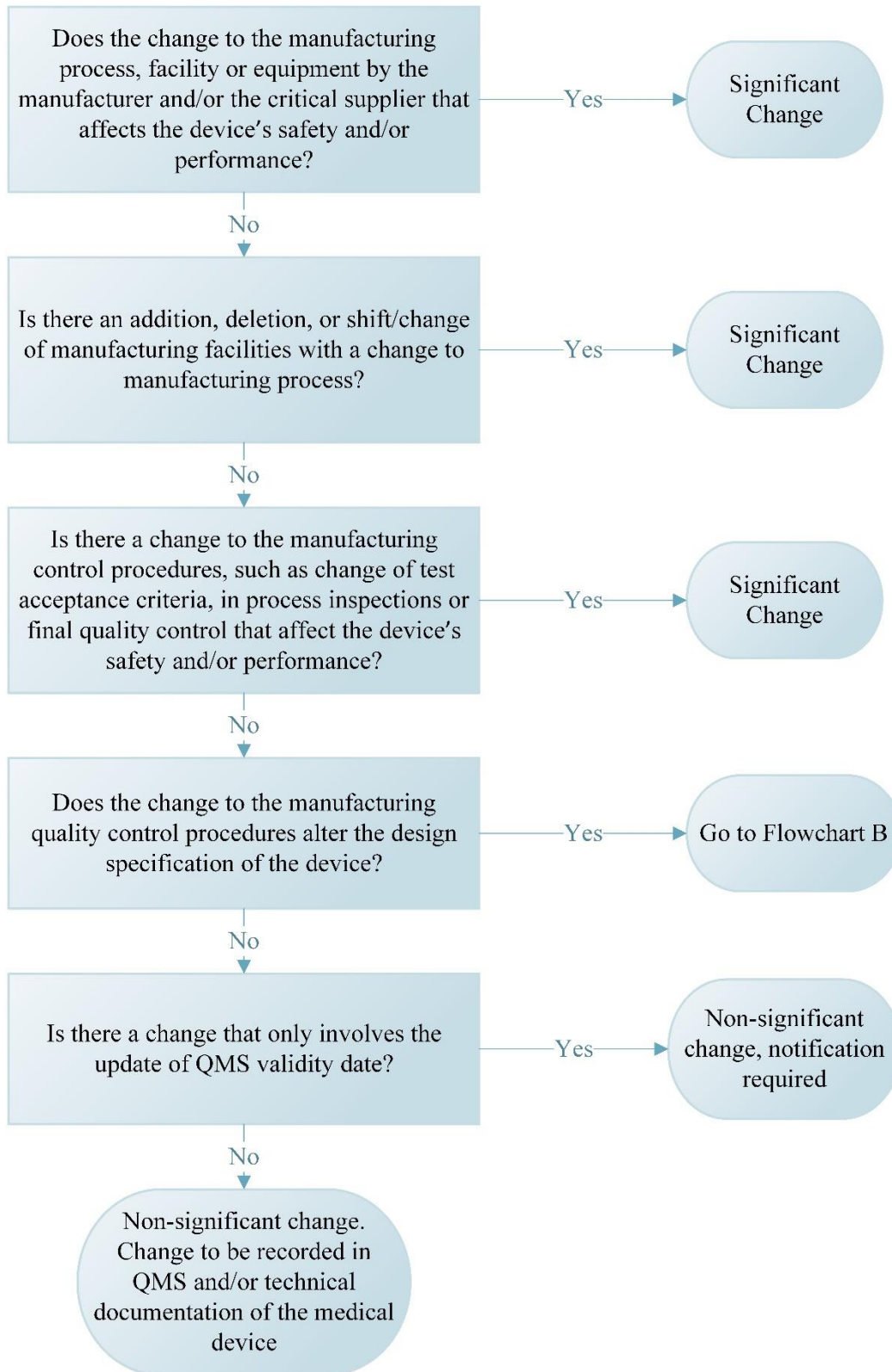
456 **Main Flowchart: General Changes made to Medical Devices and In Vitro Diagnostic (IVD)**  
457 **Medical Devices**



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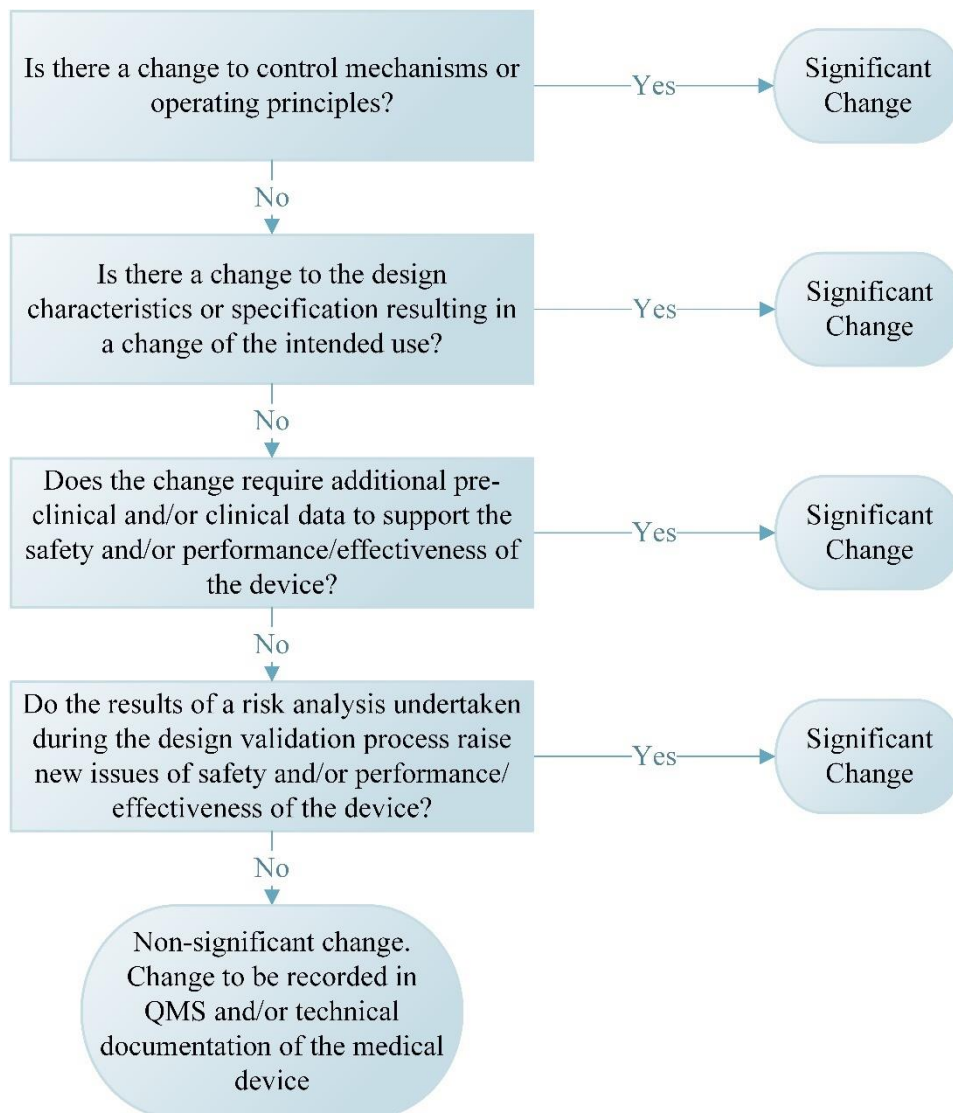
**Flowchart A: Changes in Manufacturing Processes, Facility and/or Quality Management System (including QC) for Medical Devices and In Vitro Diagnostic (IVD) Medical Devices**



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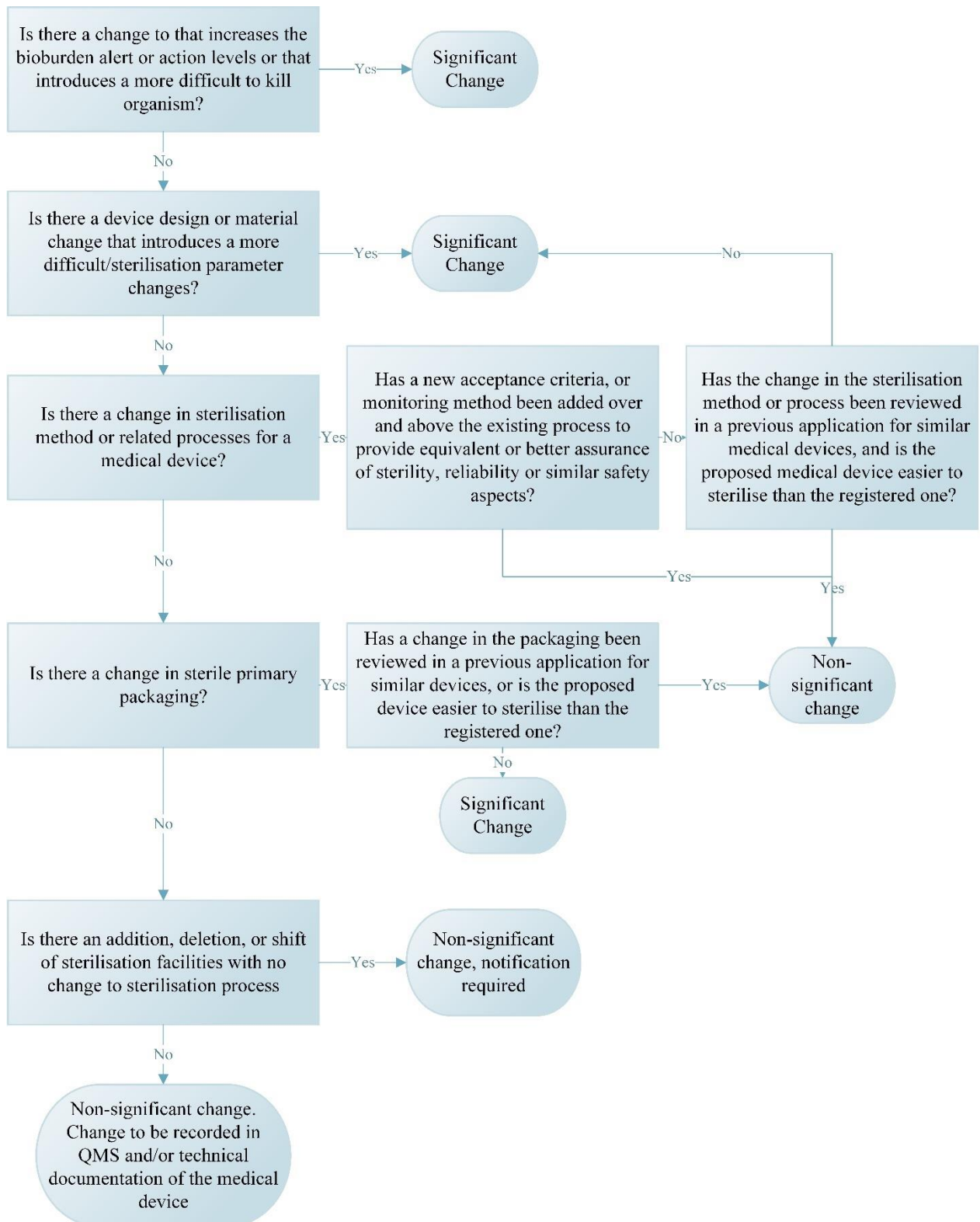
**Flowchart B: Changes in Design for Medical Devices and In Vitro Diagnostic (IVD) Medical Devices**



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**Flowchart C: Change to Sterilisation Facility and its Process and/or Quality Management System**



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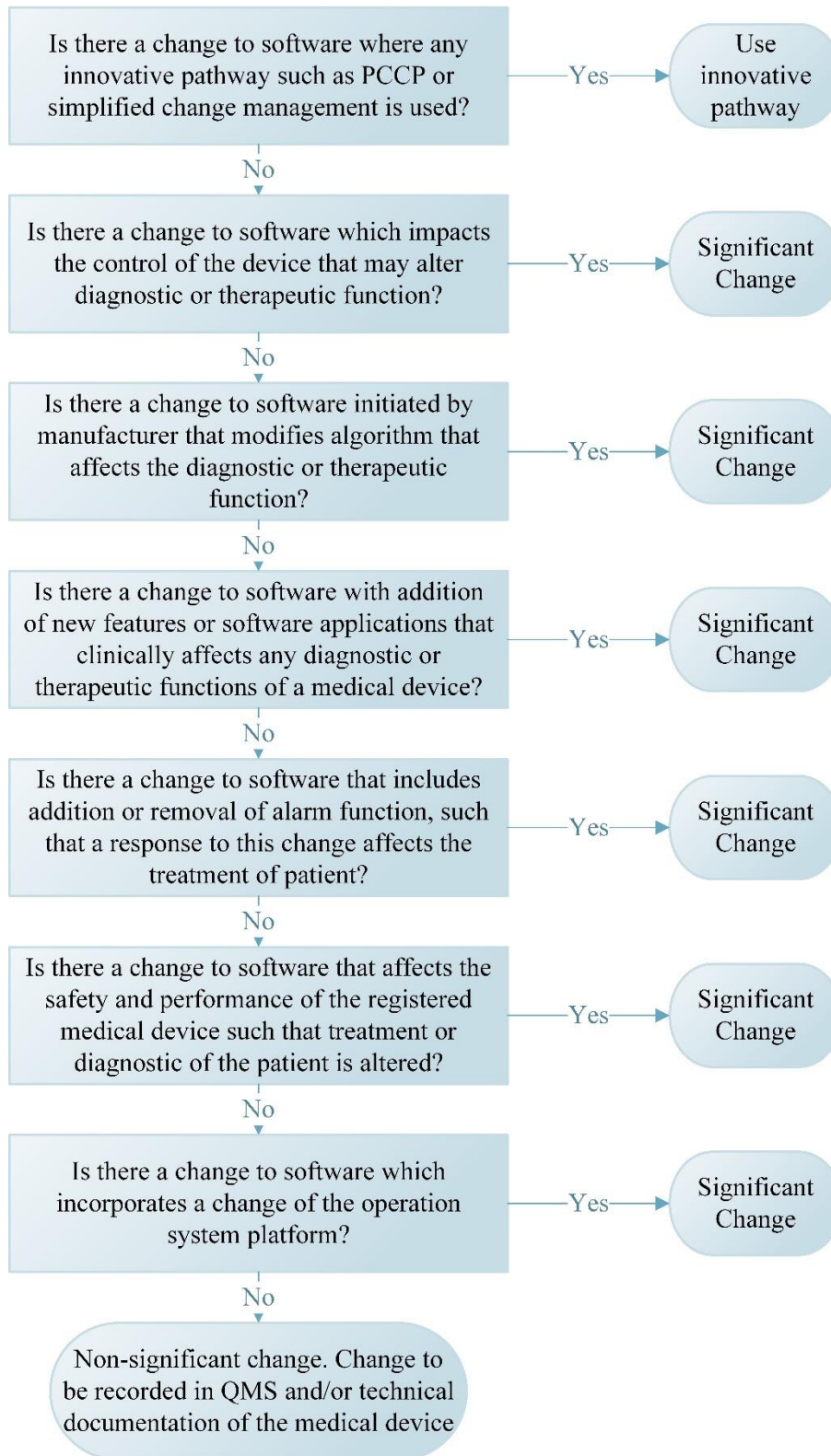
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**Flowchart D: Changes to Software for Medical Devices**

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\* Software refers to SaMD and/or Software embedded/SiMD in medical device system.

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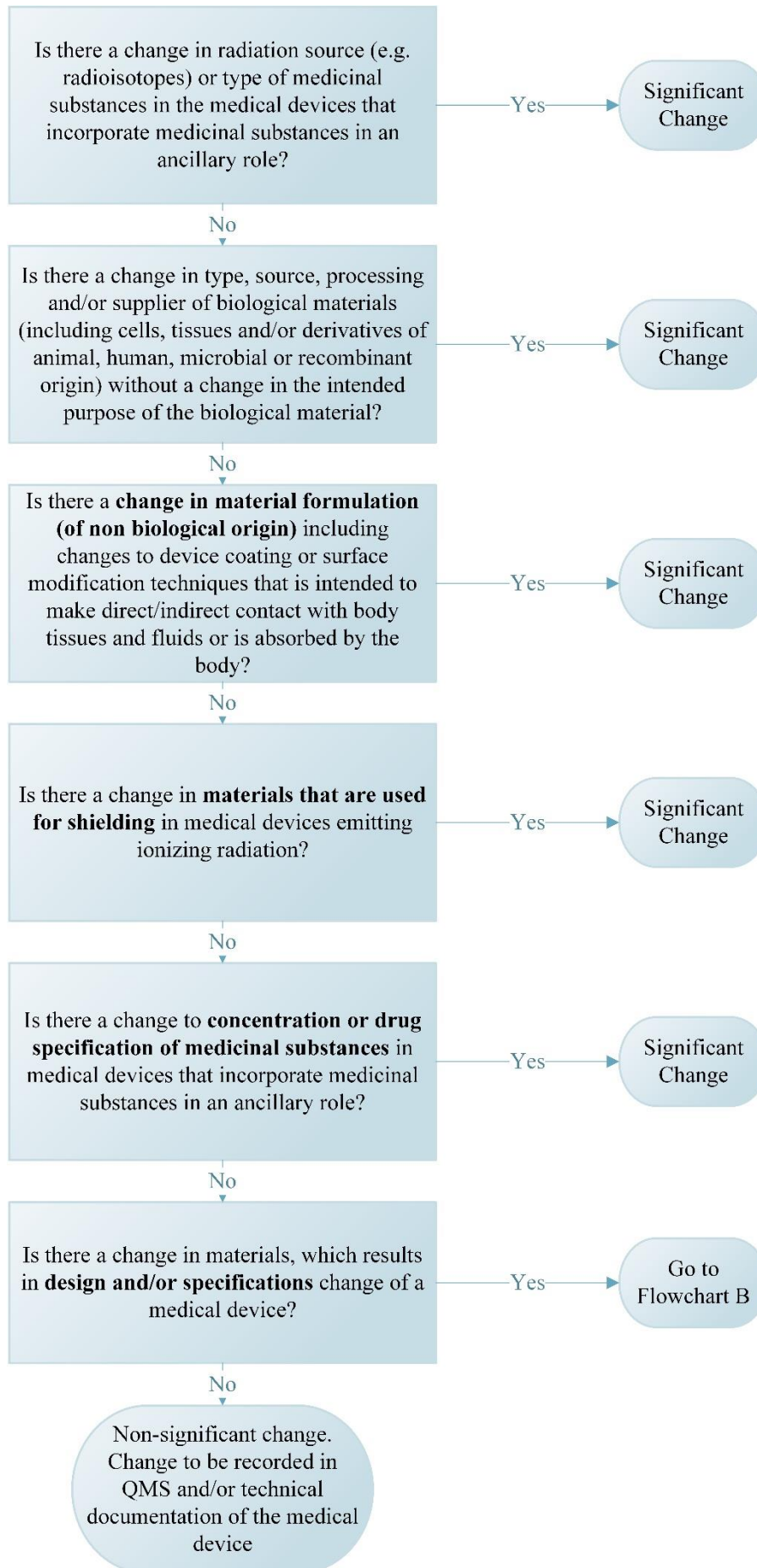


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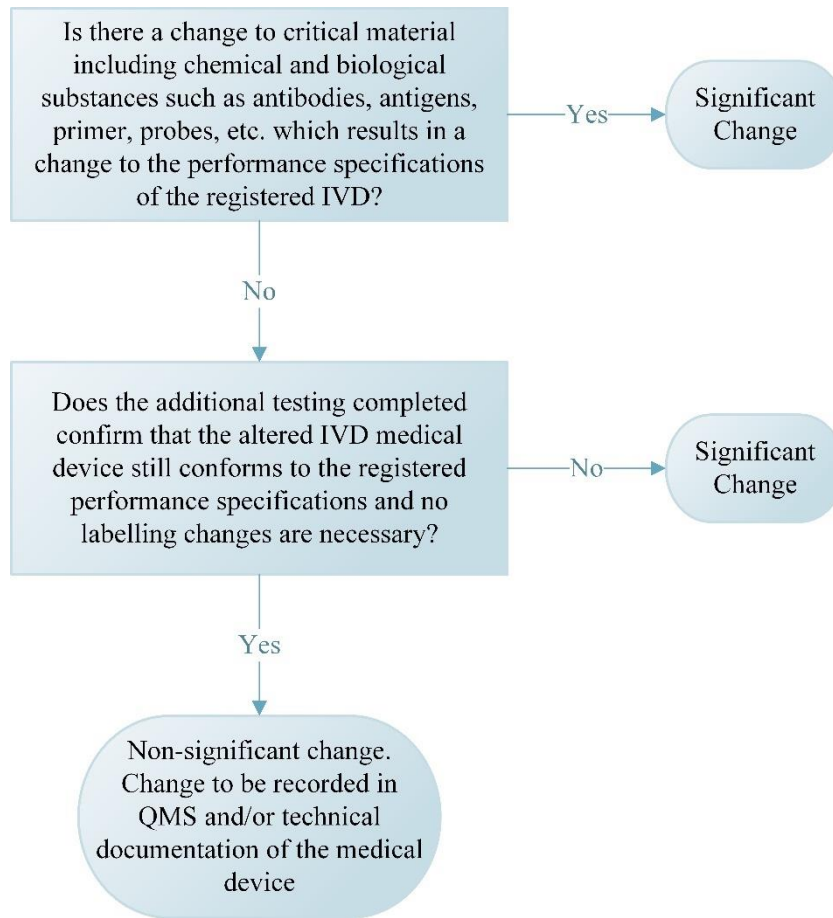


**Flowchart E1: Changes in materials for General Medical Devices**



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**Flowchart E2: Changes in materials for In Vitro Diagnostic (IVD) medical devices**



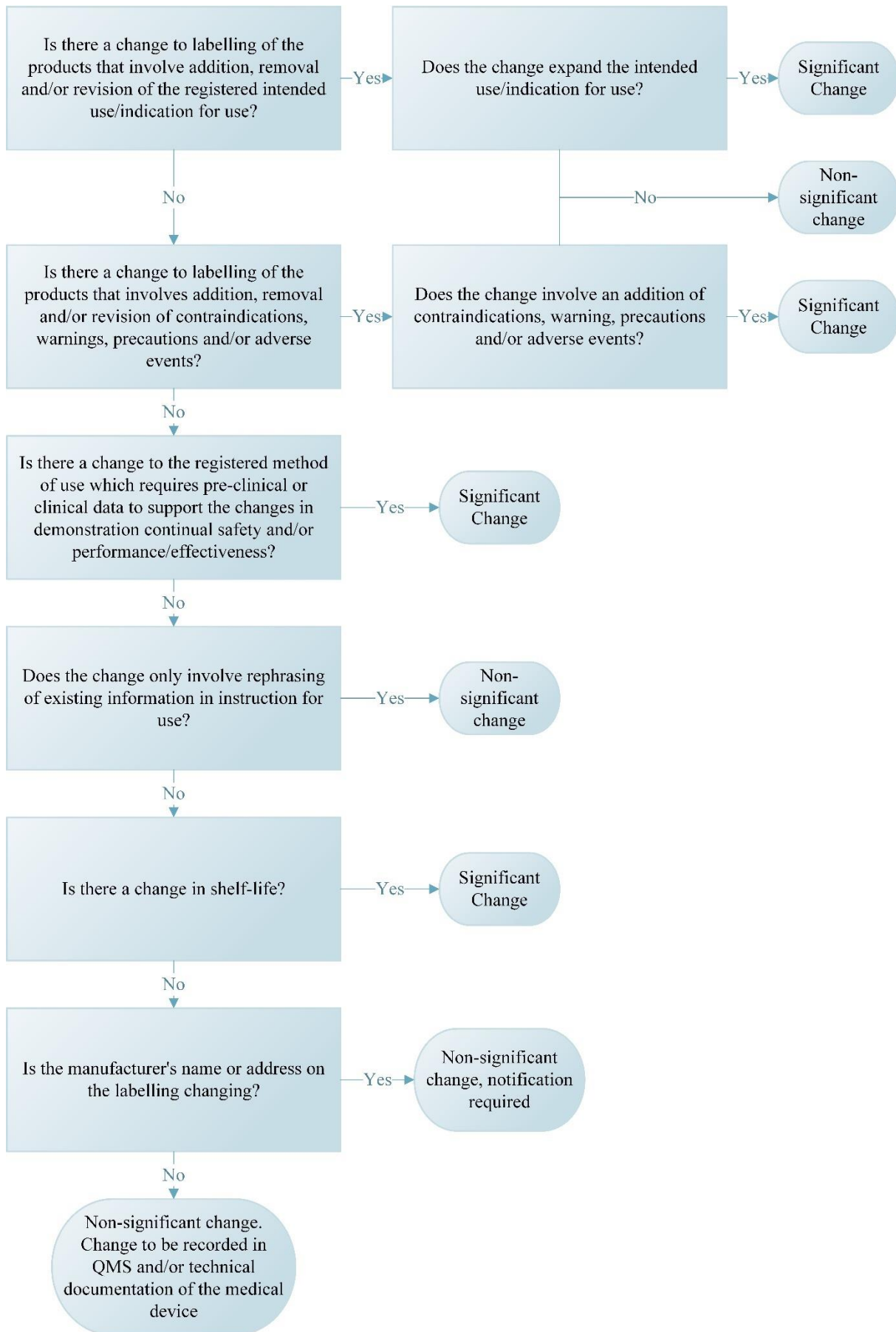
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**Flowchart F: Changes to Labelling of Medical Devices and In Vitro Diagnostic (IVD) Medical Devices**



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491 **10.0 APPENDIX 2 -Examples of changes and reporting requirements**

492 **Changes in manufacturing processes, facility and/or Quality Management System**

Example	Category (Significant, Non-significant)
<p>Changes to QMS Certificate, such as:</p> <p><i>Change/addition/removal of manufacturing site,</i></p> <p><i>Change of scope.</i></p>	Significant
<p>Change to manufacturing processes (including changes made to outsourced processes) that may affect the safety and/or performance/effectiveness of the medical device, such as:</p> <p><i>Change in the equipment used for cutting, resulting in the change in length of sutures,</i></p> <p><i>Change of centrifugation to filtration process which results in better molecule separation,</i></p> <p><i>Change of implant manufacturing process from casting to 3D printing,</i></p> <p><i>Change from manual operation to automatic operation, without changing the product specification.</i></p>	Significant
<p>Change in specification of registered medical device due to change in critical supplier, such as:</p> <p><i>Change in biological components sources or biological manufacturing processes in general,</i></p> <p><i>Change of supplier of plastic raw material of catheter,</i></p> <p><i>Change of supplier of biological component with different manufacturing process.</i></p>	Significant
<p>Changes to Manufacturing QC process issues, such as:</p> <p><i>Removal of two test parameter or modification of acceptance criteria,</i></p> <p><i>Change in the sampling processes for QC testing.</i></p>	Significant
<p>Changes to QMS Certificate, such as:</p> <p><i>Change of zip code on the certificate, typo errors and correction.</i></p>	Non-significant
<p>Changes to Manufacturing QC process, such as:</p> <p><i>New QC specification with additional testing,</i></p> <p><i>Change of measuring and/or monitoring equipment without changing test parameter.</i></p>	Non-significant

Changes to Manufacturing QC process issues, such as:  <i>Change in non-critical supplier that is fully qualified that has no change in finished product performance specifications.</i>	Non-significant
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**Changes in design for general medical devices**

<p style="text-align: center;"><b>Example</b></p>	<p style="text-align: center;"><b>Category (Significant, Non-significant)</b></p>
<p>All changes to the control mechanisms, operating principles and/or design characteristics of a medical device, such as:</p> <p><i>Change from a quantitative assay to a qualitative assay,</i></p> <p><i>Addition of a footswitch to an X-ray system that previously do not operate via a footswitch mechanism,</i></p> <p><i>Change of a substrate of an immunological test.</i></p>	<p style="text-align: center;">Significant</p>
<p>Change in the design characteristics that allows for additional or broader intended use/indication for use, such as:</p> <p><i>A smaller sized hip prosthesis or fracture fixation screw that are significantly different from their predicate designs,</i></p> <p><i>Addition of urine as specimen in the intended use/indication for use for creatinine test.</i></p>	<p style="text-align: center;">Significant</p>
<p>Change that have pre-clinical and/or clinical data identified new risks that adversely affects the safety and/or performance/effectiveness of the device, such as:</p> <p><i>The original heat-sealing package barrier found risk of leakage and change to sterile packaging barrier.</i></p>	<p style="text-align: center;">Significant</p>
<p>Change results of a risk analysis undertaken during the design validation process raise new issues of safety and/or performance, such as:</p> <p><i>Change from an internal direct current (DC) power source to an external alternating current (AC) source or vice versa,</i></p> <p><i>During the clinical validation process, ceramic dental cap has found durability issues, other materials have to be considered,</i></p> <p><i>Change to the cable design and grip of a steerable ablation catheter, which results in improved deliverability and improved procedural times.</i></p>	<p style="text-align: center;">Significant</p>
<p>Change to the design, manufacturing, or components whether it change its intended performance or not, such as:</p> <p><i>All changes in specifications (including shelf life and stability) of an IVD medical device,</i></p> <p><i>Changes in biological or chemical components of reagents.</i></p>	<p style="text-align: center;">Significant</p>
<p><i>Change of the secondary packaging with no impact on storage conditions or stability.</i></p>	<p style="text-align: center;">Non-significant</p>

<i>Change of colour of the cap of a reagent.</i>	Non-significant
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**Changes to sterilisation facility and its process and/or Quality Management System**

Example	Category (Significant, Non-significant)
Change of the sterilisation process, such as: <i>Change from ethylene oxide to gamma radiation sterilization.</i>	Significant
Change that increases the bioburden alert or action levels or that introduces a more difficult to kill organism, such as: <i>A change that introduces additional pre-sterilisation transport steps.</i>	Significant
Device design or material change that introduces a more difficult to sterilise feature, such as: <i>Change to the packaging where a single pouched sterile device is put into a double pouch.</i>	Significant
<i>Change from biological indicator to parametric release or change from batch release to parametric release.</i>	Significant
<i>Change in moist heat sterilisation parameters.</i>	Significant
<i>Change from a pre-blended sterilant (EtO and CHCs) to EtO post-blended with nitrogen. The ultimate concentration of EtO in the sterilant is the same in both cycles.</i>	Non-significant
<i>Change from using Air (mixture of 80% Nitrogen and 20% Oxygen) to pure Nitrogen in the aeration process to avoid explosive gas mixtures.</i>	Non-significant

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**Changes to Software for Medical Devices and IVD Medical Devices**

Example	Category (Significant, Non-significant)
<p>Change to software which impacts the control of the device that may be alter diagnostic or therapeutic function, such as:</p> <p><i>Software change causing the change of critical steps for laser delivery on eye treatment.</i></p>	Significant
<p>Change to software initiated by manufacturer that modifies the algorithm that affects the diagnostic or therapeutic function, such as:</p> <p><i>An X-ray Lung Nodule Assessment Software is used along with a Digital Radiography System to support physicians in the visualization, identification, evaluation and reporting of pulmonary lesions/nodules in chest images. An algorithm change improves the detection rate for small nodules.</i></p> <p><i>Changes in the software that modifies the quality controls interpretation or cut off calculation of an IVD.</i></p>	Significant
<p>Change to software with addition of new features or software applications that affect any diagnostic or therapeutic functions of a medical device, such as:</p> <p><i>Insulin Pump - Software changes that allow for wireless communication with compatible (continuous) blood glucose monitors.</i></p>	Significant
<p>Change to software that includes addition or removal of alarm function, such that a response to this change affect the treatment of patient, such as:</p> <p><i>Electrocardiogram Addition to software of an early warning alarm to signal a potential cardiac event such as atrial fibrillation,</i></p> <p><i>Modification of the software to add or remove alarms to monitor the diagnostic procedure on an infectious disease analyzer.</i></p>	Significant
<p>Change to software that affect the safety and performance/effectiveness of the registered medical device such that treatment or diagnostic of the patient is altered, such as:</p> <p><i>Blood Oxygen Monitor - A software change that allows the monitor to report blood CO2 concentrations with higher accuracy up to 0.5% deviation,</i></p> <p><i>Upgrade of software version changes the performance characteristics like specificity or sensitivity of the In-vitro diagnostic medical device.</i></p>	Significant
<p>Change to software incorporating a change to the operation system platform, such as:</p>	

<i>A change in the software together with operating system change from Linux to another operating system platform.</i>	Significant
<i>Addition or change of OS version(s) which does not backward compatible. For example: From Windows to iOS.</i>	Significant
<i>A simple bug fixes to correct the display error on the data table from the software analysis result.</i>	Non-significant
<i>Change in software which only introduces non-therapeutic and non-diagnostic features such as printing, faxing, improved image clarity or reporting format.</i>	Non-significant
<i>Change in software to disable certain functions that does not interact with other functions.</i>	Non-significant
<i>Change for compatible with large OS update patch within the same platform. Such as: From Windows X 21H1 to Windows 21H2.</i>	Non-significant
Change in software to alter colors and location of menu on graphic user interface of medical devices that does not affect safety and performance/effectiveness of the device but results in version change and doesn't alter usability of the interface.	Non-significant
Change in software to add languages for users that does not accompany changes in the main features and misunderstanding in translation for intended use/indication for use, principle of operation, and performance/effectiveness.	Non-significant
Change in the distribution/storage method of software among physical media (USB, CD, DVD), digital means (download), etc.	Non-significant
Change in software to strengthen the cybersecurity such as:  <i>Adding encryption to the configuration file of the device,</i>  <i>Adding passcode requirements for remote users, in addition to the password needed to access the device, and</i>  <i>Adding a timeout for remote user or changing the access of the restricted user/customer to appropriate levels.</i>	Non-significant
Change in software to disallow use of the specific characters that are invalid as defined in the instrument host interface specification for the prevention of Specimen Identification (ID) barcode information truncation.	Non-significant
Change in software to return the system into specification of the most recently cleared device regarding DICOM (Digital Imaging and Communications in Medicine standard; <a href="http://dicom.nema.org/">http://dicom.nema.org/</a> ) conformance allowing the automatic fetching of prior studies from radiology information system using PACS (Picture Archiving and Communication System).	Non-significant

Change management to registered Medical Devices  
GHWP/WG2-WG1-WG3/PF001:2024

Change in software to correct the bottle size parameter of the cleaning solution to prevent the fluid detection errors.	Non-significant
Change in IVD analyzer software to ensure new data of the administrative records for reagents is not merged with the existing data in the table within the software by correcting software code in the control unit of the analyzer to modify the table to add new columns.	Non-significant
Changes in software including the addition of product indication for use or its operating principles including diagnostic algorithm such as machine learning that may alter diagnostic or therapeutic function.	Significant
Change in accuracy of Machine Learning Medical Device software via modification and expansion of the training dataset without any changes to labeled product design specification.	Non-significant
Change in IVD analyzer software to rewrite an incorrectly worded software requirement and to modify code in the control unit of the analyzer without modifying the core algorithm (such as detection or measurement module algorithm).	Non-significant

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**Changes in materials for medical devices**

Example	Category (Significant, Non-significant)
<p>Change in radiation source (e.g., radioisotopes) or type of medicinal substances in the medical devices that incorporate medicinal substances in an ancillary role, such as:</p> <p><i>Change in the drug of a drug eluting stent.</i></p>	Significant
<p>Change in type, source, processing and/or supplier of biological materials (including cells, tissues and/or derivatives of animal, human, microbial or recombinant origin) without a change in the intended purpose of the biological material, such as:</p> <p><i>Change in source of hyaluronic acid from Streptococcus zooepidemicus to Streptococcus equi.</i></p>	Significant
<p>Change in material or material formulation (of non-biological origin) including changes to device coating or surface modification technique in a medical device that is intended to make direct/indirect contact with body tissues and fluids or is absorbed by the body, such as:</p> <p><i>Introduction of a colorant change into the insertion hub of a Peripherally Inserted Central Catheter (PICC) that is part of the fluid path for fluid administration or withdrawal from a patient,</i></p> <p><i>A change of material to a cardiovascular catheter that comes in contact with body tissue (e.g., change to/from polyether block amide (PEBA), Polyamide or polyether ether ketone (PEEK).</i></p>	Significant
<p>Change to concentration or drug specification of medicinal substances in medical devices that incorporate medicinal substances in an ancillary role, such as:</p> <p><i>Change in the concentration of the drug in a drug eluting stent,</i></p> <p><i>Change in the concentration of antibiotics or a change to a different antibiotic in a catheter coated with antibiotic.</i></p>	Significant
<p><i>Change in supplier or vendor of non-critical material, but the material meets the manufacturer's previously reviewed specification,</i></p> <p><i>Introduction of a colorant change into the flush port of a Peripherally Inserted Central Catheter (PICC). The flush port is an access port for flush syringes for IV-line clearance or volume block and is not intended to be used for fluid administration or withdrawal from a patient.</i></p>	Non-significant

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**Changes in materials for IVD medical devices**

<p style="text-align: center;"><b>Example</b></p>	<p style="text-align: center;"><b>Category (Significant, Non-significant)</b></p>
<p>Changes which need testing of additional samples, such as:</p> <p><i>Change of sources or types of materials (conjugate, antibodies, antigens, primers, or substrate),</i></p> <p><i>Change to the sample preparation, such as the inclusion of a stabilizer for an IVD that is intended to simplify preparation requirements or increase sample stability.</i></p>	<p style="text-align: center;">Significant</p>
<p>Change in material, which results in design specifications change, such as:</p> <p><i>Formulation changes of reagents of test kits (buffer concentration, addition of preservatives),</i></p> <p><i>Change in the synthesis/purification methods of biologicals components,</i></p> <p><i>Change from a liquid to solid reagent and vice versa.</i></p>	<p style="text-align: center;">Significant</p>
<p><i>A change in supplier or vendor of the non-critical material, but the material meets the manufacturer's previously reviewed specification,</i></p> <p><i>Change of sources of non-critical materials, such as magnesium stearate from an animal to vegetable source in a reagent of an IVD kit with no change in performance specification.</i></p>	<p style="text-align: center;">Non-significant</p>

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**Changes to Labelling**

<b>Example</b>	<b>Category (Significant, Non-significant)</b>
All changes to the labelling of medical devices that involve addition, removal and/or revision of warnings, precautions and/or contraindications.	Significant
Labelling changes that modify the registered method of use; or involve a change from 'professional use only' to 'home use.'	Significant
Change involves a reduction of intended use/indication for use not arising due to medical device safety and/or performance concerns.	Non-significant, but generally reportable
Changes to the label due to typo error.	Non-significant

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