VDE Recommendation

Market access of continuous learning AI systems in medicine

VDE DGBMT

VDE

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Content

Abstract

Artificial intelligence (AI) systems offer completely new possibilities for the diagnosis and treatment of diseases for the benefit of patients. In recent years, a growing number of AI systems have gained access to regulated markets such as Europe and the USA as medical devices. However, these have generally been static AI systems, where the learning process is completed before putting into service and the underlying AI model does not change. This is to ensure that verification and validation relate to a specific stage of development of the AI system. This approach excludes continuous learning AI systems from market access and thus prevents the use of a continuous learning process as an essential technical advantage of AI systems.

The aim of this VDE-DGBMT recommendation is, against the background of the future European Artificial Intelligence Act (AIA) and the current legislation on medical devices, to point out a solution for the current innovation-inhibiting approach for continuous learning AI systems in the European market. The core for this is a so-called “anticipatory CE conformity assessment”, which provides for the planning and approval of intended changes already before putting into service.

The VDE-DGBMT recommendation is primarily addressed to the national competent authorities and Notified Bodies as well as to the European legislator.

Abbreviations and definitions

- **Artificial intelligence (AI):** Set of methods or automated entities that together build, optimize and apply a model so that the system can, for a given set of predefined tasks, compute predictions, recommendations, or decisions (1)
- **AI system:** Engineered system featuring AI (1)
- **Artificial intelligence act (AIA):** Proposal for a Regulation of the European Parliament and of the Council laying down harmonized rules for artificial intelligence and amending certain Union legislative acts
- **Bias:** Systematic difference in treatment of certain objects, people, or groups in comparison to others (1)
- **Continuous learning:** Incremental training of an AI system that takes place on an ongoing basis during the operation phase of the AI system life cycle (1)
- **Data drift:** Accuracy of the model's predictions decays over time due to changes in the statistical characteristics of the production data (e.g. image resolution has changed, or one class has become more frequent in data than another) (1)
- **Machine learning (ML):** Process of optimizing model parameters through computational techniques, such that the model's behavior reflects the data or experience (1)
- **Machine Learning-Enabled Device Software Function (ML-DSF):** A device software function that implements an ML model trained with ML techniques (2)
- **Medical Device Regulation (MDR):** Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC
- **Medical device software (MDSW):** Medical device software is software that is intended to be used, alone or in combination, for a purpose as specified in the definition of a "medical device" in the medical devices regulation or in vitro diagnostic medical devices regulation (3)
- **Overfitting:** Generation of a ML model that corresponds too closely to the training data, resulting in a model that finds it difficult to generalize to new data (4)
- **Quality management system (QMS):** Part of a management system with regard to quality (5)

Continuous learning AI systems in medicine

Artificial intelligence (AI) systems in medicine have become increasingly important in recent years. In the US and European markets, new AI systems are becoming approved and placed on the market as medical devices (6,7).

An essential part of the development of AI systems is their training with suitable training data. The approach to this can vary. In one case, models of AI systems are trained and tested during development before moving to the market phase[1] and remain unchanged during it (static AI systems[2]). In another case, models of continuous learning AI systems (also referred to as dynamic AI systems[2]) are further trained with new data during the market phase with the goal of improving the performance of the AI model. Continuous learning can also overcome limitations in the initial availability of data, as well as achieve broader applicability of the model to more input data and higher generalizability.

The problem arises that continuous learning AI systems do not have a fixed technical development status, as this changes regarding the underlying model, during the market phase. This has led to the fact that continuous learning AI systems for medical applications are currently not approved as medical devices for the European Union market.

Requirements for changes to CE-marked medical devices derived from legislation and technical standards

In Europe, medical devices are subject to the requirements of Regulation (EU) 2017/745 (hereinafter referred to as MDR, Medical Device Regulation) (8) or, as in vitro diagnostic devices, Regulation (EU) 2017/746[3] (hereinafter referred to as IVDR, In vitro Diagnostic Regulation). Before placing on the market, manufacturers of medical devices must demonstrate the conformity of their products with the requirements of the MDR or the IVDR. After completion of the conformity assessment procedure, manufacturers issue an EU declaration of conformity and affix the corresponding CE marking to the product.

According to Annex I, Chapter II, Section 17.1 MDR, software must be designed to ensure repeatability, reliability and performance in accordance with its intended use. The CE conformity assessment and subsequent placing on the market is therefore usually coupled with a defined technical development status. In the further life cycle, however, medical devices are usually subject to technical changes which, depending on their scope and criticality, may also require a renewed CE conformity assessment.

In view of the practical relevance, the European legislator has therefore specified the handling of changes to medical devices several times in the MDR. Thus, Article 10, Section 9, Sentence 2, MDR requires that “changes in device design or characteristics [...] shall be adequately taken into account in a timely manner”. In the manufacturer’s quality management system (QMS), the control of design and development changes is implemented in a corresponding process (Article 10 Section 9 Paragraph 3 MDR).

1 The term „market phase“ here refers to the placing on the market and operation of AI systems. In the technical community, this is also referred to as the „production phase“.
2 Cf. German Notified Bodies Alliance, Ed., Questionnaire “Artificial Intelligence (AI) in medical devices”.
3 Since AI systems in medicine are typically subject to the requirements of the MDR due to their intended purpose, this document does not consider applications as in vitro diagnostic devices.

In the case that manufacturers perform conformity assessment based on a QMS and a technical documentation assessment according to Annex IX MDR, changes to an approved device must be approved by the Notified Body that issued the EU technical documentation assessment certificate if these changes could affect the safety and performance of the device or the conditions of use prescribed for the device (Annex IX, Chapter II, Section 4.10., Sentence 1 MDR). A similar provision is found in Annex X MDR for conformity assessment based on type examination. According to Annex X Section 5.2. MDR, modifications to the approved device, including restrictions to its intended purpose or conditions of use, must be approved by the Notified Body that issued the test certificate if such modification may affect the conformity of the device with the essential safety and performance requirements or with the intended conditions of use of the device. Notified Bodies must provide a procedure for evaluating changes in these cases (Section 4.9. Annex VII MDR). Based on the procedure, the Notified Body must decide whether the respective changes require a new CE conformity assessment.

Furthermore, in the event of changes to the intended purpose and conditions of use of the approved product, the MDR stipulates a new conformity assessment to be carried out (Annex X, Section 5.3. MDR).

This approach has also found its way into technical standards. According to section 7.3.9 on the control of development changes in EN ISO 13485, changes must be approved and evaluated regarding their influence on the intended purpose as well as on safety, performance and the applicable regulatory requirements. Furthermore, it must be determined which verification and validation activities will be used to check that the changes have been implemented as planned. There is also a feedback loop to risk management here. In the case of medical device software, changes are planned, implemented and controlled in the software maintenance process.

It is evident from the above provisions that not every change leads to a reassessment of the medical device. This is particularly evident regarding Annex IX, Chapter I, Section 2.4., Sentence 4 MDR, according to which “only substantial changes” to the quality management or the product range covered by it are considered by the Notified Body.

Guidance on the classification of changes

In 2014, under the old European regulatory framework, the *Notified Body Operations Group (NBOG)* published recommendations in a guide on how to assess various changes with regard to CE conformity assessment (9). The NBOG guidance gives the following examples of **substantial changes** to medical device software:

- Change affecting device control,
- Change in algorithm affecting diagnosis or therapy,
- Changes affecting the way data is interpreted by the user,
- Replacement of user input with closed-loop input,
- Introduction of a new essential software function,
- Introduction or removal of an alarm function as well as
- Significant change of the operating system

This contrasts with **non-substantial changes**, such as the introduction of new software function(s) that are not essential for the intended purpose, a minor change of the user interface appearance or the deactivation of a software function. A similar approach to the delimitation with regard to the criticality of changes can be found in guideline MDCG 2020-3 (10).

In analogy to the NBOG document, Zinchenko and co-authors describe in a publication when changes to an AI model should be considered significant and non-significant (11). As examples of significant changes, the authors cite changes related to:

- efficiency and safety (e.g., improvement of processing time / recognition rate or functional enhancements such as saliency maps),
- the input data (e.g., compatibility with new manufacturer data or additional input data, both without change of purpose) as well as
- the functionalities (e.g., new patient target groups and conditions of use, both with change of purpose).

Non-significant changes with no effect on the intended purpose concern:

- Bug fixes (e.g., changing the display of output data / report format),
- Error reports and logs (e.g., changes in the display) or
- the user interface (e.g., changes in window sizes or colors).

The view of the significance of changes described in the two documents implies that continuous learning AI systems cannot be compliant because continuous changes would require new CE conformity assessments in most cases.

In Section A of the questionnaire "Artificial Intelligence (AI) in medical devices", the German Notified Bodies Alliance (IG-NB) comments on the certifiability of AI systems as follows: "Static AI (AI that has learned and operates in a learned state) is in principle certifiable. Dynamic AI (AI that continues to learn in the field) is not certifiable in principle, as the system must be verified and validated (among other things, the functionality must be validated against the intended use)" (12).

In the view of the IG-NB, there must therefore be a defined stage of development at the time of the verification and validation activities[4]. Consequently, continuous learning AI systems in medicine that do not have a defined technical development status due to continuous learning are, in principle, not certifiable.

New regulatory approaches

In 2019, the FDA proposed a new regulatory framework for market access of AI systems in medicine in a discussion paper (13). Thus, the safety and performance of these AI systems should be ensured through a comprehensive QMS based on Good Machine Learning Practices (GMLP). In 2021, FDA, Health Canada, and the English Medicines and Healthcare products Regulatory Agency (MHRA) published a related guidance document (14). Under certain conditions, the FDA discussion paper also provides market access for continuous learning AI systems. The core of this new regulatory approach is the so-called **Predetermined Change Control Plan (PCCP)**, in which the manufacturer shall disclose planned future changes to the AI model and their evaluation prior to market access, as the FDA recently detailed in a draft guidance document (2).

The PCCP consists of a detailed **description of the changes**, a **change log**, and an **impact assessment**. The detailed description shall describe the modifications to the device characteristics and performance that result from the changes. The change protocol shall include a description of the implementation of the proposed changes and the associated verification and validation activities. Finally, the impact assessment is to evaluate the benefits and risks of the planned changes. The PCCP is to be reviewed and approved by FDA prior to market approval. If the changes to the AI system in the market phase are within the scope of the indicated and approved changes, there is no need to go through a new approval process.

AI-specific regulatory activities have also been taking place at the European level in recent years. The EU Commission has published the draft of a European Artificial Intelligence Act (draft AIA) in 2021 (15).

4 In this document, the terms „verification" and „validation" are applied according to the definitions in ISO 9000 (5).

Therein, AI systems as medical devices are classified as so-called high-risk AI systems and are subject to special market access requirements. In principle, the draft AIA provides that high-risk AI systems will be subject to a new CE conformity assessment procedure "whenever they are substantially modified, regardless of whether the modified system is intended to be further distributed or continues to be used by the current user" (Art. 43(4)(1) draft AIA). According to recital 66 of the draft AIA, a **substantial modification** is one that could affect compliance with the AIA or one that changes the purpose of the system.

In contrast, like the approach in the FDA discussion paper, "changes to the high-risk AI system and its performance that have been pre-determined by the provider at the moment of the initial conformity assessment and are part of the information contained in the technical documentation referred to in point 2(f) of Annex IV, shall not constitute a substantial modification" (Art. 43(4)(2) draft AIA). This draft legislation of the European legislator appeared significantly later than the MDR and therefore also reflects a regulatory development against the background of new technological developments.

With the AIA, the European legislator would provide a completely new type of CE conformity assessment for continuous learning AI systems, which has so far not been explicitly provided for neither by the German Notified Bodies nor in the MDR.

Approaches to CE conformity assessment of continuous learning AI systems under the current regulatory framework

Transferring the two regulatory approaches mentioned above, a so-called "anticipatory CE conformity assessment" for continuous learning AI systems in medicine could be introduced in Europe as part of the current regulatory framework (16). The anticipatory CE conformity assessment would be characterized by the fact that it is carried out in advance, including intended changes during putting into service. For subsequent changes that are within the scope of the anticipated, further conformity assessment could be waived. Changes that cannot be foreseen and cannot necessarily be anticipated would then have to be subjected to a new conformity assessment procedure and subsequently certified (16).

Even if this approach would represent an innovation in European medical device law, it is compatible with the current legal framework of the MDR. This is already supported by the fact that the regulations referenced above (cf. section "Requirements for changes to CE-marked medical devices derived from legislation and technical standards") are formulated in an open manner. An anticipatory conformity assessment is not explicitly excluded. This is not precluded by the fact that Annex I, Chapter II, Section 17.1. MDR requires the software to be designed in such a way that repeatability is ensured. According to its meaning and purpose, the quality feature of repeatability does not refer to designing the system to be as static as possible. Otherwise, even necessary software updates or patches would result in an initially assessed system no longer being repeatable in the sense of the MDR. Rather, the regulatory requirement in the context of conformity assessment refers to the fact that repeatability is ensured for reasons of traceability of the output in the phases between the software changes made.

Furthermore, sections 5.2 and 5.3 of Annex X MDR can be interpreted in such a way that anticipated changes that have already been assessed in an initial conformity assessment procedure fulfill the protective purpose of the MDR in the same way as a subsequent assessment procedure. After all, the purpose of a reassessment of conformity is to re-evaluate the patient safety risks associated with the relevant change. This would be rendered moot if the assessment were captured on the first pass and evaluated accordingly. Overall, the approach of the FDA and the EU Commission could therefore also be implemented in regulatory terms under the current MDR.

Practical implementation of an anticipatory CE conformity assessment

At the time of conformity assessment, planned changes defined by the Notified Body could already be approved based on a PCCP as part of the technical documentation. This means that the manufacturer no longer must address these additionally in the "Control of design and development changes" process and report them to the Notified Body after putting them into service or have them approved.

In the context of anticipatory CE conformity assessment, post-market surveillance (PMS) is of particular importance in the safety architecture of continuously learning AI systems. For example, Article 61(1) of the draft AIA states that the provider (equivalent to the manufacturer as defined in the MDR) must establish and document a PMS that is proportionate to the nature of the AI technology and the risks of the high-risk AI system. Recital No. 54 of the draft AIA adds that this should be a "robust" PMS system. Further, the GMLP guidance provides that the performance of AI models in the market phase is monitored and risks are managed through re-training (14). With respect to continuous learning AI systems, appropriate controls to manage risks related to overfitting, bias, or model degradation (e.g., due to data drift) should be implemented by the manufacturer (14). For example, in the context of statistical process control (SPC), various forms of statistical control charts can be used to monitor the performance of AI systems in the market phase (17). In this regard, manufacturers can also rely on various software packages, e.g., strucchange®, Scikit-multiflow (Python), or Massive Online Analysis (MOA) (18–20).

Example of the application of an anticipatory CE conformity assessment

To illustrate, we explain the anticipatory CE conformity assessment using a concrete product example.

The example is an AI system that automatically analyzes angio-CT images of the brain in the hospital emergency room. Once the AI system has identified a potential occlusion of a major vessel, it recommends that the radiologist in charge review these images, supporting triage in parallel with the standard treatment workflow in the clinic.

As part of an anticipatory CE conformity assessment, the manufacturer describes in the PCCP that he intends to use images from a second manufacturer's CT scanner for continuous learning of the AI model during the first 6 months after putting into service. The manufacturer specifies acceptance criteria with respect to image characteristics and describes how compliance with the CT image acceptance criteria will be monitored.

The manufacturer states that this change to the AI system does not require a change in intended purpose but serves to improve the generalizability of the AI model. In the PCCP, the manufacturer indicates that the images from the CT scanner will be reviewed by radiologists within a specified time period for potential vascular occlusions by the second manufacturer. As part of the post-market surveillance, it specifies acceptance criteria for selected quality criteria related to the AI model that allow for ongoing performance monitoring. The manufacturer also describes the software tools used and implements an automatic alarm function and corresponding instructions for action as soon as the quality criteria fall below a critical value.

The Notified Body reviews the PCCP as part of the initial CE conformity assessment and determines that the planned changes to the AI system are to be regarded as significant and therefore fundamentally require a renewed CE conformity assessment. However, the risk control measures appear sufficient to the Notified Body. The Notified Body approves the changes presented in the PCCP.

If the manufacturer were to use angio-CT images of additional patient groups (e.g., regarding gender or age group) for continuous learning of the AI model and these were not described and approved in the PCCP, a renewed CE conformity assessment would in principle be required.

Recommendations

In terms of anticipatory CE conformity assessment, Notified Bodies should assess a PCCP submitted by the manufacturer for continuous learning AI systems with planned changes to the model. Provided that the changes are within the approved PCCP, no new CE conformity assessment concerning changes to the model by the Notified Body should be required. This is under the premise that sufficient measures to mitigate any new risks and effective post-market surveillance have been implemented.

The Medical Device Coordination Group of the EU Commission (MDCG) should publish a guideline on the placing on the market of AI systems in medicine and provide to the Notified Bodies explicit recommendations on the handling of continuous learning AI systems. This includes specifications on the form and function of a PCCP that the manufacturer must follow. The annex of this document contains a draft outline for the PCCP as it could be introduced for the European market. Furthermore, this MDCG guideline should contain comprehensible assessment criteria for the Notified Body for the examination and approval of a PCCP. The MDCG should take care that the preparation of this guideline is done in close coordination with the requirements of the future AIA.

Literature

1. ISO/IEC, editor. ISO/IEC 22989 Information technology - Artificial intelligence - Artificial intelligence concepts and terminology [Internet]. 2022. Available from: https://www.iso.org/obp/ui#iso:std:iso-iec:22989:ed-1:v1:en
2. FDA, editor. Draft Guidance: Marketing Submission Recommendations for a Predetermined Change Control Plan for Artificial Intelligence/Machine Learning (AI/ML)-Enabled Device Software Functions [Internet]. 2023. Available from: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/marketing-submission-recommendations-predetermined-change-control-plan-artificial
3. Medical Device Coordination Group, editor. MDCG 2019-11 Guidance on Qualification and Classification of Software in Regulation (EU) 2017/745 – MDR and Regulation (EU) 2017/746 – IVDR [Internet]. 2019. Available from: https://health.ec.europa.eu/medical-devices-sector/new-regulations/guidance-mdcg-endorsed-documents-and-other-guidance_en
4. ISO/IEC, editor. ISO/IEC TR 29119-11 Software and systems engineering - Software testing - Part 11: Guidelines on the testing of AI-based systems [Internet]. 2020. Available from: https://www.iso.org/obp/ui#iso:std:iso-iec:tr:29119:-11:ed-1:v1:en:term:3.1.12
5. DIN e.V., editor. DIN EN ISO 9000 Qualitätsmanagementsysteme - Grundlagen und Begriffe [Internet]. 2015. Available from: https://www.iso.org/obp/ui#iso:std:iso:9000:ed-4:v1:en
6. FDA. Artificial Intelligence and Machine Learning (AI/ML)-Enabled Medical Devices [Internet]. 2022 [cited 2023 Jun 1]. Available from: https://www.fda.gov/medical-devices/software-medical-device-samd/artificial-intelligence-and-machine-learning-aiml-enabled-medical-devices
7. Radboud University Medical Center. AI for Radiology [Internet]. [cited 2023 Jun 1]. Available from: //www.AIforRadiology.com/
8. European Parliament and Council. Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC [Internet]. 2017/745 May 25, 2017. Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:02017R0745-20230320
9. NBOG, editor. Guidance for manufacturers and Notified Bodies on reporting of Design Changes and Changes of the Quality System [Internet]. 2014. Available from: http://www.doks.nbog.eu/Doks/NBOG_BPG_2014_3.pdf
10. Medical Device Coordination Group, editor. MDCG 2020-3 Guidance on significant changes regarding the transitional provision under Article 120 of the MDR with regard to devices covered by certificates according to MDD or AIMDD [Internet]. 2020. Available from: https://health.ec.europa.eu/medical-devices-sector/new-regulations/guidance-mdcg-endorsed-documents-and-other-guidance_en
11. Zinchenko V, Chetverikov S, Akhmad E, Arzamasov K, Vladzymyrskyy A, Andreychenko A, et al. Changes in software as a medical device based on artificial intelligence technologies. Int J Comput Assist Radiol Surg. 2022 Oct 1;17(10):1969–77.

12. German Notified Bodies Alliance, editor. Questionnaire „Artificial Intelligence (AI) in medical devices“ (Ver. 4) [Internet]. 2022. Available from: http://www.ig-nb.de/
13. FDA, editor. Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD) - Discussion Paper and Request for Feedback [Internet]. 2019. Available from: https://www.fda.gov/MedicalDevices/DigitalHealth/SoftwareasaMedicalDevice/ucm634612.htm
14. FDA, editor. Good Machine Learning Practice for Medical Device Development: Guiding Principles [Internet]. 2021. Available from: https://www.fda.gov/medical-devices/software-medical-device-samd/good-machine-learning-practice-medical-device-development-guiding-principles
15. European Commission. Proposal for a Regulation on a European approach for Artificial Intelligence | Shaping Europe's digital future [Internet]. 2021/0106 (COD) 2021. Available from: https://digital-strategy.ec.europa.eu/en/library/proposal-regulation-european-approach-artificial-intelligence
16. Schreitmüller Z. Regulierung intelligenter Medizinprodukte: eine Analyse unter besonderer Berücksichtigung der MPVO und DSGVO. 1. Auflage. Baden-Baden: Nomos; 2023. 346 p. (Schriften zum Bio-, Gesundheits- und Medizinrecht).
17. Feng J, Phillips RV, Malenica I, Bishara A, Hubbard AE, Celi LA, et al. Clinical artificial intelligence quality improvement: towards continual monitoring and updating of AI algorithms in healthcare. Npj Digit Med. 2022 May 31;5(1):1–9.
18. Zeileis A, Leisch F, Hornik K, Kleiber C. strucchange: An R Package for Testing for Structural Change in Linear Regression Models. J Stat Softw. 2002 Jan 10;7:1–38.
19. Montiel J, Read J, Bifet A, Abdessalem T. Scikit-Multiflow: A Multi-output Streaming Framework [Internet]. 2018 [cited 2023 Feb 20]. Available from: http://arxiv.org/abs/1807.04662
20. Bifet A, Holmes G, Pfahringer B, Kranen P, Kremer H, Jansen T, et al. MOA: Massive Online Analysis, a Framework for Stream Classification and Clustering. JMLR Workshop Conf Proc. 2010;11.

Appendix

Structure of a Predetermined Change Control Plan (PCCP) for anticipatory CE conformity assessment[5].

A. Description of Modifications

Planned modifications	*Description of individual proposed device modifications, including:* • *Types of modifications, e.g., improvement of quality characteristics (e.g., higher sensitivity and specificity), modifications related to device inputs, or modifications related to the device's use and performance (e.g., for use within a specific subpopulation)* • *Implementation methods, e.g., ML methods, including architecture and parameters, data pre-processing, or both*
Impact assessment	*Discussion of benefits and risks of implemented modifications, including:* • *Comparison of modified and original device* • *Appropriateness of the chosen approaches to ensure the safety and effectiveness of the device* • *Potential interactions between individual modifications given the collective impact of all planned modifications*

B. Modification Protocol

B.1 Data management

Person(s) in charge	*Who is involved in the data management? Name, function (e.g., Data Scientist)*
Procedure	*Description of procedure of management of new data, including:* • *Outline how those new data will be collected, annotated, curated, stored, retained, controlled, and used by the manufacturer for each modification, incl.* - *Quality assurance (QA) plan for determining which new data are appropriate for inclusion as part of an expanded training data set* - *data augmentation strategy that allows for additional training and independent test data to be added* • *Clarification of the relationship between the modification protocol data and the data used to train and test the initial and subsequent versions of the ML-DSF, incl.* - *Approach to the reference standard determination* • *Description of control methods preventing data or performance information leaking into the development process during modification development or assessment* - *strategy to monitor and document test dataset independence as well as control access to both the training and test datasets as additional data are being included and any revised algorithm is being retrained and tested*

B.2 Re-training

Person(s) in charge	*Who is involved in the re-training? Name, function (e.g., ML engineer)*
Procedure	*Description of re-training procedure, including:* • *Outline of re-training strategy that describes the objective of the retraining (e.g., modifications of processing steps and ML architecture)* • *Training intervals of new algorithm* • *Modified algorithm components as a result of the learning process* • *Definition of criteria that must be met during the re-training process to trigger a more comprehensive performance evaluation using the test dataset*

5 Based on the FDA draft guidance „Marketing Submission Recommendations for a Predetermined Change Control Plan for Artificial Intelligence/Machine Learning (AI/ML)-Enabled Device Software Functions" (2).

B.3 Performance evaluation

Person(s) in charge	*Who is involved in the performance evaluation? Name, function (e.g., ML engineer)*
Procedure	*Description of procedure for performance evaluation, including:* • *Appropriate metrics as performance targets* • *Test procedures and protocols, which may be applicable for that device and type of change* • *Intervals for technical evaluation* • *Definition of- appropriate measures to minimize information leakage about the test data set if part of it is re-used in multiple evaluations* • *Planned real-world monitoring of performance across data acquisition systems*

B.4 Update

Person(s) in charge	*Who is involved in the update procedure? Name, function (e.g., ML engineer)*
Procedure	*Description of update procedure, including:* • *Update plan including expected frequency of updates and whether the updates will be global (all devices use the same version of the algorithm) or local (multiple versions of the algorithm targeted for specific sub-populations are distributed)* • *Version tracking and control* • *Obsolescence planning* • *Requirements for host software/hardware requirements* • *Planned 'beta' release of the updated medical device algorithm concurrent with the previous version*

B.5 Communication with users

Person(s) in charge	*Who is involved in the communication with users? Name, function (e.g., RA manager)*
Procedure	*Description of communication procedure with users, including:* • *Notification of users of updates and any information that will be conveyed to users about the update (e.g., changes labelling or instruction for use)*

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