Software AI Best Practices for QMS and Regulatory Submissions

Annual IVD Regulatory Meeting
April 27-28, 2022

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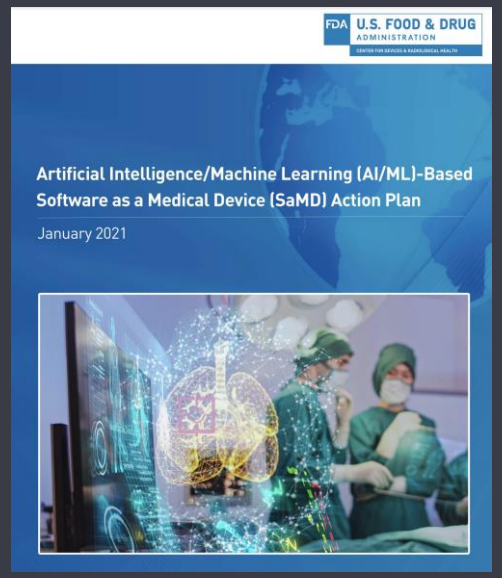
Agenda

- Quick intro
- Regulatory stuff
  - FDA AI/ML Developing Regulatory Landscape
- Quality stuff
  - QMS: Incorporate AI/ML in Design Controls and QMS

Intro

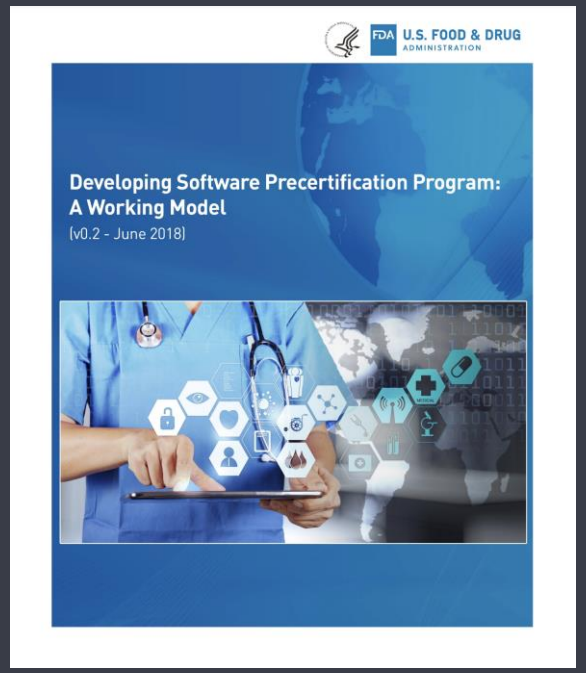
- Expert Consultant, NDA Partners
- Previous: QA leadership positions @
- 2017: FDA Digital Health Software Pre-Cert pilot
- >2008: Agile/Scrum, QMS/SDLC tools/Design Controls/DHF automation, ….
- MSEE, Doctor of Regulatory Science (USC)

FDA AI/ML Developing Regulatory Landscape

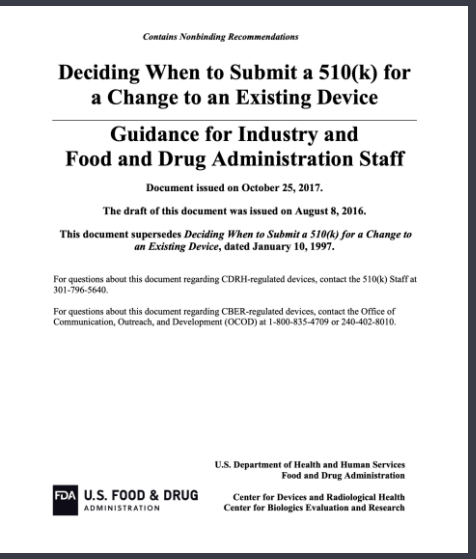


2021

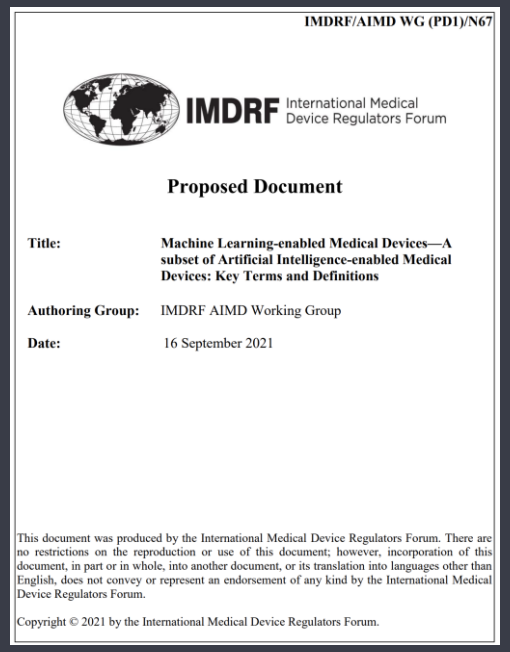
2019

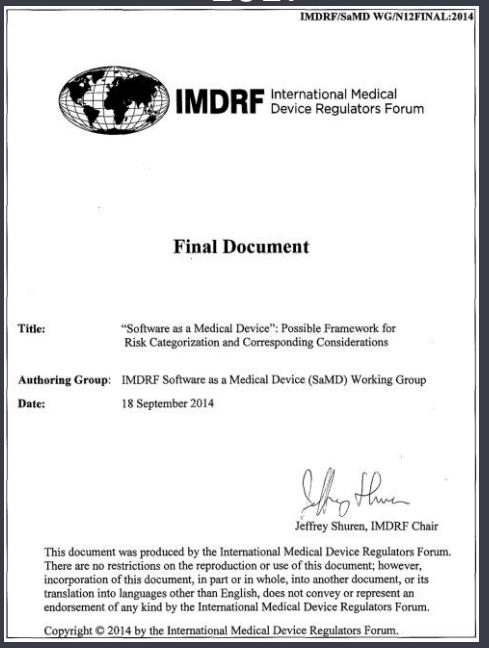


2018



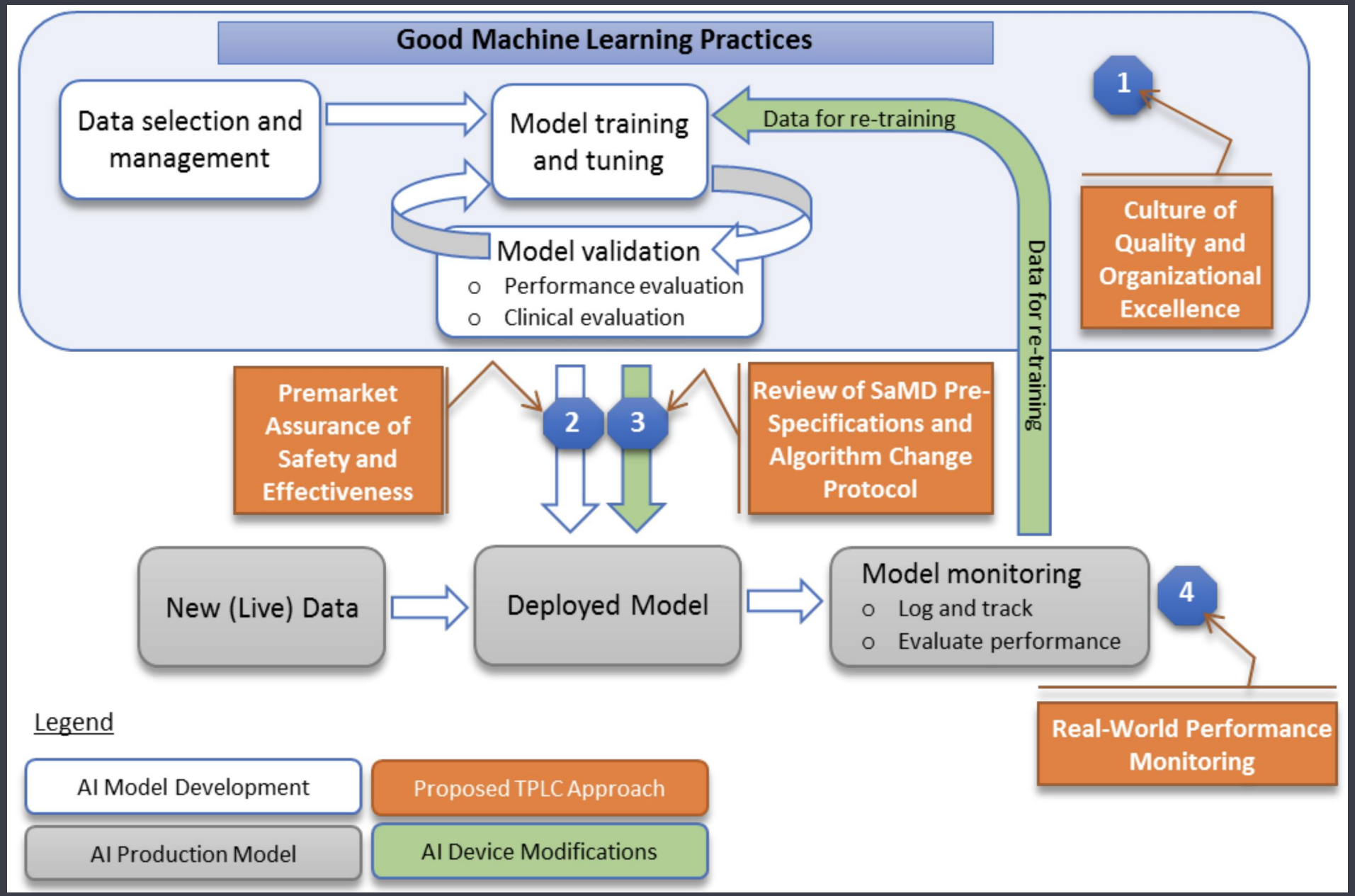
2017





2014

FDA's proposed regulatory framework: AI/ML-based SaMD discussion paper



2019

FDA's TPLC approach on AI/ML workflow

SPS (SaMD Pre-Specifications) and ACP (Algorithm Change Protocol)

FDA envisions a "predetermined change control plan" in premarket submissions, containing:

SPS: "what" the manufacturer intends the algorithm to become as it learns

- retraining and model update strategy

- Draws a "region of potential changes" around the initial specifications and labeling of the original device.
- Anticipated modifications to:
  - "performance"
  - "inputs"
  - changes to "intended use"

ACP: "how" the algorithm will learn and change while remaining safe and effective

- implement changes in a controlled manner

- Methods for risk control; Step-by-step delineation of the data and procedures to be followed
  - Data Management
  - Retraining
  - Performance Evaluation
  - Update Procedures

SPS and ACP, cont..

2019

AI/ML-based SaMD with approved SPS and ACP

YES

Software modifications decision tree requires new 510(k)?

Approved SPS + ACP

NO

YES

NO

FDA premarket review for reasonable assurance of safety and effectiveness
+
Establish SPS + ACP

Modification outside of "agreed SPS + ACP"?

NO

Document

YES

Premarket submission cleared or approved

Approved SPS + ACP

Modifications lead to a new intended use?

NO

Focused FDA review of SPS and ACP

YES

New approved SPS + ACP

FDA premarket review

Legend

Proposed regulatory pathway for new AI/ML-based SaMD

Proposed regulatory pathway for modifications for AI/ML-based SaMD

Endpoint for AI/ML modification

FDA's AI/ML-Based SaMD "Action Plan"

- Update the proposed regulatory framework (AI/ML-based SaMD paper)
  - Issue Draft Guidance on the Predetermined Change Control Plan

- Support development of GMLP (Good Machine Learning Practice)

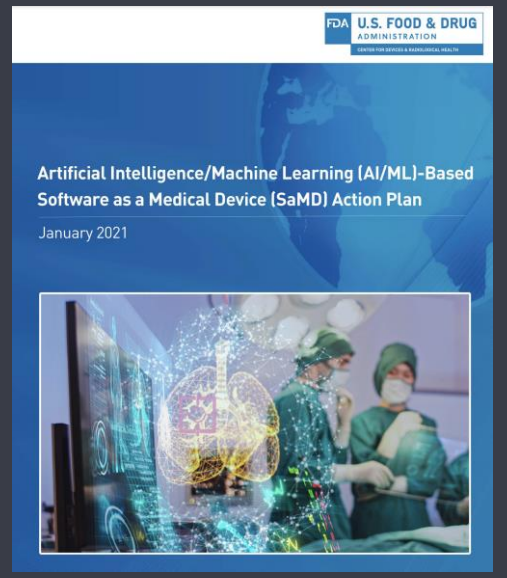
FDA U.S. FOOD & DRUG ADMINISTRATION | Health Canada Santé Canada | Medicines & Healthcare products Regulatory Agency

Good Machine Learning Practice for Medical Device Development: Guiding Principles

October 2021

- Support patient-centered approach, transparency
- Support efforts related to algorithm bias & robustness

- Advance real-world performance (RWP) programs



2021

AL/ML SaMD Categories: FDA's perspective

- Category #1: Machine's learning occurs during development. Once algorithm is in use, it no longer changes unless updated by a development team.
- Category #2: Software continuously learns and can update itself in response to real-world use.
- The examples of AI/ML-enabled medical devices marketed in the U.S. today fall within Category #1.
- FDA anticipates that as technology advances, medical devices will incorporate continuously learning technologies (Category #2), as well.

List of Artificial Intelligence and Machine Learning (AI/ML)-Enabled Medical Devices

Date of Final Decision	Submission Number	Device	Company	Panel (Lead)
06/17/2021	K203514	Precise Position	Philips Healthcare (Suzhou) Co., Ltd.	Radiology
06/16/2021	K202718	Qmenta Care Platform Family	Mint Labs, Inc., D/B/A. QMENTA	Radiology
06/11/2021	K210484	LINQ II Insertable Cardiac Monitor, Zelda AI ECG Classification System	Medtronic, Inc.	Cardiovascular
06/10/2021	K203629	IDx-DR	Digital Diagnostics Inc.	Ophthalmic
06/02/2021	DEN200069	Cognoa Asd Diagnosis Aid	Cognoa, Inc.	Neurology
05/19/2021	K210237	CINA CHEST	Avicenna.AI	Radiology
04/30/2021	K210001	HYPER AiR	Shanghai United Imaging Healthcare Co.,Ltd.	Radiology
04/23/2021	K203314	Cartesion Prime (PCD-1000A/3) V10.8	Canon Medical Systems Corporation	Radiology
04/23/2021	K203502	MEDO-Thyroid	MEDO DX Pte. Ltd.	Radiology
04/21/2021	K210556	Preview Shoulder	Genesis Software Innovations	Radiology
04/20/2021	K203610	Automatic Anatomy Recognition (AAR)	Quantitative Radiology Solutions, LLC	Radiology
04/19/2021	K203469	AI Segmentation	Varian Medical Systems	Radiology

- Varian Medical Systems Inc: AI Segmentation (K203469; April, 2021)

The significant differences in the subject device compared with the predicate device are:

1. Use of AI-based algorithms for automated segmentation and contouring
    a. Note: These algorithms are static and non-adaptive; they do not alter their behavior over time based on user input.
2. Cloud deployment and hosting of software components and algorithms

Implementing QMS for AI/ML

AI/ML QMS Considerations

- Is your QMS agile and efficient for today's software development?
  - Software releases: Quarterly? Monthly? Biweekly??

- Agile/Scrum method, and now AI/ML, will only require it more

- Question?

  AI/ML technology is here,

  ……. industry and users are ready

  …… FDA is ready, BUT

  …… Is your QMS ready for AI/ML??

AI/ML SaMD has unique QMS needs

Traditional Medical Devices

Design and Development → Manufacturing/ Operations (+ Suppliers) → Post-Market/ Commercialization

- Much longer (months – years)
- Less iterative

- Complaint Handling
- Adverse Event Reporting

(Compliance) Best Practices

SaMD

Software Design and Development (+ Open-source/SOUP/OTS SW) → Post-Market/ Commercialization

- Much shorter (weeks – months)
- Highly iterative

- Real-World Performance (RWP)

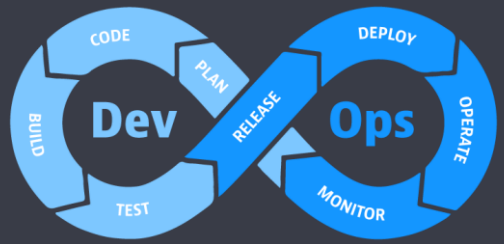
Best Practices (Efficiency)

Software Industry

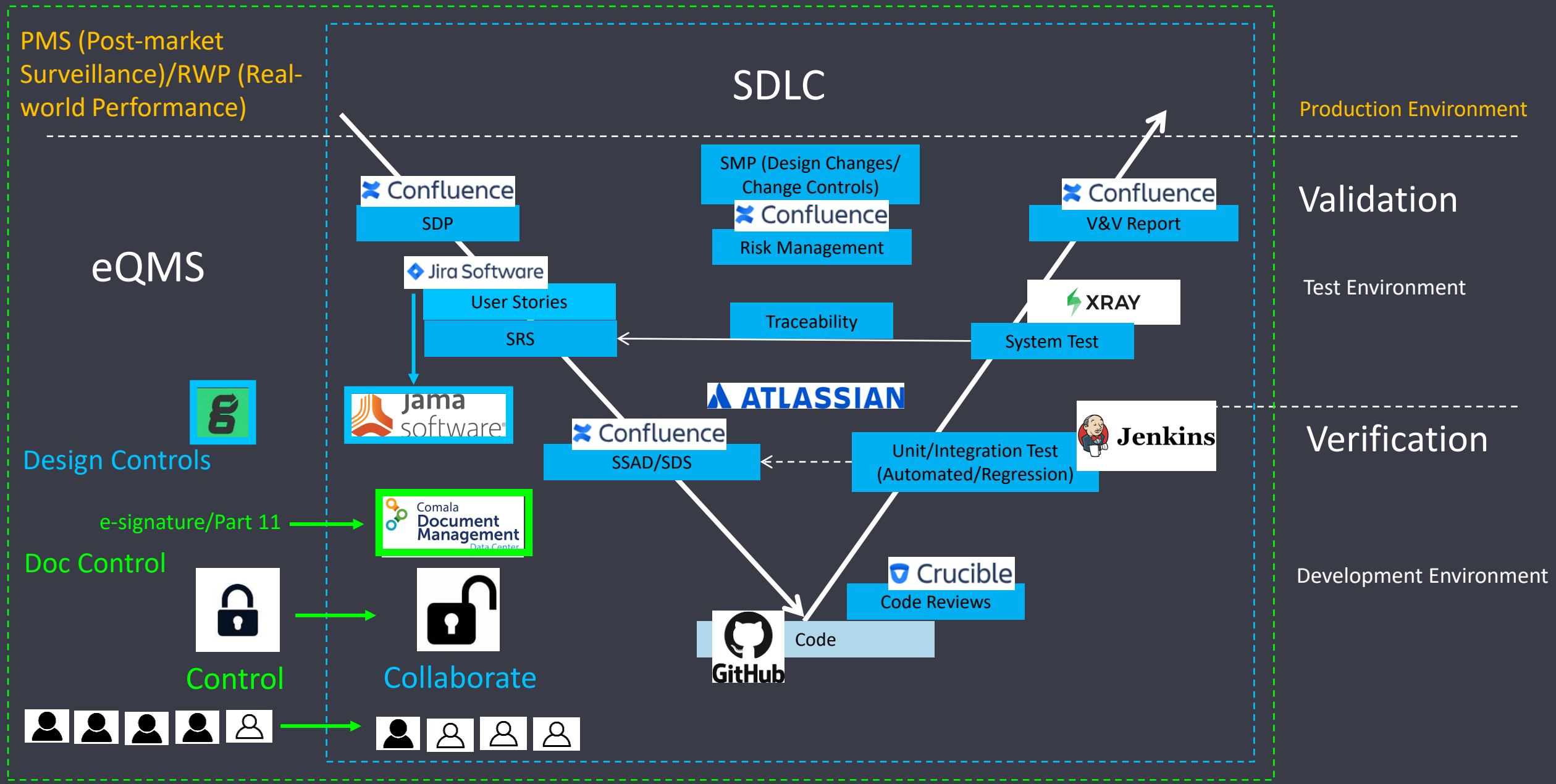
DevOps/ Continuous Integration (CI)

DevOps = Combines software development (Dev) and IT operations (Ops)

Short SDLC, Continuous delivery, high quality



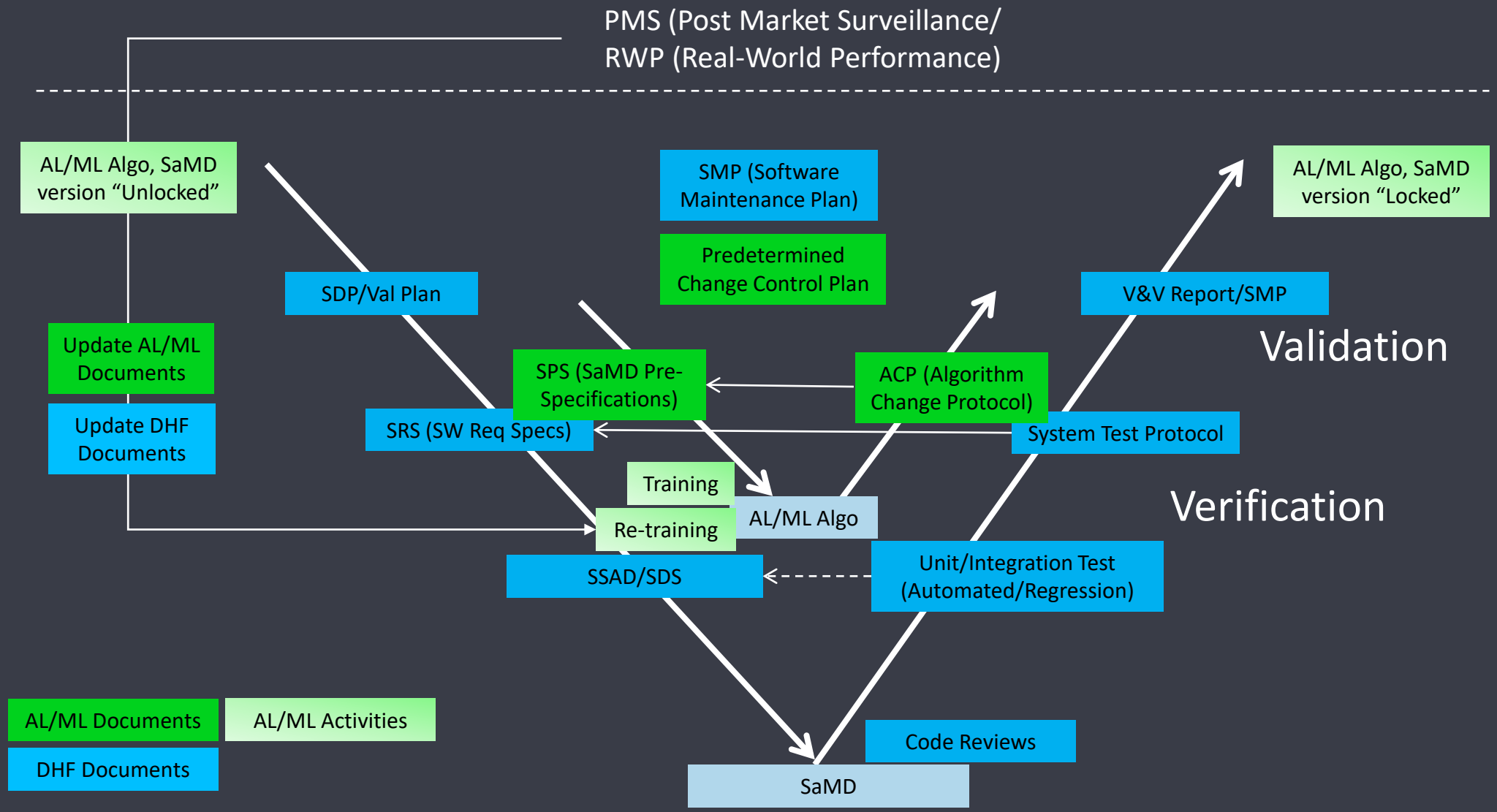
Building QMS around SDLC and Automating Design Controls/DHF using tools



Building agile and efficient QMS for highly-iterative software technologies

- Use software industry best practices; be agile
  - Agile/Scrum SDLC method
  - DevOps, Continuous Integration (CI)
- Follow GMLP (Good Machine Learning Practice)
- Use state-of-the-art SDLC tools (e.g. Atlassian and plug-ins)
  - Semi-automate Design Controls and DHF production and maintenance
- Build QMS around SDLC tools
  - Design Controls: Ideally integrated w/ or included within eQMS (Greenlight Guru?)
    - Standalone: e.g. JAMA (JIRA/Atlassian plug-in)
  - Doc Control: Consider building e-records/e-signatures/Part 11 functionality in SDLC/DHF tools (e.g. Comala-Atlassian plug-in)
  - PMS: RWP (proactive approach w/ AL/ML/SaMD performance/clinical metrics; not complaint handling/AER per se)
- Remove Logistical barriers, inefficiencies:
  - Bring the (non-software) audience (reviewers/approvers) into SDLC environment
  - Hire documentation engineer if necessary
    - Let all SMEs do what they do best (e.g. software engineer develop software)
    - Design Assurance Engineers (design controls compliance) already a standard practice

Handling AI/ML documentation w/ Design Controls/DHF



Recap

- AI/ML in medical devices is here, and it's a great thing
- Regulatory landscape is evolving but heading in a right-direction (thanks FDA)
- QMS for AI/ML: Lagging behind?
  - Innovation is also needed here….
  - We need to be talking more on how to best handle not only AI/ML in particular but also (dynamic nature of) software in general

Thank You

Questions?