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Modifications to AI/ML-based SaMD

The Proposed Regulatory Framework by the FDA

Swiss Medtech SaMD Event, 25.03.2021

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Disclaimer

- This talk is based on the **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 issued by the **FDA**
- The views and opinions expressed in the following presentation are those of the individual author
- I am a Software Engineer – I like programming

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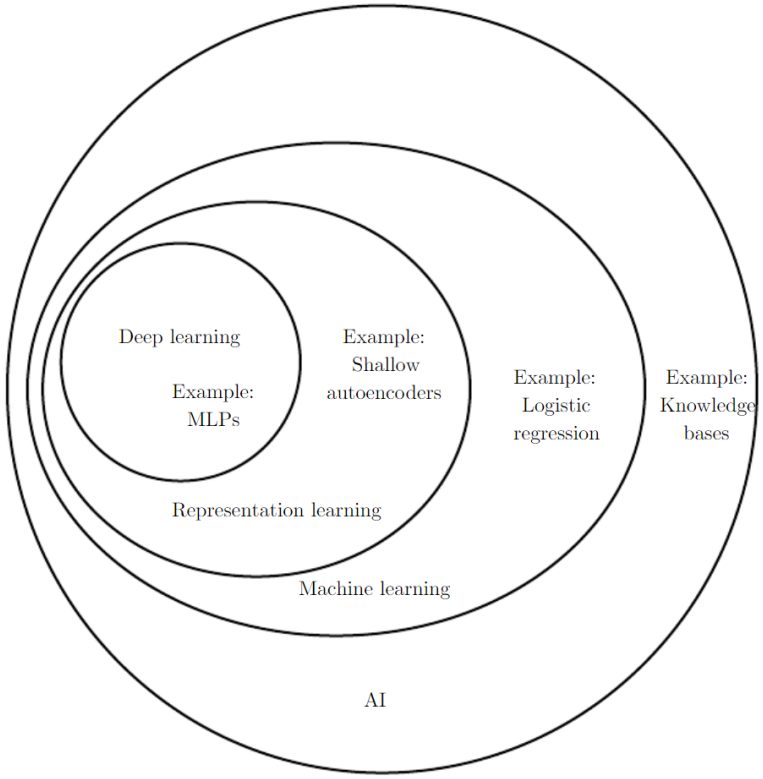
Introduction – AI/ML

AI:

- Artificial Intelligence
- The science and engineering of making intelligent machines, especially intelligent computer programs[1]

ML:

- Machine Learning, an AI technique
- Learning a specific task based on training data (experience)
- Performing the learnt task on new, previously unseen test data



[1] http://jmc.stanford.edu/articles/whatisai/whatisai.pdf

Introduction – AI/ML-based SaMD

Locked: same input always produces the same output (fixed function, deterministic).
Adaptive: same input can result in different outputs. The Algorithm changes its behavior.

SaMD:

- Regulated by the FDA
- Manufacturers submit a marketing application to FDA prior to initial distribution (type and requirements based on the risk of the SaMD)
- Modifications:
  - Premarket submission may be required (**risk-based**)
  - Guidance document on when to submit a 510(k) for a software change
  - Typically considered to be **locked**

AI/ML-based SaMD:

- Currently regulated the same way as “regular” SaMD
- Great benefit: can learn from real-world use and experience; can improve its performance (is **adaptive**)

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Introduction – Current State

Locked: same input always produces the same output (fixed function, deterministic).
Adaptive: same input can result in different outputs. The Algorithm changes its behavior.

Current state:

- FDA has approved several AI/ML-based SaMD (typically **locked** algorithms)
- Changes would likely require FDA premarket review
- The traditional paradigm of FDA's regulation was not designed for **adaptive** technologies
- FDA issued a discussion paper in April of 2019: [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]

When is a premarket submission required for an adaptive SaMD with AI/ML?

(probably almost always under the current approach)

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AI/ML-based SaMD – Risk Categorization

Proposed regulatory framework Proposal:

- Total Product Lifecycle (TPLC) regulatory approach
- Facilitating a rapid cycle of product improvement
- Based on the risk categorization principles of the International Medical Device Regulators Forum (IMDRF):

State of healthcare situation or condition	Significance of information provided by SaMD to healthcare decision		
	Treat or diagnose	Drive clinical management	Inform clinical management
Critical	IV	III	II
Serious	III	II	I
Non-serious	II	I	I

Significance: intended use of the information provided by the SaMD

State of healthcare situation or condition: intended user, disease, condition or population

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AI/ML-based SaMD – Types of Modifications

Categories of modifications:

- **Performance** – clinical and analytical performance
- **Inputs** – change in inputs used and their clinical association to the output
- **Intended use** – change of the IMDRF risk categorization

Types of modifications:

Type 1: modifications related to **performance** with **no change** to the **inputs** or **intended use**.

Type 2: modifications related to **inputs** with **no change** to the **intended use**.

Type 3: modifications related the **intended use**.

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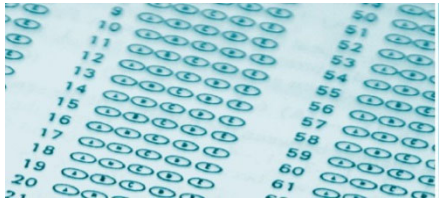
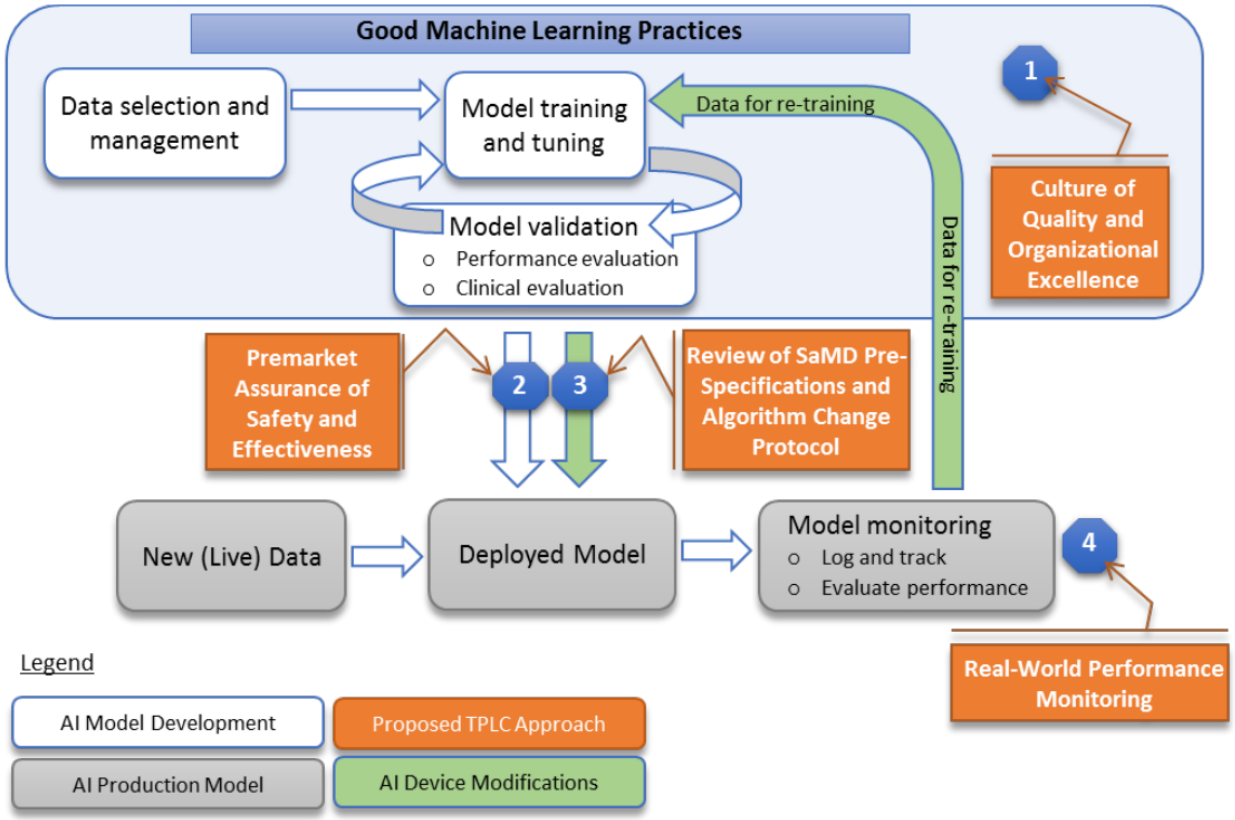


TPLC Approach – Overview



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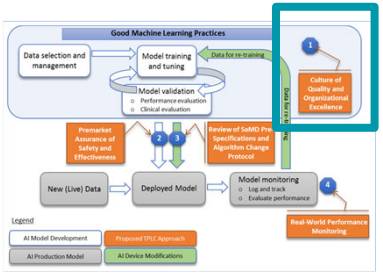
TPLC Approach – 1. Culture of Quality

Quality:

- Manufacturers must have an established an appropriate quality system
- Conformity to appropriate standards and regulations
- Embrace the excellence principles of culture of quality and organizational excellence (Software Precertification Program)
- Demonstrate analytical and clinical validation as described in the SaMD: Clinical Evaluation Guidance

Good Machine Learning Practices (GMLP):

- Perform and “live” GMLP
- Analyze relevance of available data to the clinical problem
- Separation between training, tuning and test datasets
-



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TPLC Approach – 2. Premarket Assurance of Safety and Effectiveness

Predetermined change control plan:

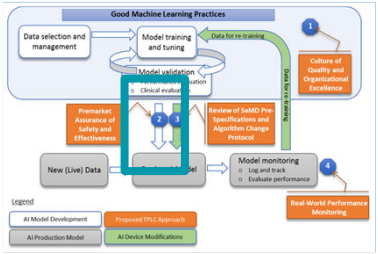
- Can be submitted during the initial premarket review (voluntary)
- Plan anticipating future modifications to the SaMD
- Consisting of **SaMD Pre-Specifications (SPS)** and the associated methodology **Algorithm Change Protocol (ACP)**

SaMD Pre-Specifications (SPS) :

- Anticipated modifications to **performance**, **inputs** or **intended use**
- Draws a region of potential changes around the initial specifications
- The **"what"** the manufacturer plans the algorithm to become

Algorithm Change Protocol (ACP) :

- Plan on methodology to achieve and appropriately control the risks of the intended modifications
- The **"how"** the algorithm will learn



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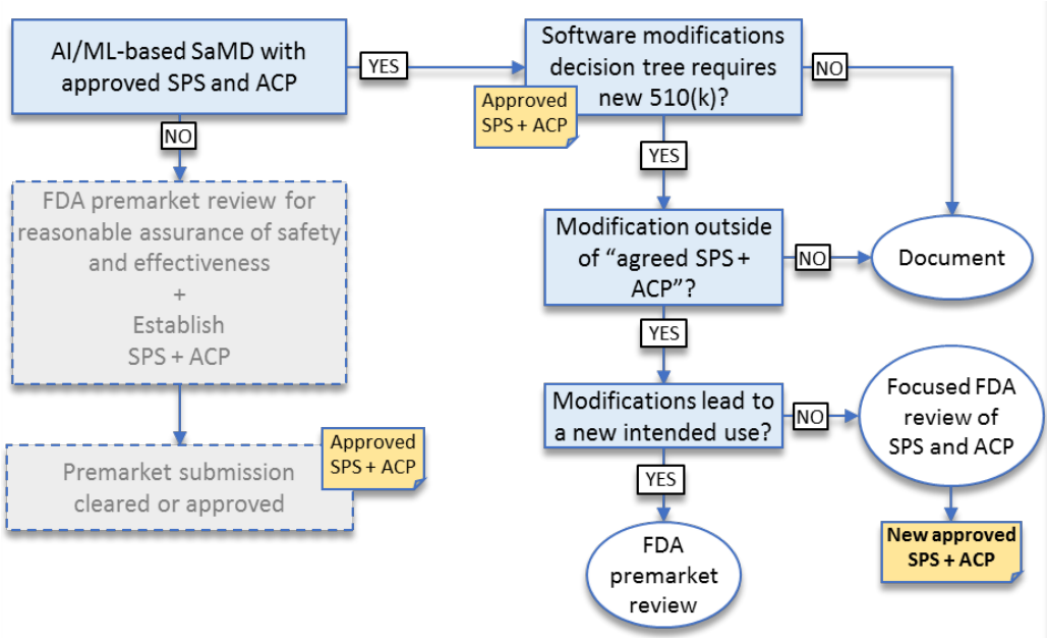
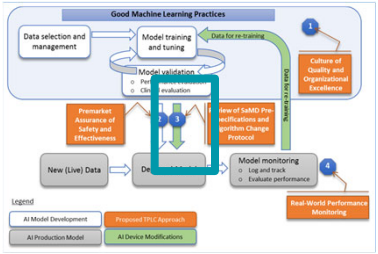
TPLC Approach – 3. Modifications with an established SPS and ACP





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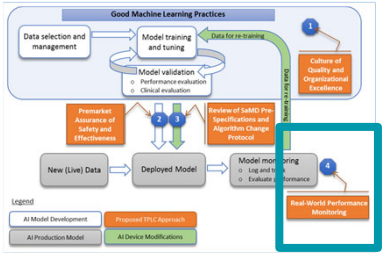
TPLC Approach – 4. Transparency and real-world performance monitoring

Transparency:

- Implement appropriate mechanisms that support transparency
- Transparency about function and modifications
- Provide periodic reporting to the FDA
- Communication procedures on how users will be notified of updates
- …

Real-world performance monitoring:

- Gathering real-world data for insight, improvement opportunities
- Respond proactively to safety or usability concerns
- …



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Conclusions – State and Personal

FDA …

- … acknowledges that the current framework was not designed for adaptive techniques
- … **proposed** a concrete framework on how AI/ML-based SaMD **could** be handled in future
- … requested **feedback** from the community (hence *Discussion Paper and Request for Feedback*)
- … presented an Action Plan on how they intend to proceed

Personally as a developer I think …

- … the proposed, TPLC-based framework makes sense
- … its great that FDA involves the community and industry
- … there are still open questions

[1] http://jmc.stanford.edu/articles/whatisai/whatisai.pdf

Conclusions – Comparison to the EU

	Today	Tomorrow
FDA	- No special way to deal with AI/ML-based SaMD - Proposed a new framework - Mainly locked algorithms	- AI/ML tailored regulatory framework - Shift towards quality & transparency - Manufacturers get more responsibility
EU	- No special way to deal with AI/ML-based MDSW - Only locked algorithms	- Expected to publish plans - Maybe Salvatore will tell us?

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Outlook

According to the recently published Action Plan (January 2021):

- FDA will develop an update to the proposed regulatory framework
- Issuance of a Draft Guidance on the Predetermined Change Control Plan (in 2021)
- Encourage harmonization of Good Machine Learning Practices
- Hold a public workshop on how device labelling supports transparency/trust in AI/ML-based devices
- Support regulatory science efforts to develop methodology for the evaluation of AI/ML-based devices
- Support the piloting of real-world performance monitoring

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References

Sources:

- FDA Discussion Paper (April 2019): https://www.fda.gov/media/122535/download
- FDA Action Plan (January 2021): https://www.fda.gov/media/145022/download
- AI/ML Topics and Image: https://www.deeplearningbook.org/

More Information:

- FDA AI/ML-Based SaMD: https://www.fda.gov/medical-devices/software-medical-device-samd/artificial-intelligence-and-machine-learning-software-medical-device
- Introduction to machine learning for students and practitioners: https://www.deeplearningbook.org/

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Questions

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