Intro to Regulatory Affairs in Software as Medical Devices (SaMD)

Yu-Wen Wang, Dec 15, 2022

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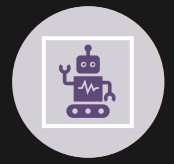
This presentation focuses on standalone software.

All the references are in the notes

Agenda

What can be considered a SaMD

Cybersecurity



AI/ML (Artificial Intelligence / Machine Learning) SaMD

What is SaMD?

Device : means an instrument, apparatus, contrivance or other similar article, or an in vitro reagent, including a component, part or accessory of any of them, that is manufactured, sold or represented for use in

- diagnosing, treating, mitigating or preventing a disease, disorder or abnormal physical state, or any of their symptoms
- restoring, modifying or correcting the body structure or the functioning of any part of the bodies
- diagnosing pregnancy
- caring during pregnancy or at or after the birth of the offspring, including caring for the offspring, or
- preventing conception

Software is not a medical device	The software is a medical device and part of a medical device.
The software is a medical device and accessories of a medical device.	The software is a stand-alone medical device

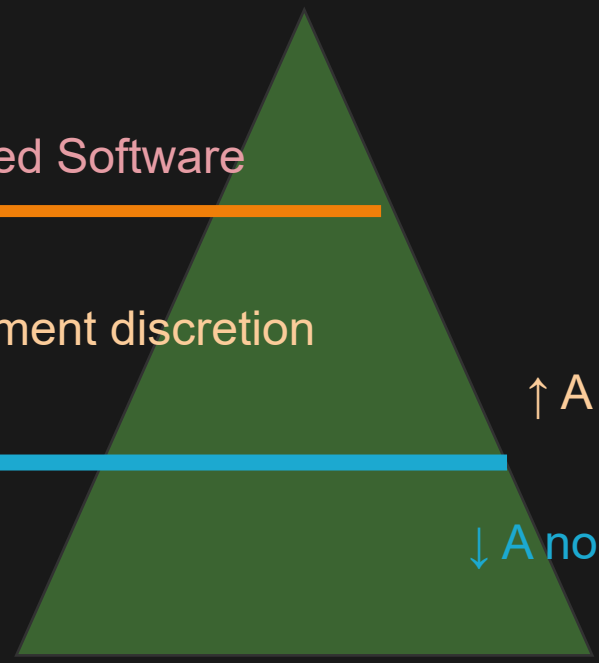
Some Examples – Are Them Also Regulated?

- Period tracking apps
- Baby monitors (measures the oxygen level and the heart rate and rhythm of babies)
- Telemedicine Software
- Patient Data Management Systems
- Clinical Decision Support Software
- Software for medical training purposes
- Patient portal (e.g. **carnetsante.gouv.qc.ca)**
- Software provides classifications of tumour stage
- Pre-hospital Electrocardiograph (ECG) System

MANUAL ON BORDERLINE AND CLASSIFICATION IN THE COMMUNITY REGULATORY FRAMEWORK FOR MEDICAL DEVICES
MDCG 2019-11 Guidance on Qualification and Classification of Software in Regulation (EU) 2017/745 – MDR and Regulation (EU) 2017/746 – IVDR
FDA guidance - Changes to Existing Medical Software Policies Resulting from Section 3060 of the 21st Century Cures Act
FDA guidance - Policy for Device Software Functions and Mobile Medical Applications

Regulations for SaMDs - Overview

Conditions
- Meet the definition of device - Regulated as a device
- May meet the def. of SaMD but regulatory authorities intended to not put regulatory oversight
- Does not meet the definition of device



↑ Regulated Software

↕ Enforcement discretion

↑ A medical device

↓ A non-medical device

Note: Depends on which regulatory body you are working with:

- the definition of Medical Device and/or Software as Medical Device varies
- the enforcement discretion list(s) varies

Based on the Intended Use - HC

Health Canada ‘s interpretation of medical purposes:

- Intended to acquire, process, or analyze a medical image, or a signal from an in vitro diagnostic device or a pattern/signal from a signal acquisition system or imaging device, OR
- Intended for the purpose of supporting or providing recommendations to health care professionals, patients or non-healthcare professional caregivers about prevention, diagnosis, treatment, or mitigation of a disease or condition.

Software that does not have a direct impact on the diagnosis, treatment, or management of an individual's disease, disorder, abnormal physical state or symptoms

- Software intended for administrative support of a healthcare facility,
- Software that enables clinical communication and workflow including patient registration, scheduling visits, voice calling, video calling,
- Software intended for maintaining or encouraging a healthy lifestyle, such as general wellness apps, and
- Software intended to serve as electronic patient records or tools to allow a patient to access their personal health information.

Based on the Intended Use - FDA

21st Century Cures Act amended the definition of “Device” in the FD&C Act to **exclude** certain software functions:

(A) for administrative support of a health care facility, including […];

(B) for maintaining or encouraging a healthy lifestyle and is unrelated to the diagnosis, cure, mitigation, prevention, or treatment of a disease or condition; (General Wellness Devices)

(C) to serve as electronic patient records, including patient-provided information, to the extent that such records are intended to transfer, store, convert formats, or display the equivalent of a paper medical chart, so long as—

> (i) such records were created, stored, transferred, or reviewed by health care professionals, or by individuals working under supervision of such professionals;
>
> (ii) such records are part of health information technology[…]
>
> (iii) such function is not intended to interpret or analyze patient records, including medical image data, for the purpose of the diagnosis, cure, mitigation, prevention, or treatment of a disease or condition;

(D) for transferring, storing, converting formats, or displaying clinical laboratory test or other device data and results, findings by a health care professional with respect to such data and results, general information about such findings, and general background information about such laboratory test or other device, unless such function is intended to interpret or analyze clinical laboratory test or other device data, results, and findings...

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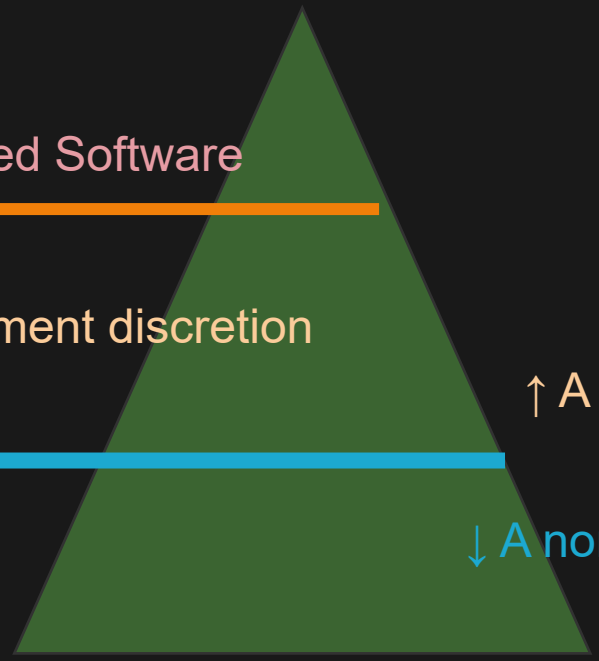

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Clinical/Patient Decision Support

Health Canada / FDA both determined that the software meets all of the four criteria outlined below –may not meet the device definition - therefore would not be subject to the Regulations

- Software that is not intended to acquire, process, or analyze a medical image or a signal from an IVDD or a pattern/signal from a signal acquisition system
- Software that is intended to display, analyze, or print medical information about a patient or other medical information (such as demographic information, drug labelling, clinical guidelines, studies, or recommendations).
- Software that is only intended to support a health care professional, patient or non healthcare professional caregiver in making decisions about prevention, diagnosis, or treatment of a disease or condition.
- Software that is not intended to replace the clinical judgement of a health care professional to make a clinical diagnosis or treatment decision regarding an individual patient.

FDA - Device Software Functions (DSF) and Mobile Medical Applications (MMA) Guidance: the software function

- provide or facilitate supplemental clinical care, by coaching or prompting, to help patients manage their health in their daily environment, without providing specific treatment or treatment suggestions
- help patients communicate with health care professionals by supplementing or augmenting the data or information by capturing an image for patients to convey to their health care professionals about potential medical conditions
- perform simple calculations routinely used in clinical practice

FDA - Digital Health Policy Navigator

Health Canada Software guidance

- Step 1: Is the software function intended for a medical purpose?
- Step 2: Is the software function intended for administrative support of a health care facility?
- Step 3: Is the software function intended for maintaining or encouraging a healthy lifestyle?
- Step 4: Is the software function intended to serve as electronic patient records?
- Step 5: Is the software function intended for transferring, storing, converting formats, or displaying data and results?
- Step 6: Is the software function intended to provide clinical decision support?
- Step 7: Does the Device Software Functions and Mobile Medical Applications Guidance apply?

Medical purposes

Exclusion criteria

Partially in the exclusion criteria

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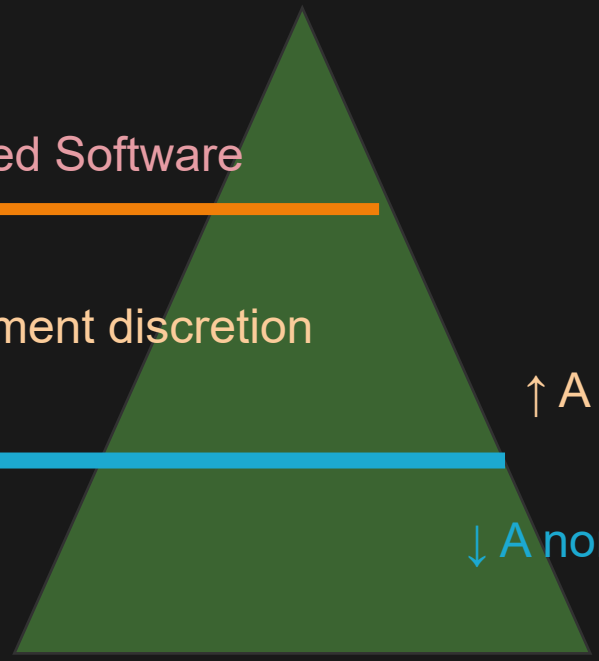

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Regulatory Concept – IMDRF

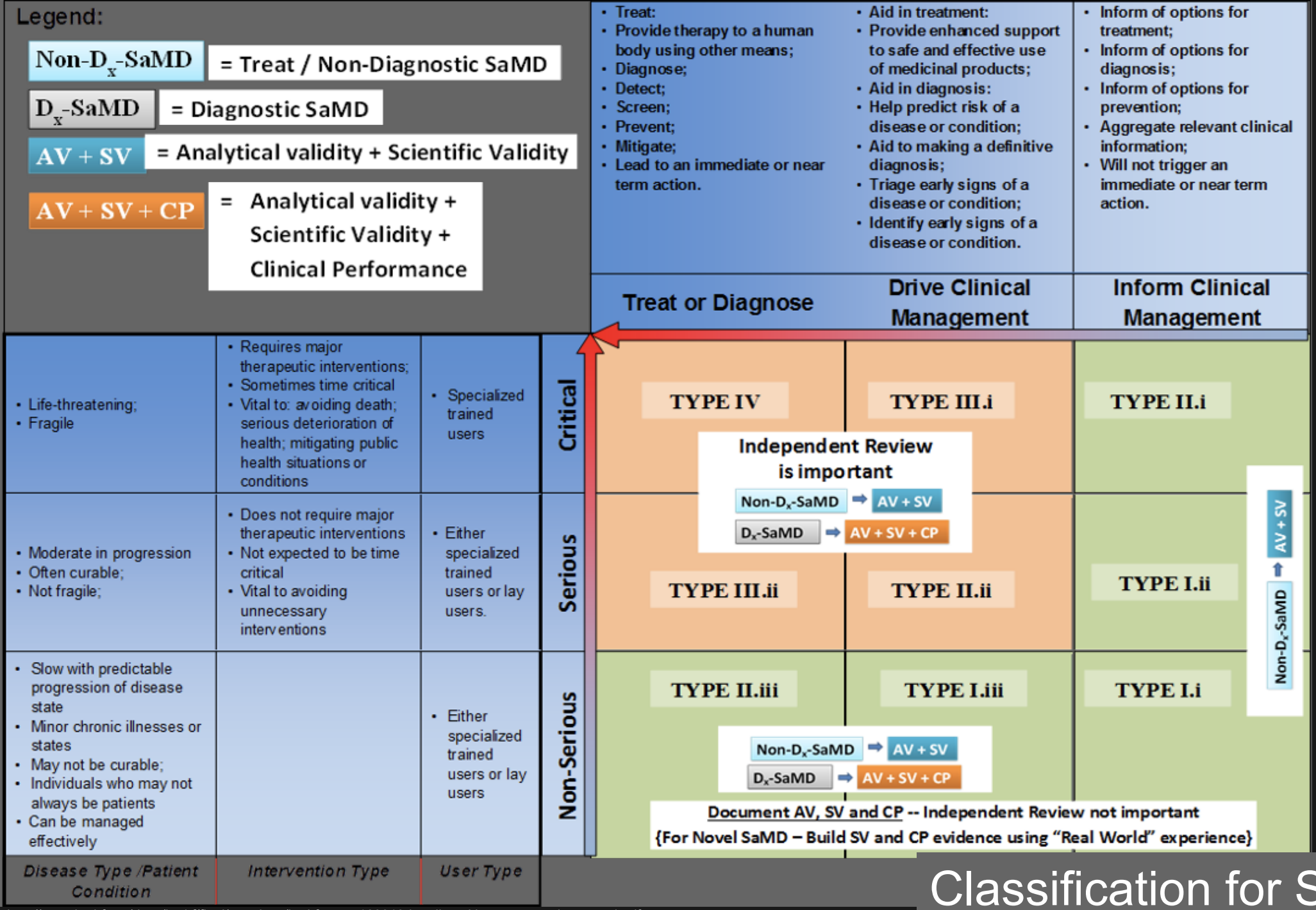
Criticality of context

- Critical situation or condition – where accurate and/or timely diagnosis or treatment action is vital to avoid death, long-term disability or other serious deterioration of health of an individual patient or to mitigating impact to public health.
- Serious situation or condition – where accurate diagnosis or treatment is of vital importance to avoid unnecessary interventions
- Non-Serious situation or condition – where an inaccurate diagnosis and treatment is important but not critical for interventions

Significance of information

- To treat or to diagnose
  - To provide therapy to a human body;
  - To diagnose/screen/detect a disease or condition
- To drive clinical management
  - To aid in treatment by providing enhanced support to safe and effective use of medicinal products or a medical
  - device.
  - To aid in making a definitive diagnosis.
  - To triage or identify early signs of a disease or conditions.
- To Inform clinical management
  - To inform of options
  - To provide clinical information by aggregating relevant information

http://www.imdrf.org/docs/imdrf/final/meetings/imdrf-meet-140829-washington-presentation-samd.pdf



Classification for SaMD - IMDRF

http://www.imdrf.org/docs/imdrf/final/meetings/imdrf-meet-160913-brazil-working-group-update-samd.pdf

Example 1:

Software that provides patients with simple tools to organize and track their health information. The information is intended to be shared with a healthcare provider as part of a pre-diabetes management plan.

No; the software is not intended for a medical purpose as outlined in the definition of device

- The software is not intended for diagnosing, treating, mitigating or preventing a disease.
- The software does not restore, modify, or correct body structure or functioning.
- The software does not diagnose pregnancy, is not intended for use during pregnancy or after birth, and the software does not prevent conception.

https://www.canada.ca/content/dam/hc-sc/documents/services/drugs-health-products/medical-devices/application-information/guidance-documents/software-medical-device-guidance-document/examples/software-medical-device-guidance-examples.pdf

Example 2:

Software that provides a diabetic patient with simple tools to organize and track their health information. The healthcare professional can input medical information for diabetes-related conditions such as kidney and eye function as well as drug dosage. The software also obtains data from a closed-loop blood glucose monitor. The software analyzes the information collected to provide early diagnosis of a diabetic emergency. When a patient experiences a diabetic emergency, the software will alert the healthcare professional and use the analyzed information to make treatment decisions based on the patient's unique health profile

Yes; the software is intended to analyze measurements from a monitoring device and is intended to provide recommendations to healthcare professionals about treatment or mitigation of diabetes.

https://www.canada.ca/content/dam/hc-sc/documents/services/drugs-health-products/medical-devices/application-information/guidance-documents/software-medical-device-guidance-document/examples/software-medical-device-guidance-examples.pdf

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Classification: The information provided by the SaMD is intended to be used to diagnose a diabetic emergency and make treatment decisions. Therefore, the software is treating and diagnosing.

An accurate diagnosis of diabetic emergency is vital to avoid death, long-term disability or other serious deterioration of health of a patient. Therefore, the software is intended for a critical situation.

https://www.canada.ca/content/dam/hc-sc/documents/services/drugs-health-products/medical-devices/application-information/guidance-documents/software-medical-device-guidance-document/examples/software-medical-device-guidance-examples.pdf

Example 3:

Breast imaging software intended for use with a digital mammography system. The software displays images from multiple modalities, including X-ray, ultrasound and magnetic resonance imaging. The software allows selection, display, manipulation, quantification (i.e. measurements such as area and distance within a region of interest), annotation, printing, and Digital Imaging and Communications in Medicine (DICOM) image transfer. Following review of the images by a primary radiologist, the software analyzes digital mammography images and identify regions of interest, such as microcalcification clusters and density masses, which may warrant further review.

Yes; the software is intended to acquire, process, or analyze medical images for healthcare professionals review and warrant healthcare professionals for further review.

https://www.canada.ca/content/dam/hc-sc/documents/services/drugs-health-products/medical-devices/application-information/guidance-documents/software-medical-device-guidance-document/examples/software-medical-device-guidance-examples.pdf

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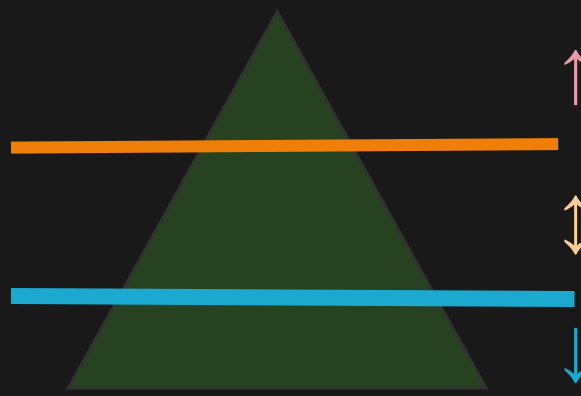
Classification: The information provided by the SaMD may trigger an immediate or near-term action. Therefore, the software is driving clinical/patient management
The information provided by the SaMD is used to aid in the next treatment intervention of a patient where the intervention is not normally expected to be time critical in order to avoid death, long-term disability, or other serious deterioration of health. Therefore, the software is intended for a Serious situation.

https://www.canada.ca/content/dam/hc-sc/documents/services/drugs-health-products/medical-devices/application-information/guidance-documents/software-medical-device-guidance-document/examples/software-medical-device-guidance-examples.pdf

Example 4:

An administrative software which has warning messages based on the current clinical practice guidance

- **US**: FDA may say it is not a medical device if the basis of information can be reviewed Independently by health care professionals (HCPs) and provide list of options.
- **Canada**: Health Canada may say that is a non-medical device and not subject to oversight if the criteria are met, and the users can be patients or non-healthcare professional caregivers.
- **EU**: MDCG says (in guidance p.20) it is a medical device function if this module provides additional information that contributes to follow-up (e.g. generate alarms)



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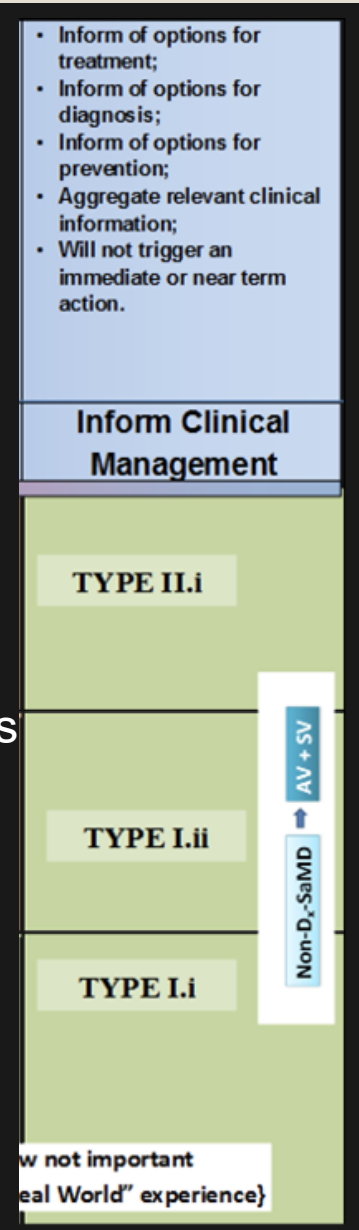

Exercise – Regulated? If so, the risk level?

- Period tracking apps
- Baby monitors
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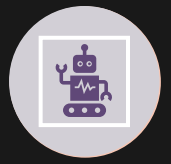
Cybersecurity

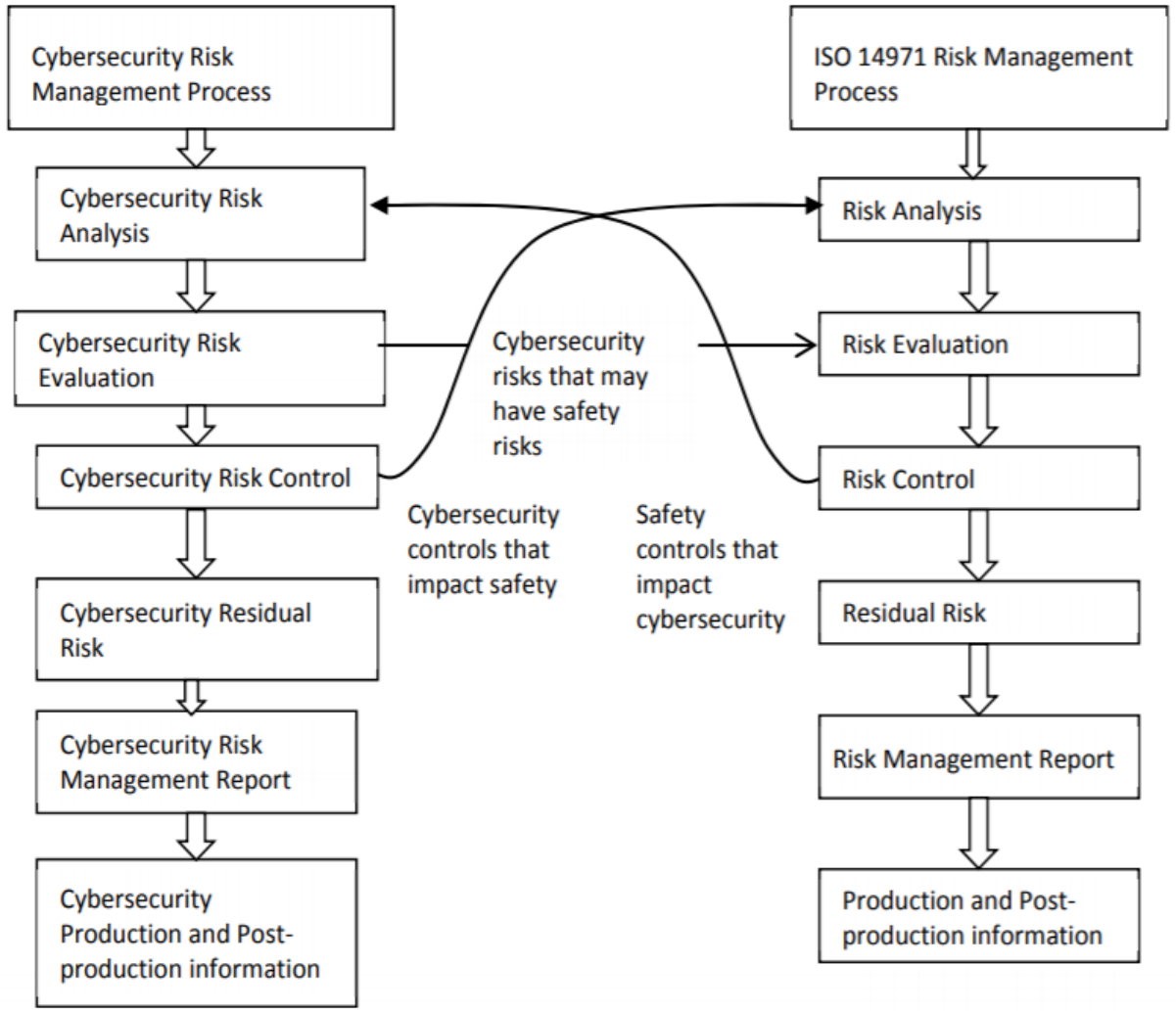


AI/ML (Artificial Intelligence / Machine Learning) SaMD

Cybersecurity

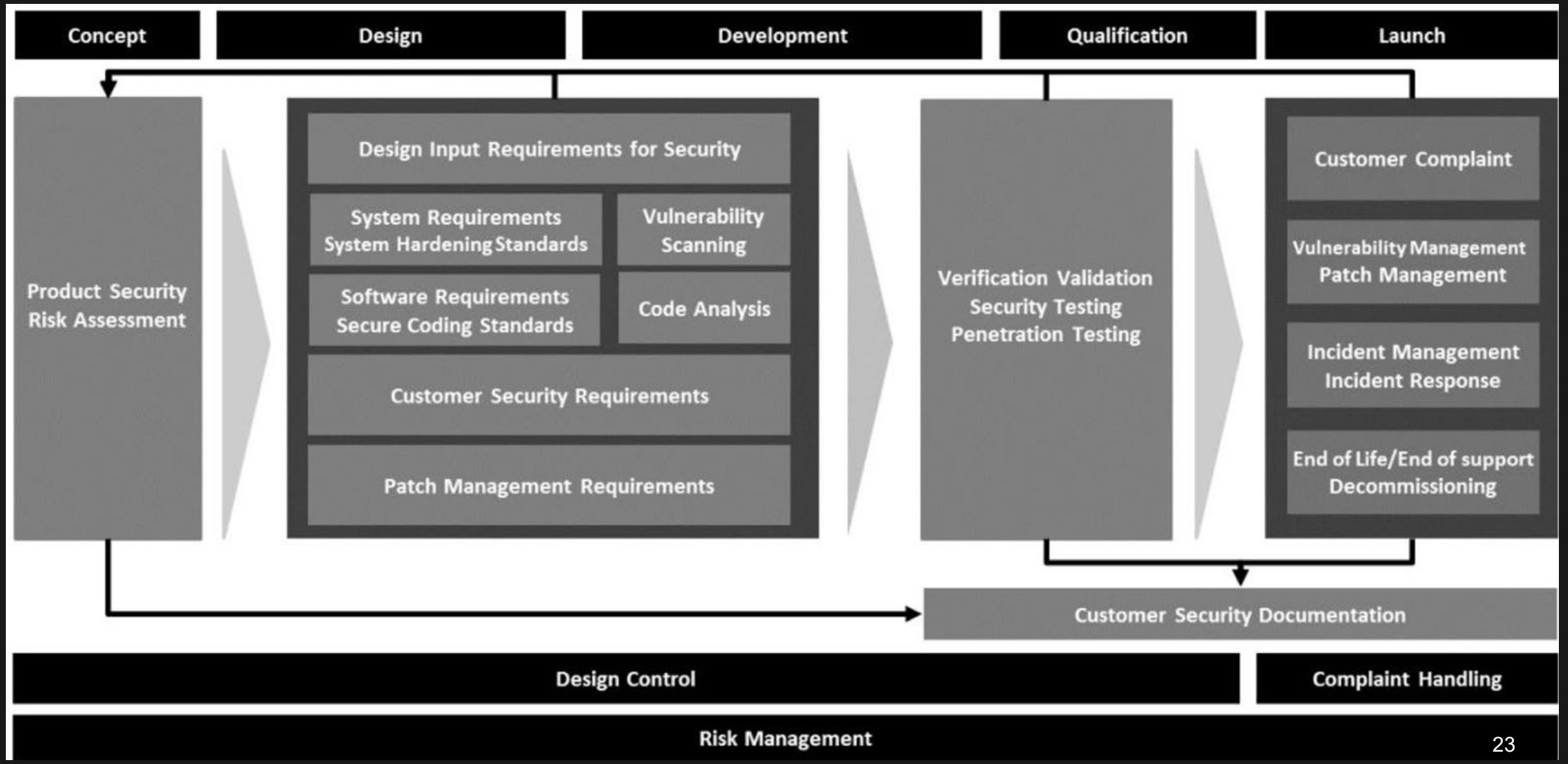
- Security Design
- Risk Management
- Testing
- Monitoring plan
- Response Plan
- Security & Safety RMP

Figure 2 - Illustrating the relationship between cybersecurity risk management process and safety risk management process as defined in ISO 14971 (AAMI TIR57:2016)

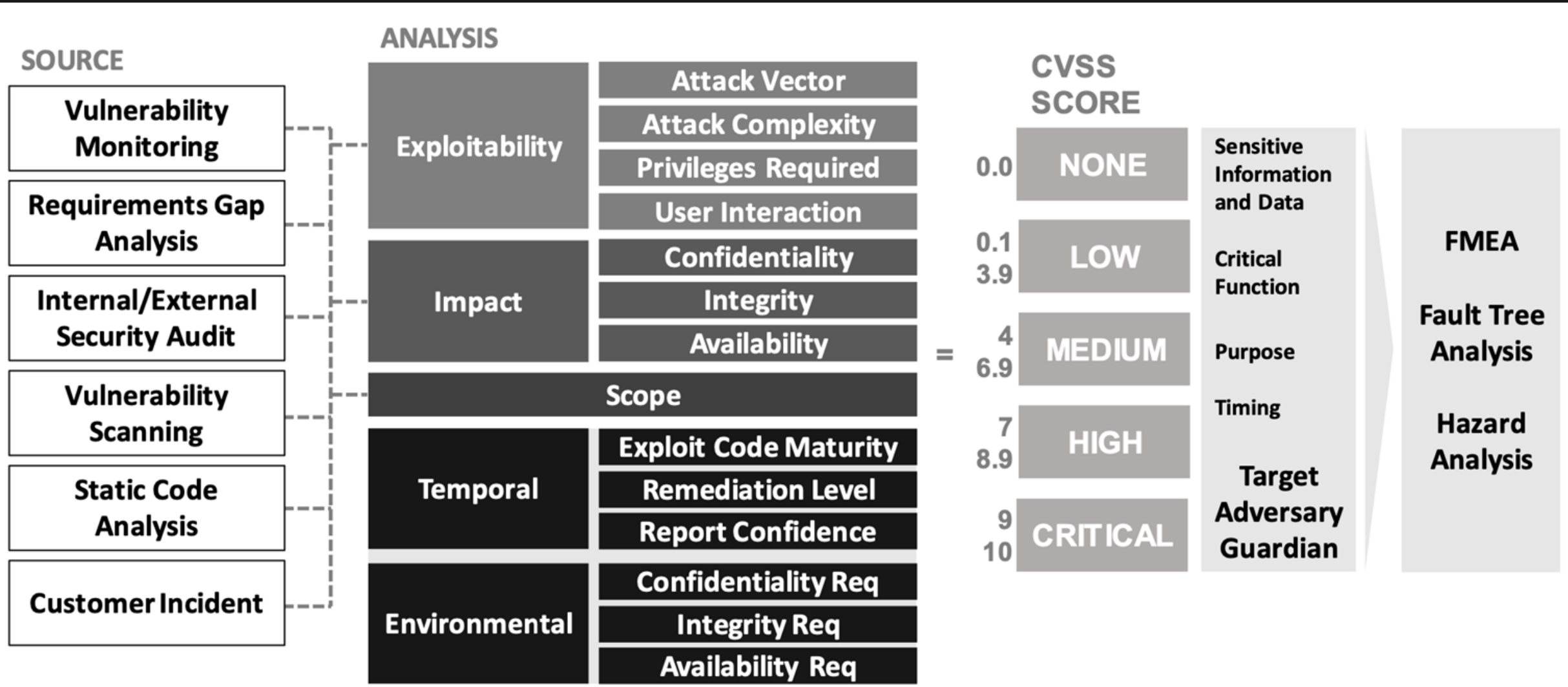


https://www.fda.gov/regulatory-information/search-fda-guidance-documents/content-premarket-submissions-management-cybersecurity-medical-devices
https://www.fda.gov/regulatory-information/search-fda-guidance-documents/postmarket-management-cybersecurity-medical-devices
https://www.canada.ca/en/health-canada/services/drugs-health-products/medical-devices/application-information/guidance-documents/cybersecurity.html
https://www.tga.gov.au/publication/medical-device-cyber-security-guidance-industry
https://ec.europa.eu/docsroom/documents/41863
http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-200318-pp-mdc-n60.pdf

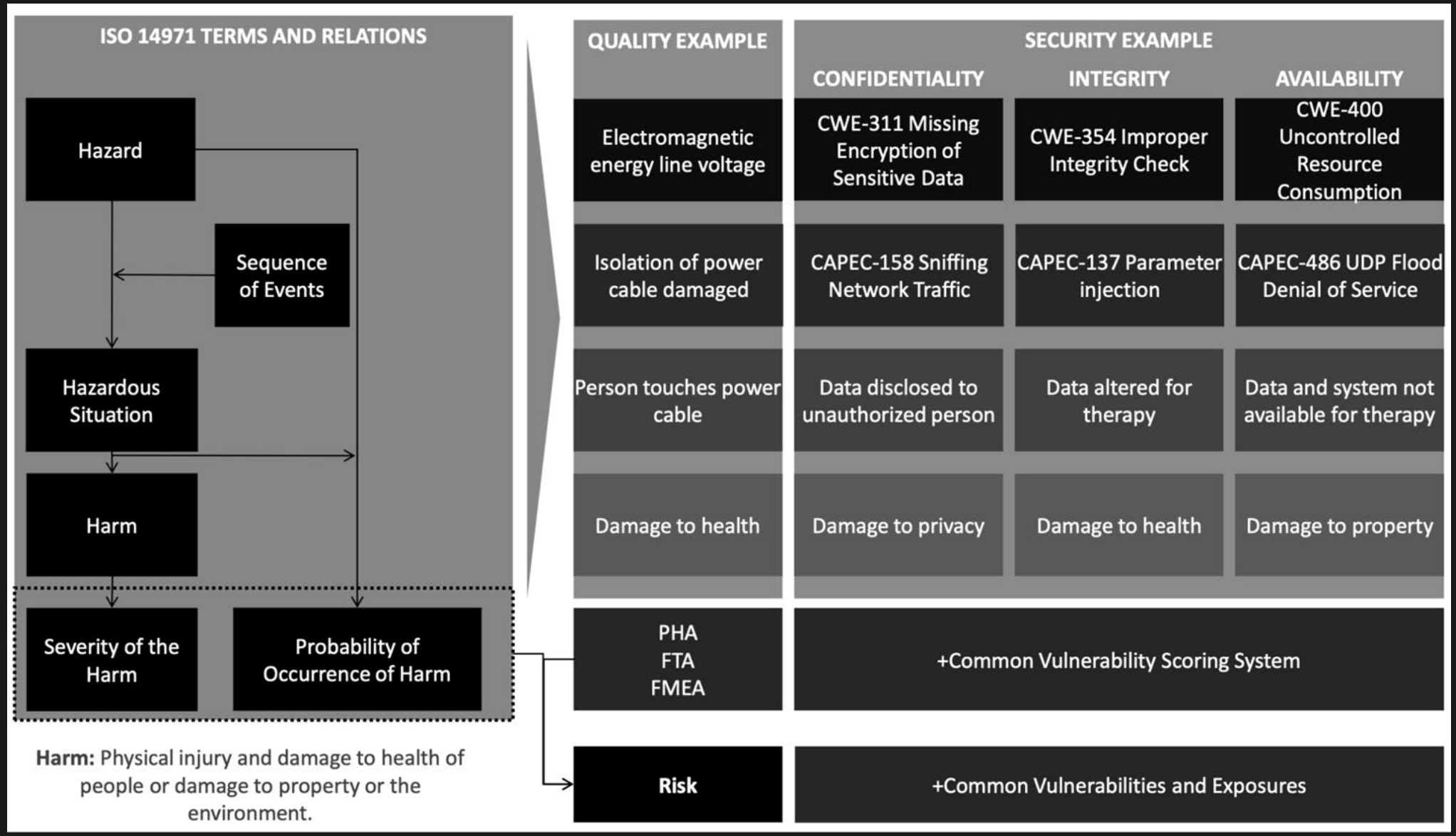
Product Security Framework



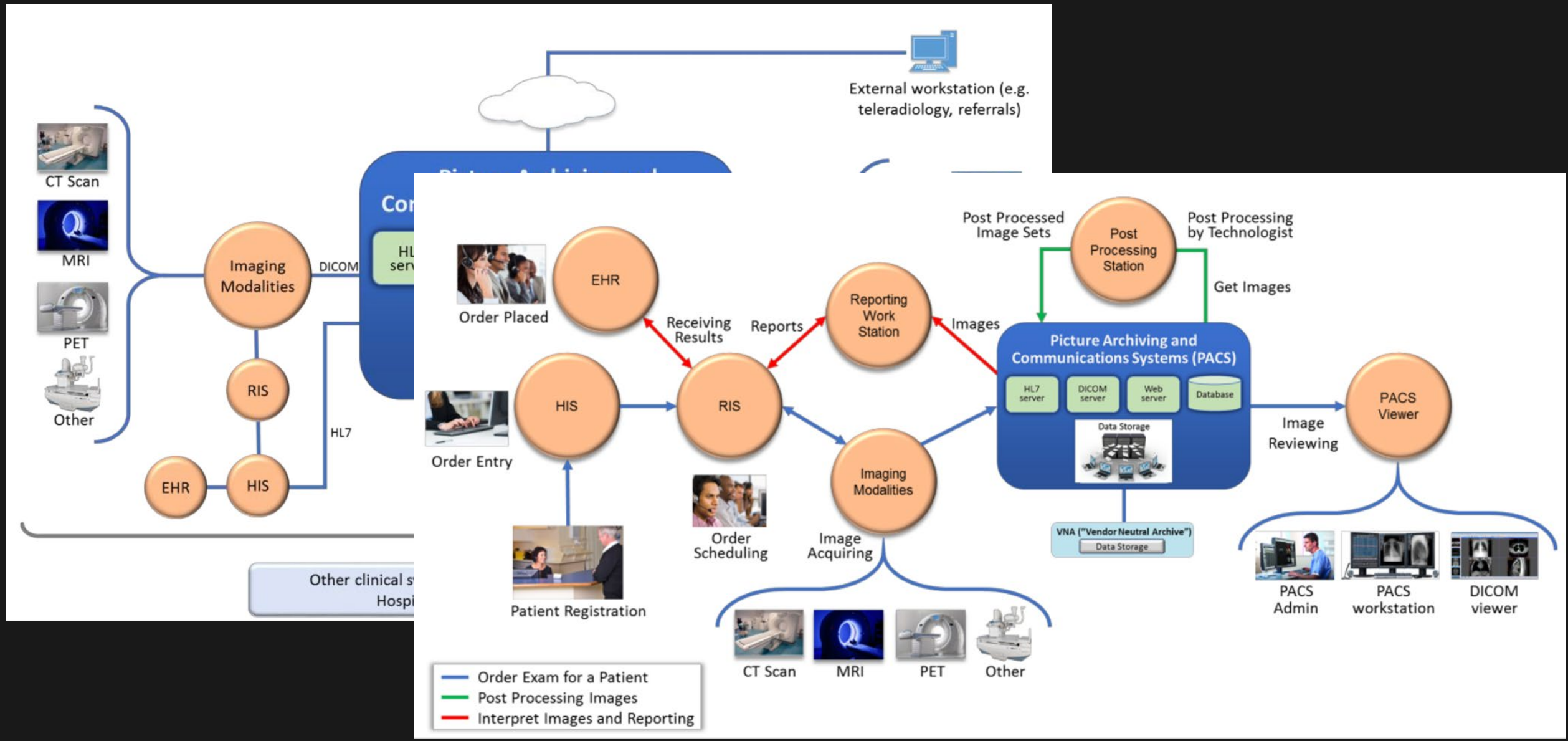
Risk Assessment Sources



Risk Assessment Mapping



Example: Medical imaging management system



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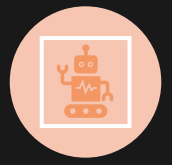
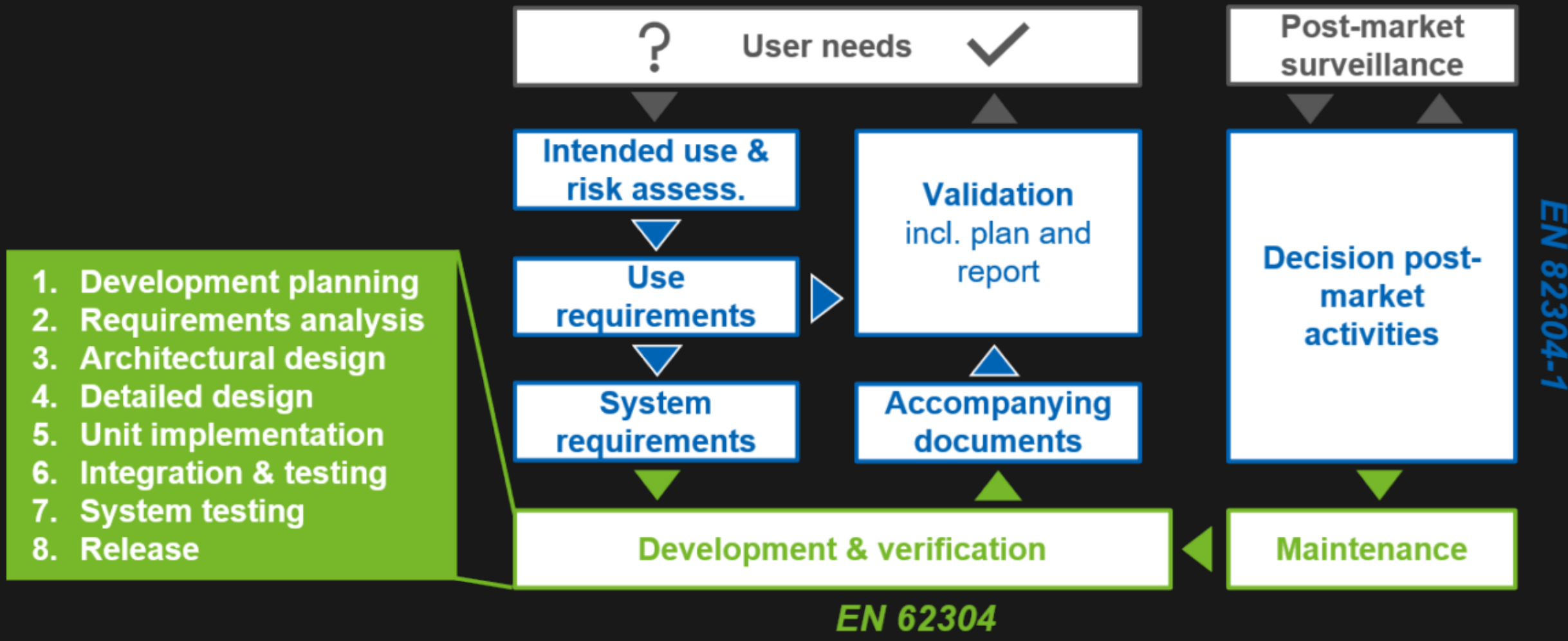


AI/ML (Artificial Intelligence / Machine Learning) SaMD

Software development life cycle

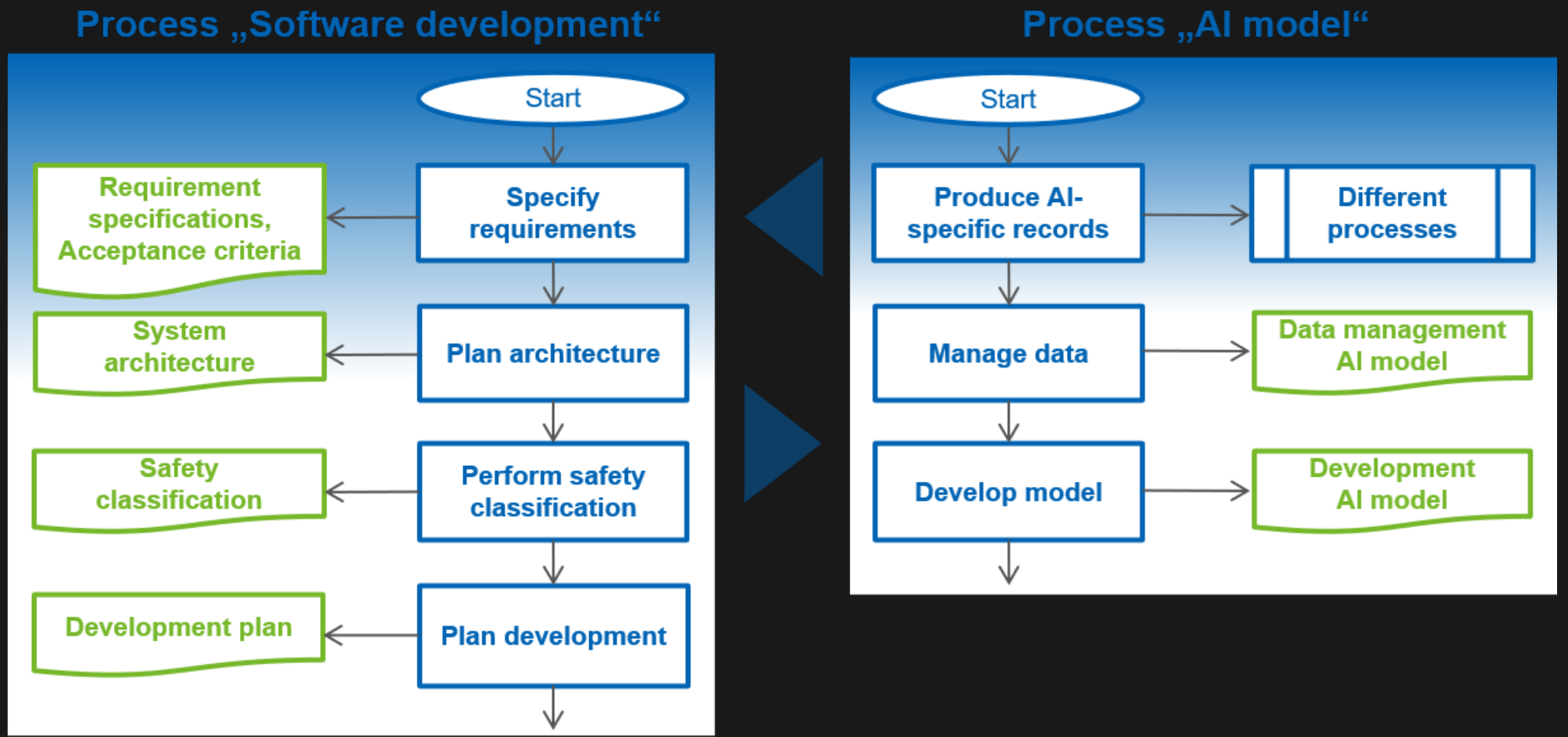
Development of AI/ML-based applications needs attention on code and model level



https://meso.vde.com/ai-based-software/

Software and AI model development

QMS processes side by side



Good Machine Learning Practice (GMLP) Guiding Principles

- Multi-Disciplinary Expertise Is Leveraged Throughout the Total Product Life Cycle
- Good Software Engineering and Security Practices Are Implemented
- Clinical Study Participants and Data Sets Are Representative of the Intended Patient Population
- Training Data Sets Are Independent of Test Sets
- Selected Reference Datasets Are Based Upon Best Available Methods
- Model Design Is Tailored to the Available Data and Reflects the Intended Use of the Device
- Focus Is Placed on the Performance of the Human-AI Team
- Testing Demonstrates Device Performance During Clinically Relevant Conditions
- Users Are Provided Clear, Essential Information
- Deployed Models Are Monitored for Performance and Re-training Risks Are Managed

https://www.fda.gov/media/160125/download
https://www.canada.ca/en/health-canada/services/drugs-health-products/medical-devices/good-machine-learning-practice-medical-device-development.html

Current Thinking Of FDA

Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD)

...per and Request for Feedback

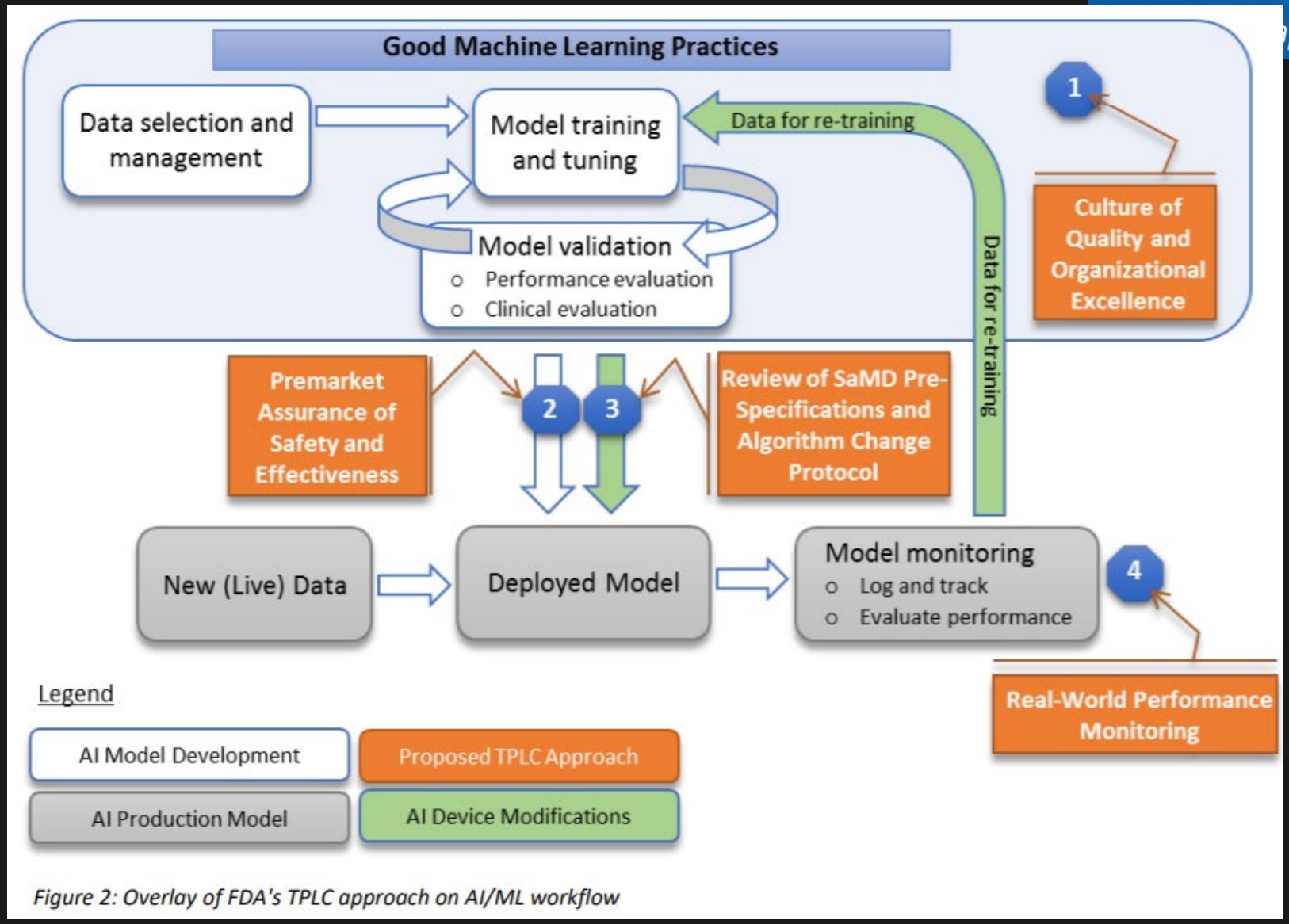


Figure 2: Overlay of FDA's TPLC approach on AI/ML workflow

https://meso.vde.com/ai-based-software/

ACP: Algorithm Change Protocol

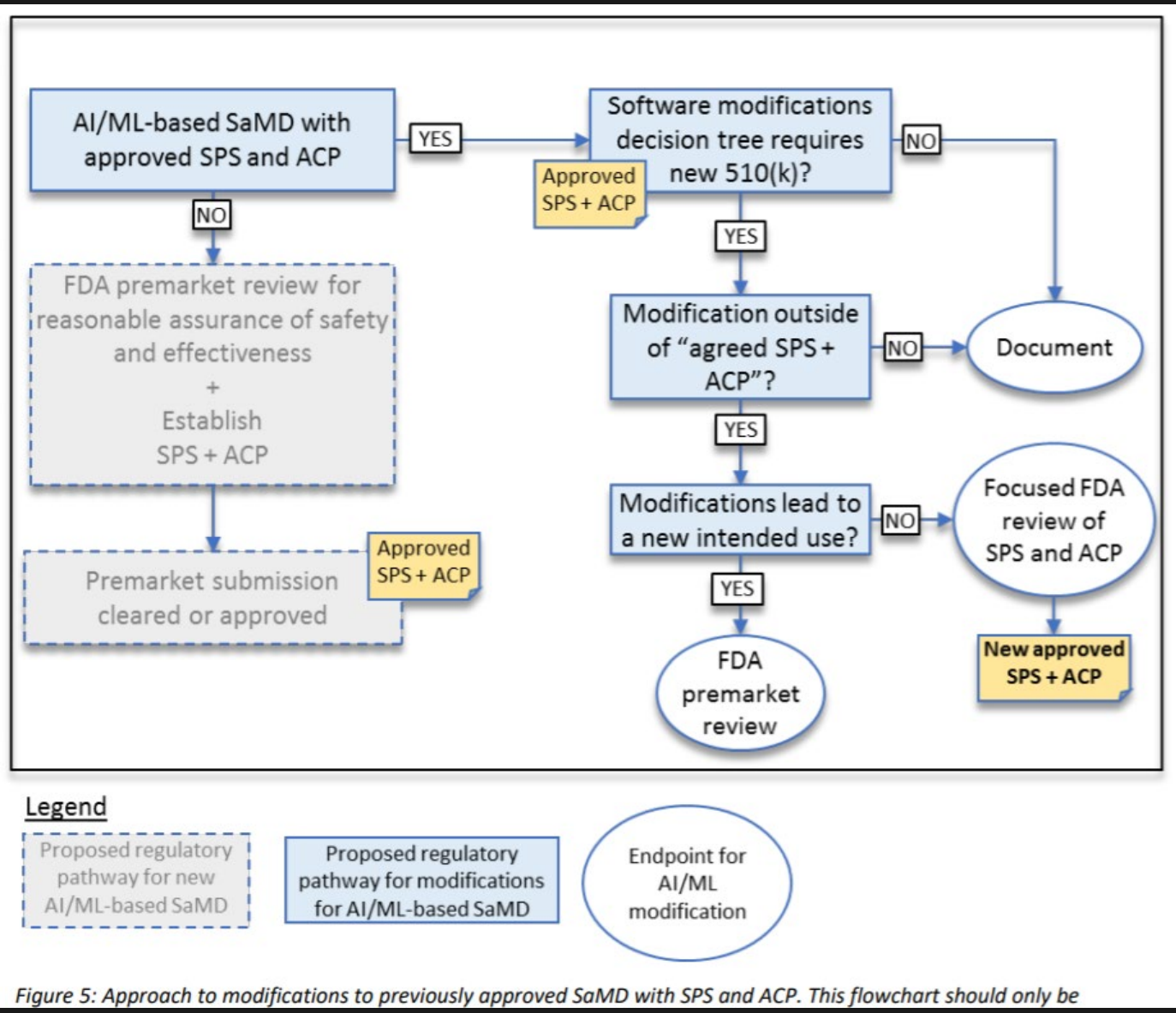


Figure 5: Approach to modifications to previously approved SaMD with SPS and ACP. This flowchart should only be

Data Management	➢ For new training & test data: • Collection protocols • Quality assurance • Reference standard determination ➢ Auditing and sequestration of training and test sets
Re-training	➢ Re-training objectives ➢ Changes related to: • ML methods, including architecture and parameters • Data pre-processing ➢ Criteria to initiate performance evaluation
Performance Evaluation	➢ Assessment metrics ➢ Statistical analysis plans ➢ Frequency and triggers for evaluation ➢ Performance targets ➢ Methods for testing with "clinicians in the loop" when necessary
Update Procedures	➢ Software verification and validation ➢ When and how updates will be implemented ➢ Plans for global and local updates ➢ Communication and transparency to users

Figure 4: Algorithm Change Protocol components

https://meso.vde.com/ai-based-software/

Thank you for your attention!

Any questions?

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