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International Medical Device Regulators Forum

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15:45 – 17:25

Session 4: Specific post-market considerations for AI MDs

IMDRF International Medical Device Regulators Forum

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15:45 – 16:00

Monitoring of endpoints (surrogate and non-surrogate)

Leo Hovestadt

Chair, Global Diagnostic Imaging, Healthcare IT & Radiation Therapy Trade Association (DITTA) & Medical Device Coordination Group Working Groups (CIE WG)

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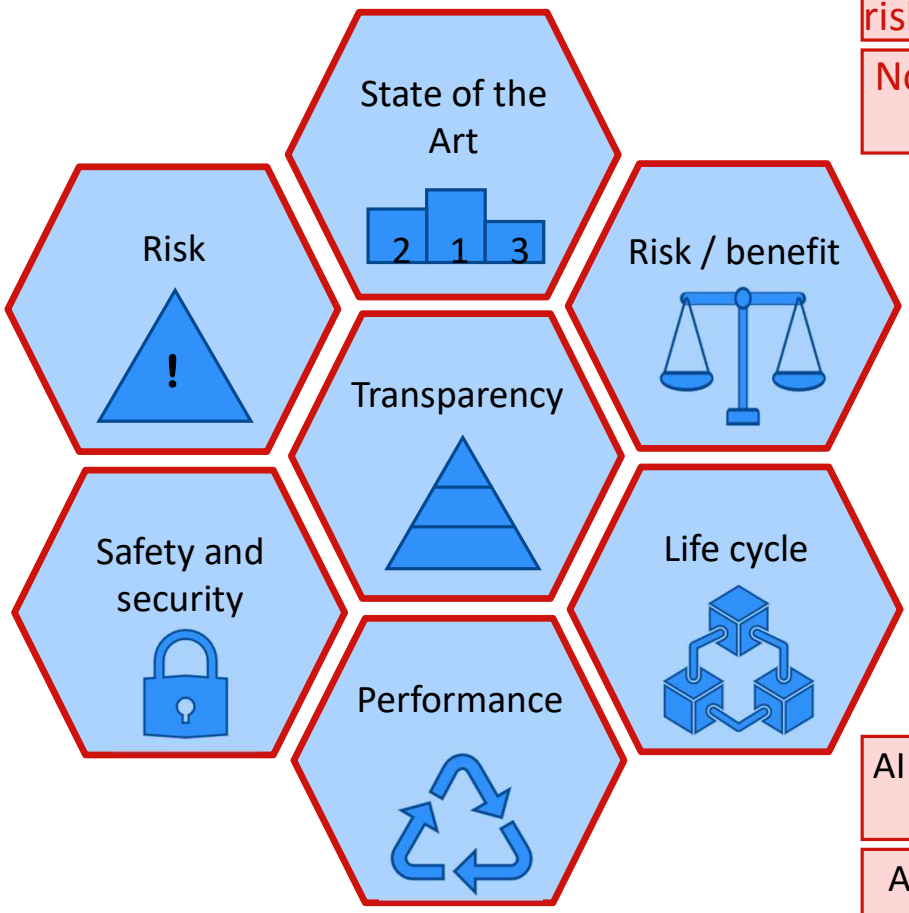
Overview – AI endpoint categories

Agenda:

- **AI endpoints categories**
- **Transparency matrix and endpoints**
- **Insider transparency: PMCF endpoints**
- **Internal transparency: IDEAL endpoints**



Not one definition of risk (SaMD, AI, Ethics, …)

Not all AI risks weighed against benefits

Regulator help is appreciated to keep regulations and standards medical device specific

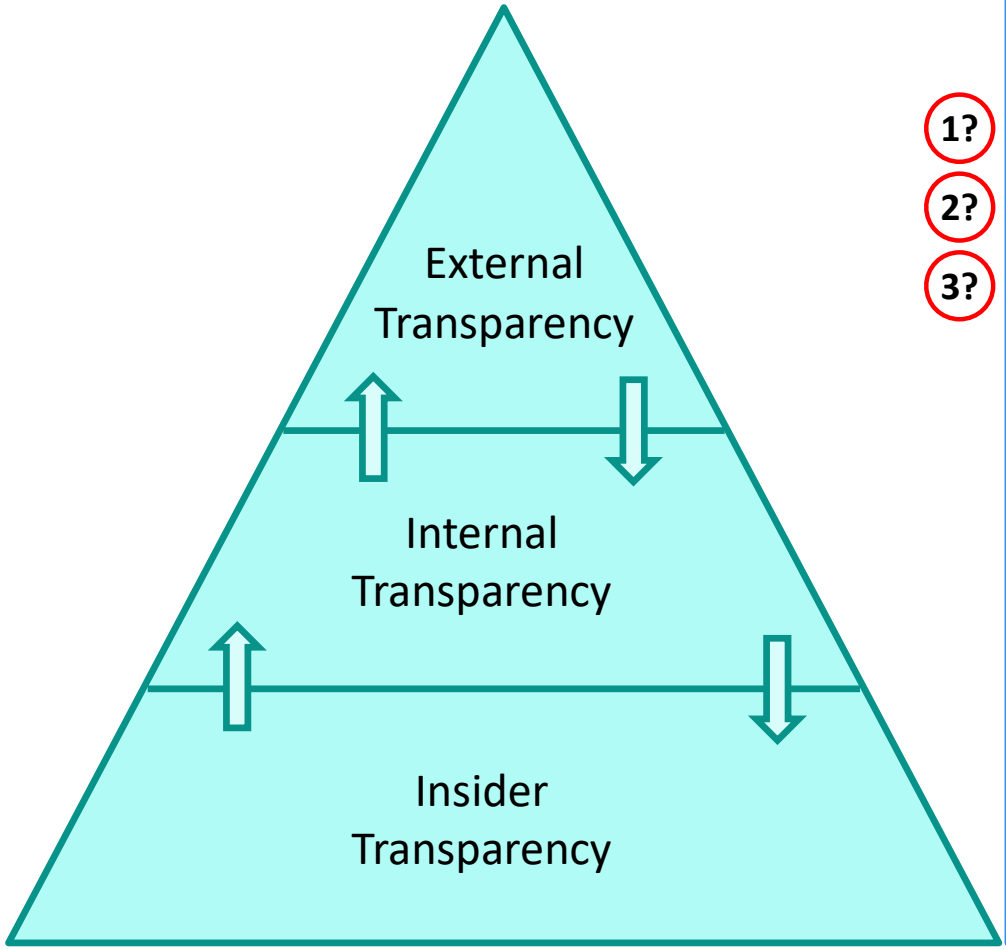
AI state of the art changes quickly

AI performance changes over lifetime

Transparency matrix and AI endpoint stakeholders

Stakeholder

- Patient
- Society
- Environment
- Health care provider
- Hospital / Insurance
- Regulator

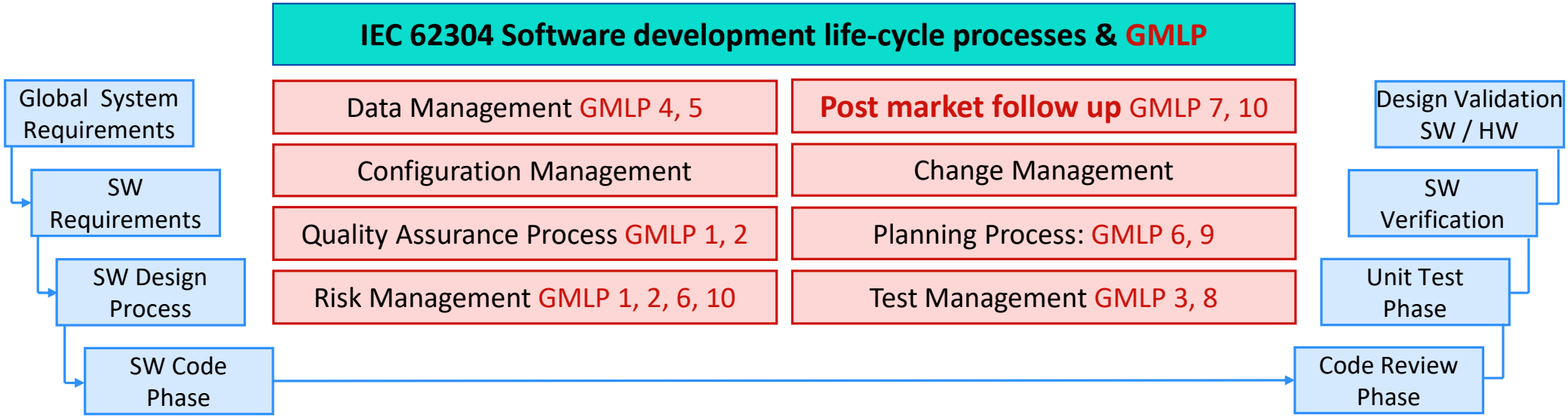


Endpoints

1?	Patient benefit / Affordable
2?	Human rights (Fairness)
3?	Environment
	Scientific (evidence)
	Cost / HTA
	Post-market performance
	Safety, Performance, Security

The transparency matrix explains easily this AI concept

Insider transparency: AI PMCF endpoints and SamD life cycle and GMLP



GMLP PMCF endpoint examples

GMLP 6, 10 Commissioning: Endpoint for overfitting of deployed model

GMLP 6 Life cycle: Endpoint for performance degradation

GMLP 7 Life cycle: Endpoint for growing usability issues

PMCF example related issues

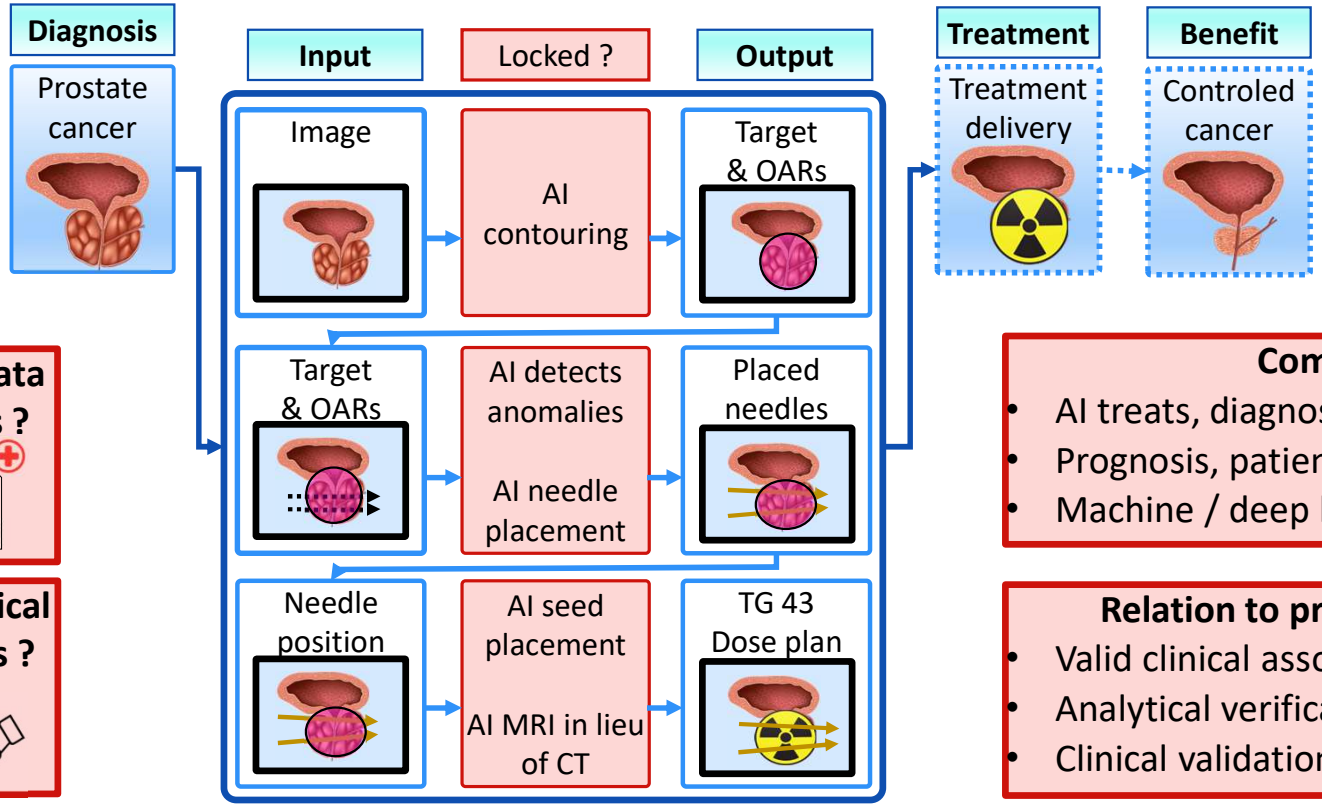
GMLP 10 Life cycle: Plan algorithm retraining and change management

GMLP 10 Life cycle: Plan usage of sandboxes

GMLP 10 End of life: Manage disposal of the training data

GMLP integrates well in IEC 62304

Insider transparency AI PMCF endpoint reflections



"Clinical" data definitions ?

Limited clinical data access ?

PMCF vs ISO 14155 ?

Complexities ?

- AI treats, diagnosis, drives, informs, …
- Prognosis, patient management…
- Machine / deep learning, unsupervised, ...

Relation to premarket endpoints?

- Valid clinical association
- Analytical verification / validation
- Clinical validation

GMLP integrates well in IEC 62304

Internal transparency: R-IDEAL endpoints for radiotherapy: reflections

Milestones	Purpose	Endpoints (Outcomes)	Study design
Stage 0 Predicate studies	• How to use the innovation (software, coils needed)? • Why and in whom to use the innovation?	• MR sequences, dedicated coils, etc. • Inter-rater reproducibility • Treatment strategies, patient selection	Phantom studies, delineation studies, planning studies, model-based studies
Stage 1 Idea	First time use of the innovation for treatment delivery in men	Proof of concept	Structured case report
Stage 2a Development	Technical optimization of the innovation for treatment delivery	Technical improvements, feasibility, and safety	Prospective small uninterrupted case series
Stage 2b Exploration	Provide proof of early clinical effectiveness and safety of the innovation	Early effectiveness: • toxicity • tumor response • local recurrence (with spacious information)	Prospective study with preferably randomized component: RCT; cmRCT; random allocation of limited available treatment slots to eligible patients; Comparison with matched (historical) controls
Stage 3 Assessment	Formal comparison of innovation against standard treatment Development of clinical guidelines?	Effectiveness compared to standard treatment: • (disease-free) survival /recurrence / toxicity • PROMs, CTC-PRO, Cost effectiveness	RCT, cmRCT, registry-based trial Scientific (evidence)? Safety, Performance
Stage 4 Long-term evaluation	Long-term outcomes of the innovation, post-marketing, and surveillance Clinical guidelines by clinicians or manufacturers ?	Long-term toxicity, long-term (disease-free) survival, rare side effects, Patient-Reported Outcomes	Prospective registries, including all patients treated with the innovation Post-market monitoring

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Back-up slide - Good Machine Learning Practices (GMLP)

1. Multi-Disciplinary Expertise Is Leveraged Throughout the Total Product Life Cycle: In-depth understanding of a model's intended integration into clinical workflow, and the desired benefits and associated patient risks, can help ensure that ML-enabled medical devices are safe and effective and address clinically meaningful needs over the lifecycle of the device.
2. Good Software Engineering and Security Practices Are Implemented: Model design is implemented with attention to the "fundamentals": good software engineering practices, data quality assurance, data management, and robust cybersecurity practices. These practices include methodical risk management and design process that can appropriately capture and communicate design, implementation, and risk management decisions and rationale, as well as ensure data authenticity and integrity.
3. Clinical Study Participants and Data Sets Are Representative of the Intended Patient Population: Data collection protocols should ensure that the relevant characteristics of the intended patient population (for example, in terms of age, gender, sex, race, and ethnicity), use, and measurement inputs are sufficiently represented in a sample of adequate size in the clinical study and training and test datasets, so that results can be reasonably generalized to the population of interest. This is important to manage any bias, promote appropriate and generalizable performance across the intended patient population, assess usability, and identify circumstances where the model may underperform.
4. Training Data Sets Are Independent of Test Sets: Training and test datasets are selected and maintained to be appropriately independent of one another. All potential sources of dependence, including patient, data acquisition, and site factors, are considered and addressed to assure independence.
5. Selected Reference Datasets Are Based Upon Best Available Methods: Accepted, best available methods for developing a reference dataset (that is, a reference standard) ensure that clinically relevant and well characterized data are collected and the limitations of the reference are understood. If available, accepted reference datasets in model development and testing that promote and demonstrate model robustness and generalizability across the intended patient population are used.
6. Model Design Is Tailored to the Available Data and Reflects the Intended Use of the Device: Model design is suited to the available data and supports the active mitigation of known risks, like overfitting, performance degradation, and security risks. The clinical benefits and risks related to the product are well understood, used to derive clinically meaningful performance goals for testing, and support that the product can safely and effectively achieve its intended use. Considerations include the impact of both global and local performance and uncertainty/variability in the device inputs, outputs, intended patient populations, and clinical use conditions.
7. Focus Is Placed on the Performance of the Human-AI Team: Where the model has a "human in the loop," human factors considerations and the human interpretability of the model outputs are addressed with emphasis on the performance of the Human-AI team, rather than just the performance of the model in isolation.
8. Testing Demonstrates Device Performance during Clinically Relevant Conditions: Statistically sound test plans are developed and executed to generate clinically relevant device performance information independently of the training data set. Considerations include the intended patient population, important subgroups, clinical environment and use by the Human-AI team, measurement inputs, and potential confounding factors.
9. Users Are Provided Clear, Essential Information: Users are provided ready access to clear, contextually relevant information that is appropriate for the intended audience (such as health care providers or patients) including: the product's intended use and indications for use, performance of the model for appropriate subgroups, characteristics of the data used to train and test the model, acceptable inputs, known limitations, user interface interpretation, and clinical workflow integration of the model. Users are also made aware of device modifications and updates from real-world performance monitoring, the basis for decision-making when available, and a means to communicate product concerns to the developer.
10. Deployed Models Are Monitored for Performance and Re-training Risks are Managed: Deployed models have the capability to be monitored in "real world" use with a focus on maintained or improved safety and performance. Additionally, when models are periodically or continually trained after deployment, there are appropriate controls in place to manage risks of overfitting, unintended bias, or degradation of the model (for example, dataset drift) that may impact the safety and performance of the model as it is used by the Human-AI team.

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Bias in the post-market phase

Anindita Saha

Assistant Director for the Digital Health Center of Excellence, U.S. Food and Drug Administration

Pat Baird

Head of Global Software Standards, Philips

European Commission

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Bias in the Post-Market Phase

Pat Baird, Philips

March 27, 2023

What do we mean by “Bias” ?

“Bias” is defined in IMDRF’s Machine Learning-enabled Medical Devices: Key Terms and Definitions:

Systematic difference in treatment of certain objects, people, or groups in comparison to others.

Note 1 to entry: Treatment is any kind of action, including perception, observation, representation, prediction or decision. (ISO/IEC TR 24027:2021)

Note**:** The term ‘Bias’ is used **in different ways in different fields.** For example, in data science, bias is often defined with a statistical/mathematical meaning while in law, bias is often used to **mean unfair or unfairly prejudiced/partial**.

ISO/IEC TR 24027 refers to systems having both “wanted” and “unwanted” bias depending on the intended purpose of an AI(-based) system.

Sources of bias include:

- **human cognitive biases** (including automation bias, societal bias, and confirmation bias),
- **data biases** (including statistical bias, data processing bias, and data aggregation bias), and
- **bias introduced by engineering decisions** (e.g., during feature engineering, via algorithm selection, and model bias)

BIBO!

We are familiar with the concept of “Garbage In, Garbage Out (GIGO)” – there is a similar term “Bias In, Bias Out (BIBO)”

Bias is like a magnifying mirror – it reflects (and possibly enhances) bias that already exists in healthcare.

Bias Examples

A system trained to detect breast cancer did not perform as well on African-American women; they weren't fully represented in the training set as the developers did not realize that tissue density varies by race.

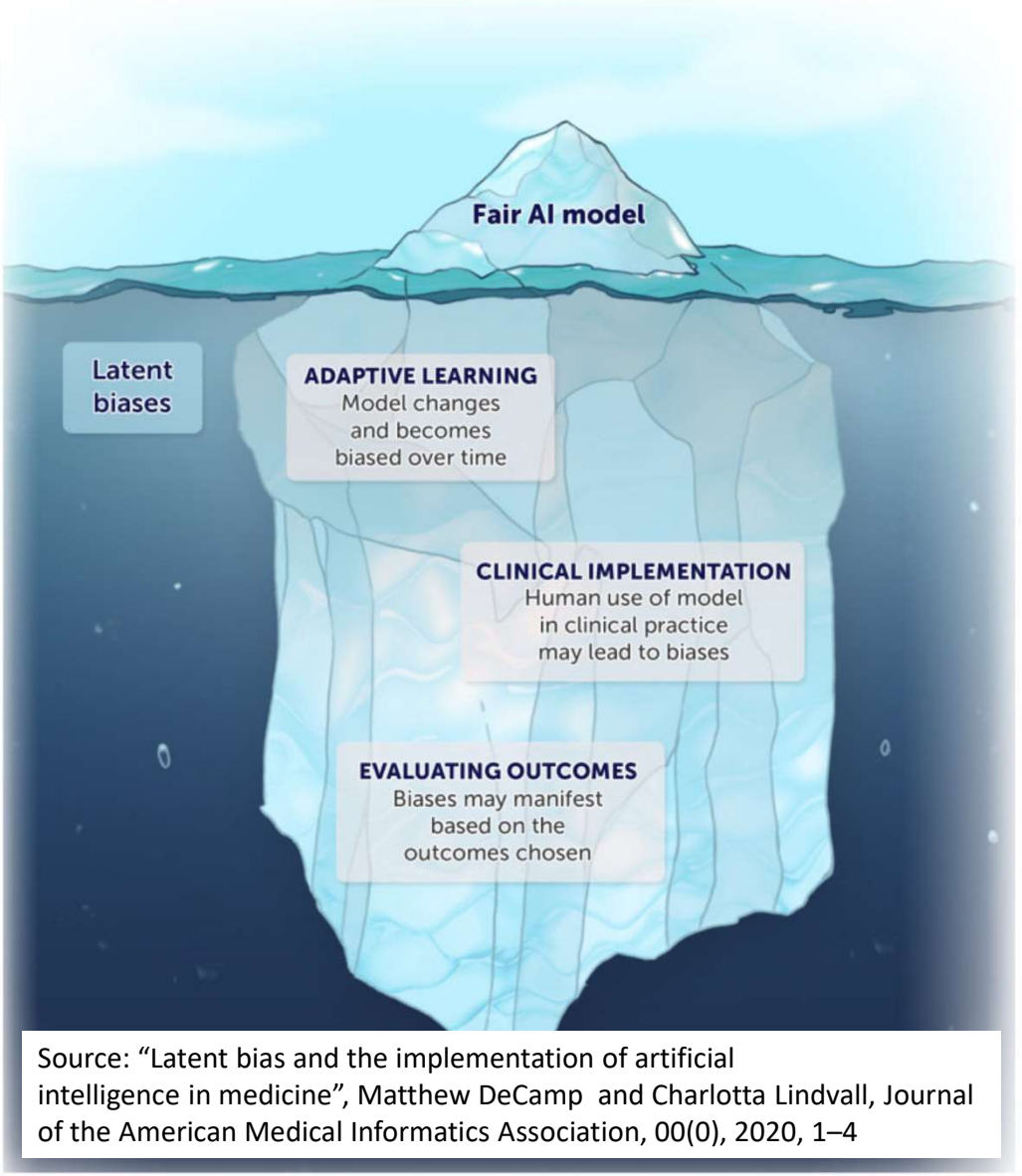
A system intended to detect early onset of a disease used healthcare costs as a proxy measure for how sick a patient is. Unfortunately, some patients are poor and could not afford proper treatment of their disease. The software concluded that people that live in poor neighborhoods were at low-risk because they didn't seek medical care..

Positive Bias: A hospital once approached me and started asking questions about the patient demographics used to train one of our products. They did not want a product that was trained with a large, diverse dataset (e.g. representing patients across the country); they wanted something that was specifically trained for **their** patients (e.g. patients living in a retirement community on the beach..)

A seemingly fair AI model could involve latent biases after clinical implementation.

"Increasing recognition of biases in artificial intelligence (AI) algorithms has motivated the quest to build fair models, free of biases. However, building fair models may be only half the challenge. A seemingly fair model could involve, directly or indirectly, what we call "latent biases." Just as latent errors are generally described as errors "waiting to happen" in complex systems, latent biases are biases waiting to happen."

One of the goals of post-market activities will be to monitor for bias..



Source: "Latent bias and the implementation of artificial intelligence in medicine", Matthew DeCamp and Charlotta Lindvall, Journal of the American Medical Informatics Association, 00(0), 2020, 1–4

Similarities & Differences

There are similar problems in post-market as there are in pre-market. For example, one of the challenges is getting data from small, rural hospitals with limited resources – this is true in the post-market phase as well. The patient demographics for those hospitals is likely different than patients in large city hospitals.

Post-market data isn't always of the same quality as pre-market data, but for the system to effectively learn, we need high quality data & need to be aware of potential bias in that data.

Additional considerations

One of my committees recently released a paper about bias management, and it included a discussion of post-market activities. The recommended data collection process was similar to our current processes; the differences were in the review of the data:

- Identify necessary changes to existing residual impact assessments of bias source/type/sequence combinations (i.e., impact level, likelihood of occurrence, likelihood of impact).
- Identify new bias source/type/sequence combinations.
- Identify new uses or foreseeable misuses of the system that may drive new or changed bias source/type/sequence combinations.
- Identify changes to the stated benefits of the system.
- Identify changes in what may be considered positive, negative, or neutral bias.
- Identify changes in the criteria for determining the acceptability of bias at both a bias source/type/sequence combination level and a system level.
- Identify new bias mitigations for existing bias source/type/sequence combinations.

Additional considerations

That committee is currently working on a paper about ML post-market considerations, and when I mentioned this presentation to them, they wanted to add:

1. Post-market might detect types of bias that were not identified during development.
2. Target demographic can change over time – the patient population may change (drift.)
3. The deployment model for the product and the listening model for post-market information might have bias (e.g. small hospital example)
4. Because we are not collecting ALL data, we might not know about ALL potential biases.

Because of these factors, for learning systems, consideration should be given for what is needed in a rollback plan.

Resources

Bias has gotten a lot of attention and many papers, guidance, and standards have already been created – the IMDRF can leverage the existing work. Example resources include:

- NMPA AI Framework
- ISO/IEC TR 24027:2021 Information technology — Artificial intelligence (AI) — Bias in AI systems and AI aided decision making
- IEEE P7003 Algorithmic Bias Considerations
- Bias in Artificial Intelligence in Healthcare Deliverables, AFDO/RAPS Healthcare Products AI Global Initiative
- CTA 2116 (draft) The Use of Artificial Intelligence in Health Care: Best Practices and Recommendations for Bias Management

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16:20 – 16:40

Change management

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Specific Post-market Considerations for AI MDs

Dr Rama Sethuraman

Director, Medical Devices,

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27 March 2023

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Regulatory Approach for Change Management in AI Medical Devices

Singapore Perspective

Health Sciences Authority

HSA's Role in Health Products Regulation

Our Role

- Ensure that pharmaceuticals, biologics, **medical devices** and health-related products in Singapore are wisely regulated to meet appropriate standards of safety, quality and efficacy throughout the product life cycle
- Ensure timely access to good quality & safe health products
- Support the health and biomedical sciences industry and facilitating its development

Our Regulatory Philosophy

1. Benefits outweigh foreseeable risks
2. Risk-based approach
3. Confidence-based approach
4. Adoption and judicious adaption of international standards & best practices
5. Forging strategic partnership both regionally in ASEAN and internationally

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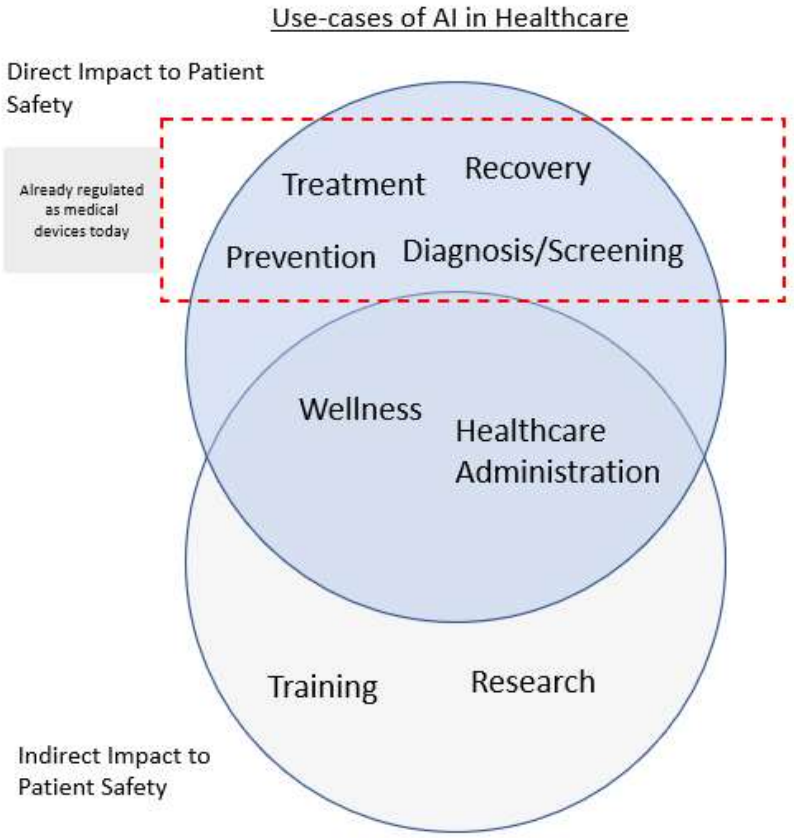
Artificial Intelligence based Medical Devices (AI-MD)



AI that is intended for **medical purposes** (i.e. diagnosis, treatment, patient monitoring) are regulated medical Devices –(AI-MD)

AI that are used in hospitals solely for administrative functions (e.g. patient appointment scheduling) are **not** regulated medical devices under HSA

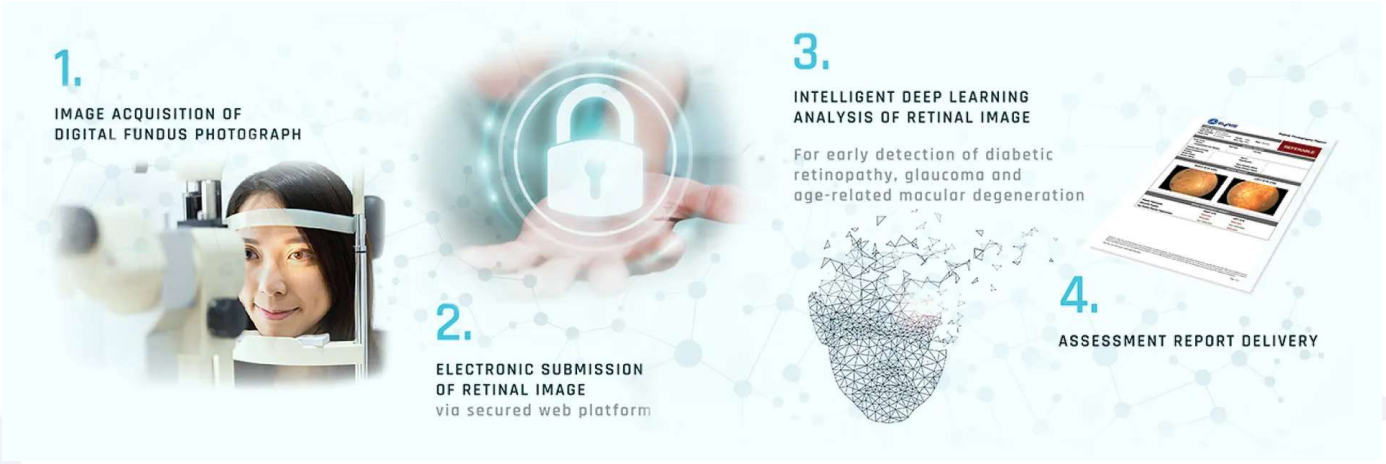
Legislative definition of "Medical Device" can be found in the First Schedule of the Health Products Act 2007: http://statutes.agc.gov.sg/

Regulating AI-MDs: Need for a Tailored Approach

- Unique manufacturing processes (model selection, training, validating, re-training, bug fixing, programming) and facilities
- Short development time and short lifecycle
- Constant change and updates (intended changes and unintended or consequential changes)
  - Learning from real world use data and improving performance
- Connectivity and Data related risks
  - Cybersecurity, Data integrity, Data security
- Continuous learning and deployment of upgrades or newer versions
  - Version controls; Traceability
  - Ability to track and revert to older versions; Recall actions

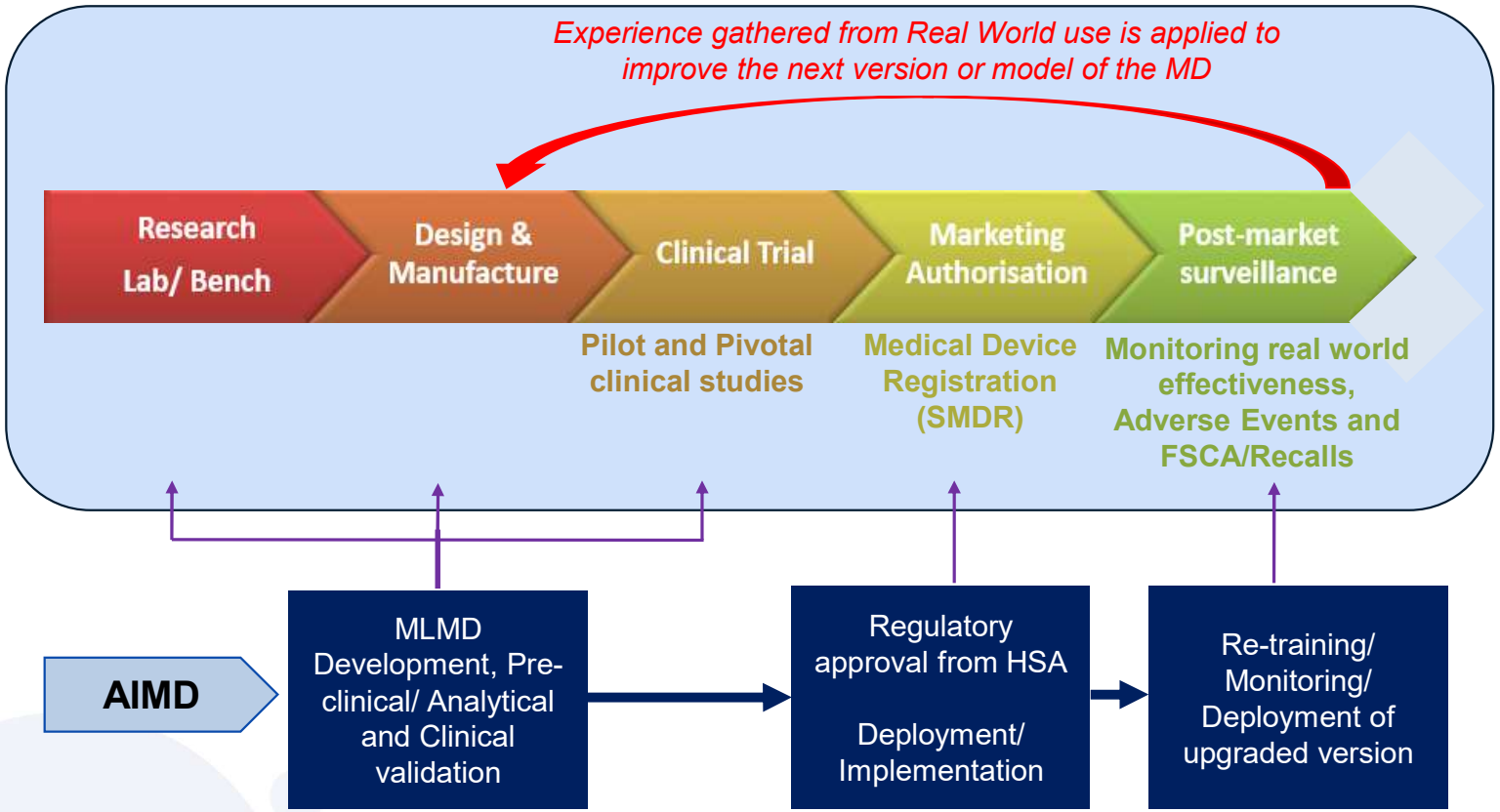
Risk Classification of AI-MDs

- Risk Classification approach for AI-MDs is similar to the approach for SaMDs
  - HSA Guidelines on Risk Classification of SaMD* and Qualification of CDSS# published in April 2022; Accessible online at: https://www.hsa.gov.sg/medical-devices/guidance-documents
  - Aligned to the IMDRF's guidelines on risk categorisation for SaMD
  - In assigning risk class, manufacturer's intent based on design and claims for their AI-MD is considered
    - Functionalities and Features (e.g. analyse, monitor, adjust or control therapy)
    - Output from the AI-MD (e.g. triage, recommend, diagnose, therapy recommendations)



*SaMD – Software as Medical Device (aka Standalone Medical Mobile applications in Regulations in Singapore)
#CDSS – Clinical Decision Support Software

Regulating AI-MD – A Lifecycle Approach



Change Management for Medical Devices

- A risk calibrated approach to regulating post-approval changes for medical devices
- Significance of the change based on the intended and any consequential impact on the registered medical device, arising from the change such as
  - Impact on the device safety/quality/efficacy
  - Impact on the approved performance specifications
  - Impact on the clinical use cases (e.g. disease condition, patient types)
  - Impact on the device functionalities
- Level of HSA's regulatory oversight titrated based on the significance of the change to the medical device; Includes
  - Evaluation and approval process
  - Notification
  - No submission required

NOTE: Changes that result in a new intended use for the medical device will require new pre-market application

Change Management for AI-MDs

- During pre-market evaluation, manufacturers are required to provide the following information for their AI-MDs
  - Specifications of their AI-MD including the input data types and parameters, clinical association with the output parameters, nature of output and indications for use that has been validated for the AI-MD
  - Procedures implemented to monitor and manage the current performance and also future retraining and implementation of changes to their AI-MDs which could include managing the training and validation datasets, re-training of algorithm, performance evaluation and upgrades
- In particular, for continuous learning algorithm based AI-MDs, the learning process including process controls, verification, ongoing model monitoring measures and the allowable range of performance specifications should be clearly defined
- All post-approval changes to the AI-MD must be managed within the processes established by the manufacturer and under their QMS
  - Any changes to the pre specified procedures and specifications would typically affect the AI-MD performance and deemed significant. Such changes would likely require evaluation and approval by HSA

Change Management for AI-MDs

Regulatory Oversight

Technical/Review Changes ***Subject to Evaluation & Approval***	• Significant changes that impact the safety/quality/efficacy of registered AI-MD or the approved performance specifications • Addition of new functionalities or new indications for use • New versions of AI-MD with enhanced performance • Change to the degree of automation of the AI-MD • *For continuous learning algorithms*: Changes to inclusion/exclusion criteria for real world input data and allowable boundaries for change to performance specifications pre-defined
Administrative Changes ***Subject to Approval***	• Changes to the administrative information submitted during registration of the AI-MD including changes that would require updates to the information listed on the Singapore Medical Device Register
Notification Changes	• Changes with typically low impact on the registered AI-MD • May be implemented immediately upon receipt of the acknowledgement email from HSA upon notification via online system
Changes that require no action	• Changes with no known or foreseeable impact on the registered AI-MD • To be managed by the manufacturer under their QMS

Regulatory Oversight Stratified based on the significance of the change

Change Management for AI-MDs - Examples

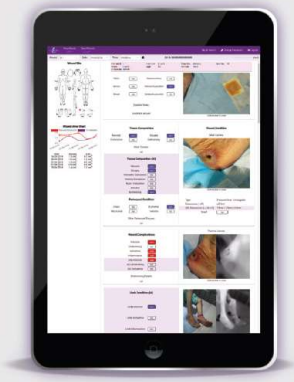
For locked and continuous learning algorithm based AI-MDs

Examples of significant changes to AI-MDs subject to evaluation and approval by HSA (Technical Changes)

- Changes to the input data to generate the same clinical output from the AI-MD – potential impact on clinical association with output
- Change to the output results presented which are based on the approved input parameters

Example – Approved wound scanner intended to report the length and width of the wound.
New output parameter will include the depth of wound. There is no change to the indication for use.

A nurse can use KroniKare Wound Scanner to capture an image of the wound for full assessment and documentation under 30 seconds at a patient's bedside.



Uploaded data vectors are automatically compiled into medical reports for monitoring wound progress and prioritising serious cases using a tablet.

For locked and continuous learning algorithm based AI-MDs

Examples of significant changes to AI-MDs subject to evaluation and approval by HSA (Technical Changes)

- Change to the output results presented by the AI-MD, which are based on the approved input parameters/ image modality and involves expansion of the approved indications for use of AI-MD

  Example –The approved software can identify certain types of intra-cranial tumours from MRI images (e.g. Meningioma and Chordoma). The change involves inclusion of an additional intra-cranial tumour (e.g. Craniopharyngioma) in the AI-MD's output

- Change to the approved workflow such that the patient result/therapy will no longer be required to be reviewed/supervised by the health care provider/trained professional/user (i.e. no human intervention is required) – Full-automation of AI-MD

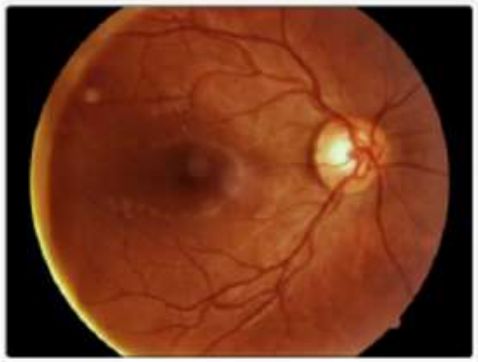
  Example – Removal of the review of the AI-MD's output results by a nurse and specialist from the workflow for deployment and use of the AI-MD.

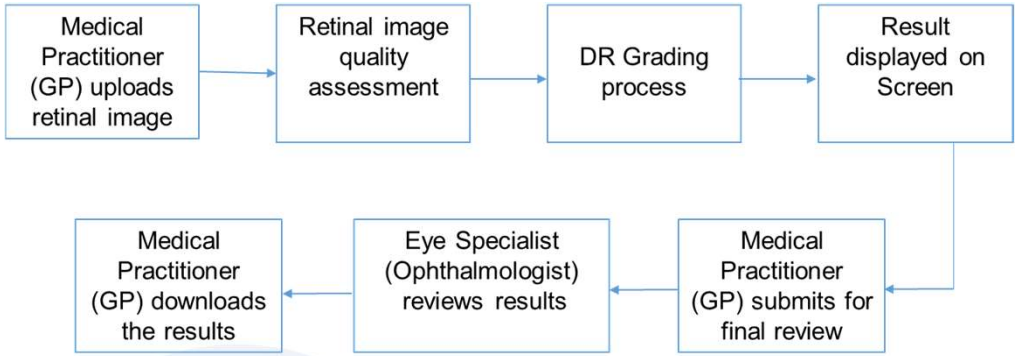
Change in the Workflow for deployment of AI-MD

AI-MD's Original intended use during pre-market evaluation:

To screen and grade Diabetic Retinopathy (DR) in patients/general population through colour fundus retinal images. The results are intended to be subsequently verified and certified by an eye specialist before forwarding to the Primary Health Care Professional as a report.

- All outputs to be reviewed by specialists





Disease Severity Level*

Non disease
1. Unable to grade
2. Normal
3. Mild NPDR

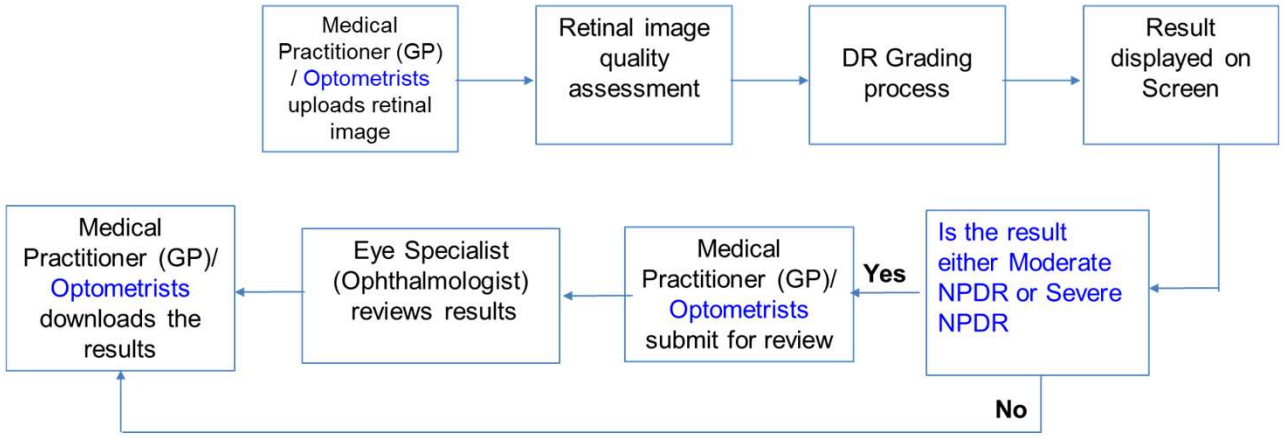
Disease
4. Moderate NPDR
5. Severe NPDR

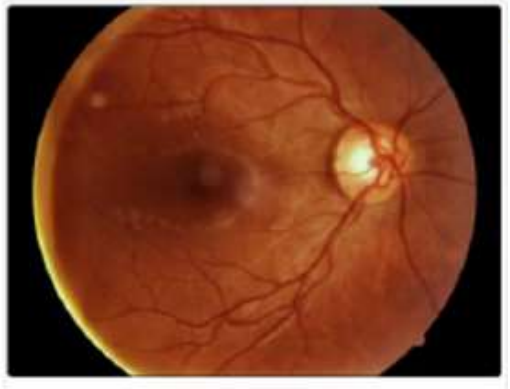
**American Academy of Ophthalmology*

Change in the Workflow for deployment of AI-MD

Change in Workflow post-approval

Only moderate NPDR or severe NPDR outputs will be referred to specialist





Regulatory Considerations:

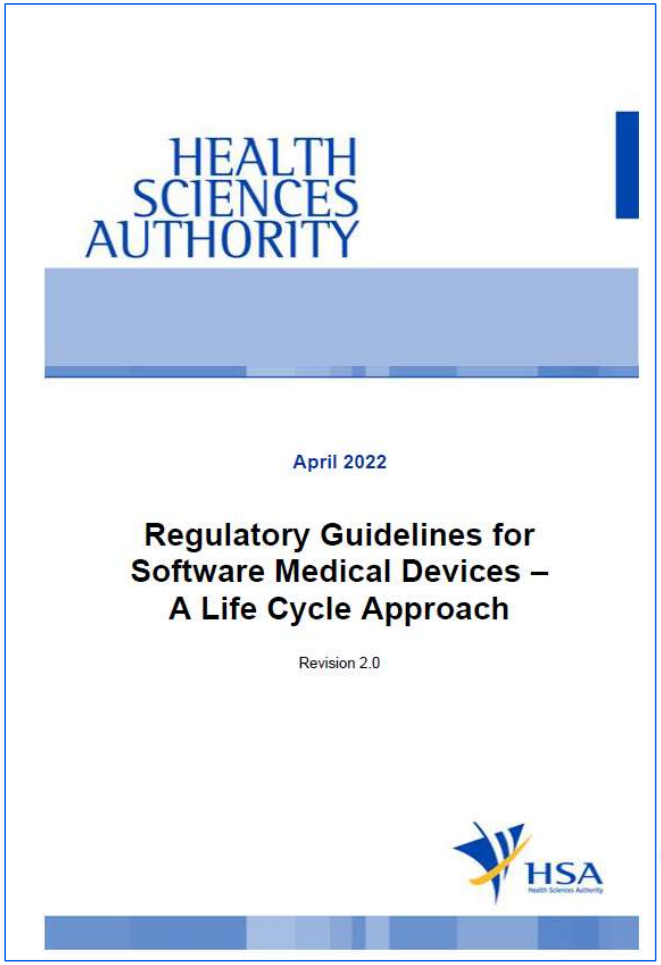
- Increased reliance on AI-MD output for Normal and Mild NDPR cases
- Need for more robust validation studies especially with mild NPDR cases
- Clear instructions to be provided for situations where the AI-MD would potentially generate incorrect outputs (i.e. moderate NPDR reported as mild NPDR)

Regulatory Guidelines for Software Medical Devices – A Life Cycle Approach

This document provides clarity on the regulatory requirements for software medical devices throughout its entire life cycle and covers:

- Quality Management System (QMS) for software medical devices
- Dealer's licensing requirements
- Pre-market product registration requirements
- Change notification
- Post-market management of software medical devices
- Cybersecurity
- Artificial Intelligence Medical Device

Reference: "Regulatory Guidelines for Software Medical Devices - A Life Cycle Approach" available at HSA | Guidance documents for medical devices



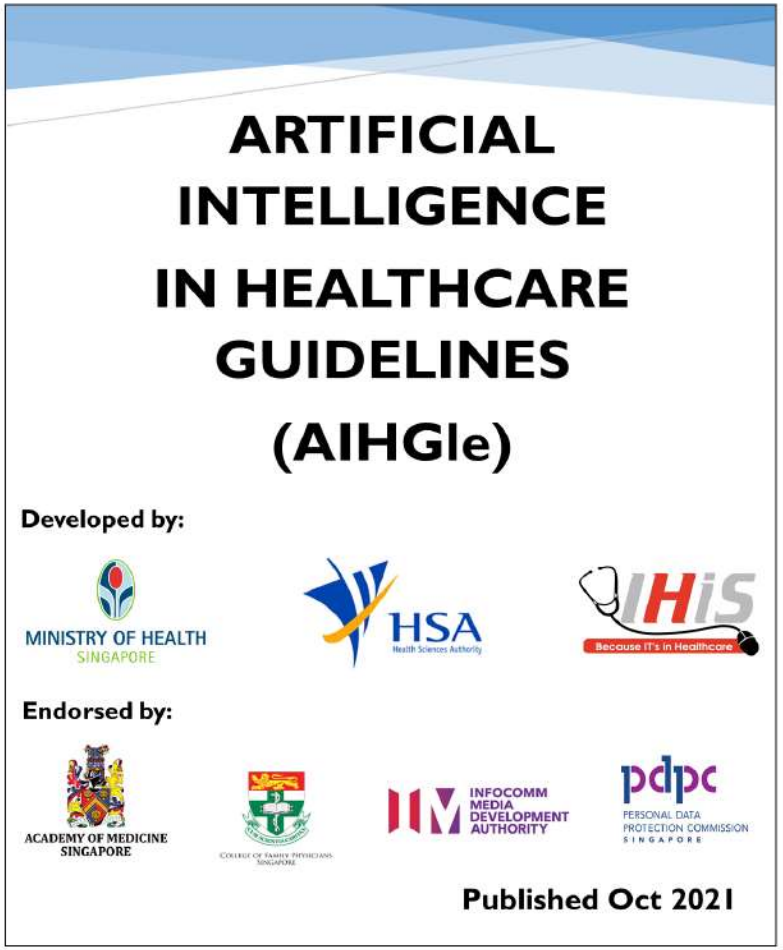
Guidelines for Implementation of AI-MDs in Healthcare

The Ministry of Health, Singapore in collaboration with the Health Sciences Authority (HSA) and Integrated Health Information Systems (IHiS), has published a guideline on good practices for AI developers and implementers (e.g. healthcare institutions – hospitals, clinicals, laboratories, etc.)

Some of the key recommendations include:

- Exercise clinical governance and oversight over the adoption and implementation
- Contingency plans to remove the AIMD from the operational workflow

Reference: https://www.moh.gov.sg/licensing-and-regulation/artificial-intelligence-in-healthcare



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Specific post-market considerations for AI MDs: Change Management

Melissa Finocchio, Chief Regulatory Officer

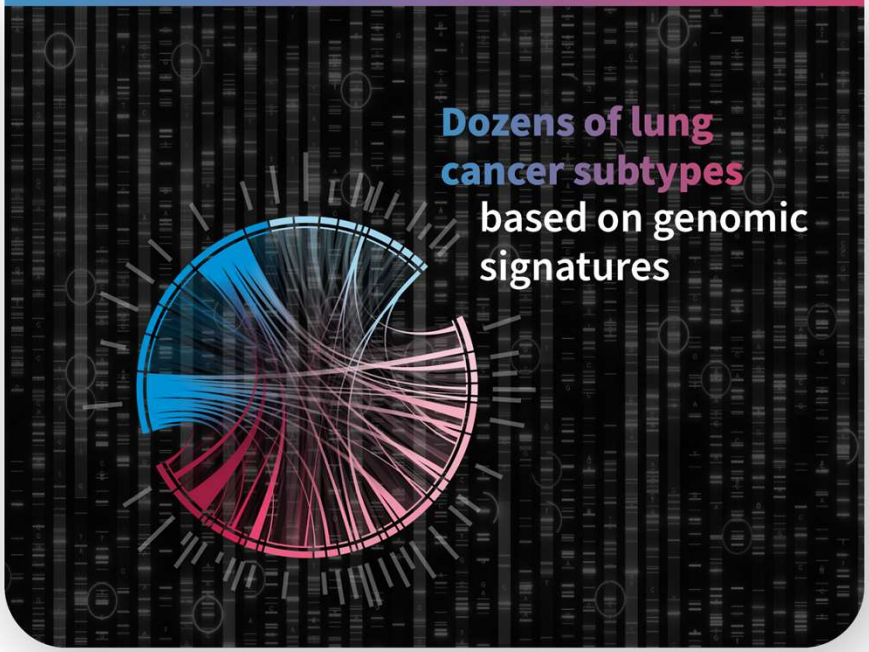
SOPHiA GENETICS

27 March 2023

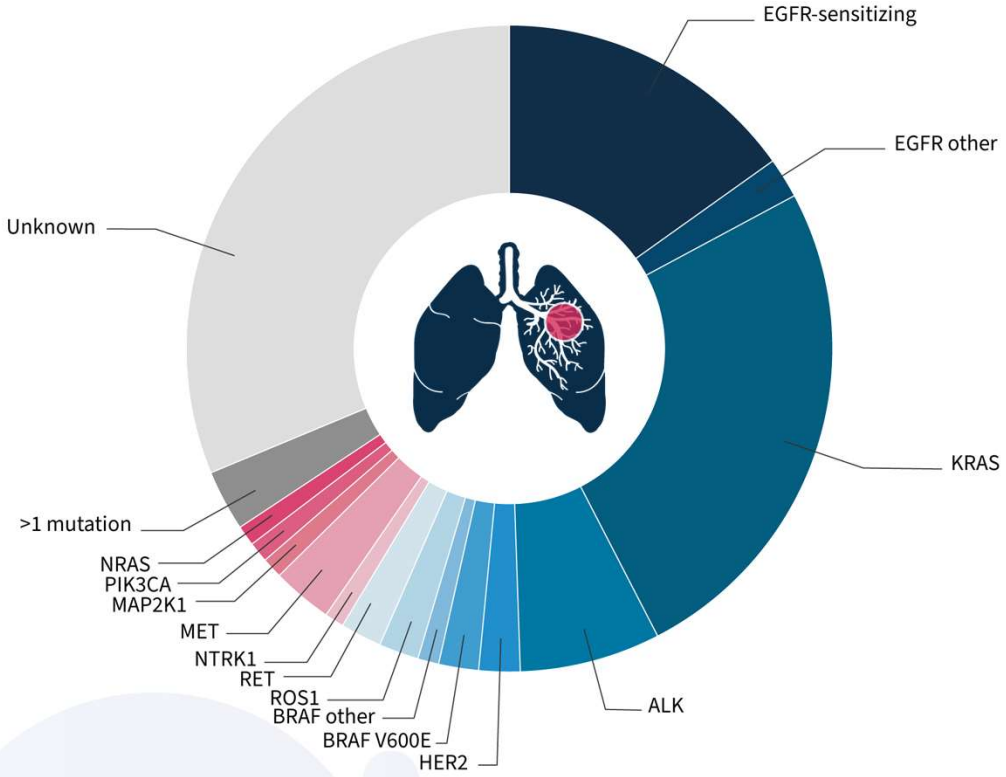
What is change?

20 years ago

Today

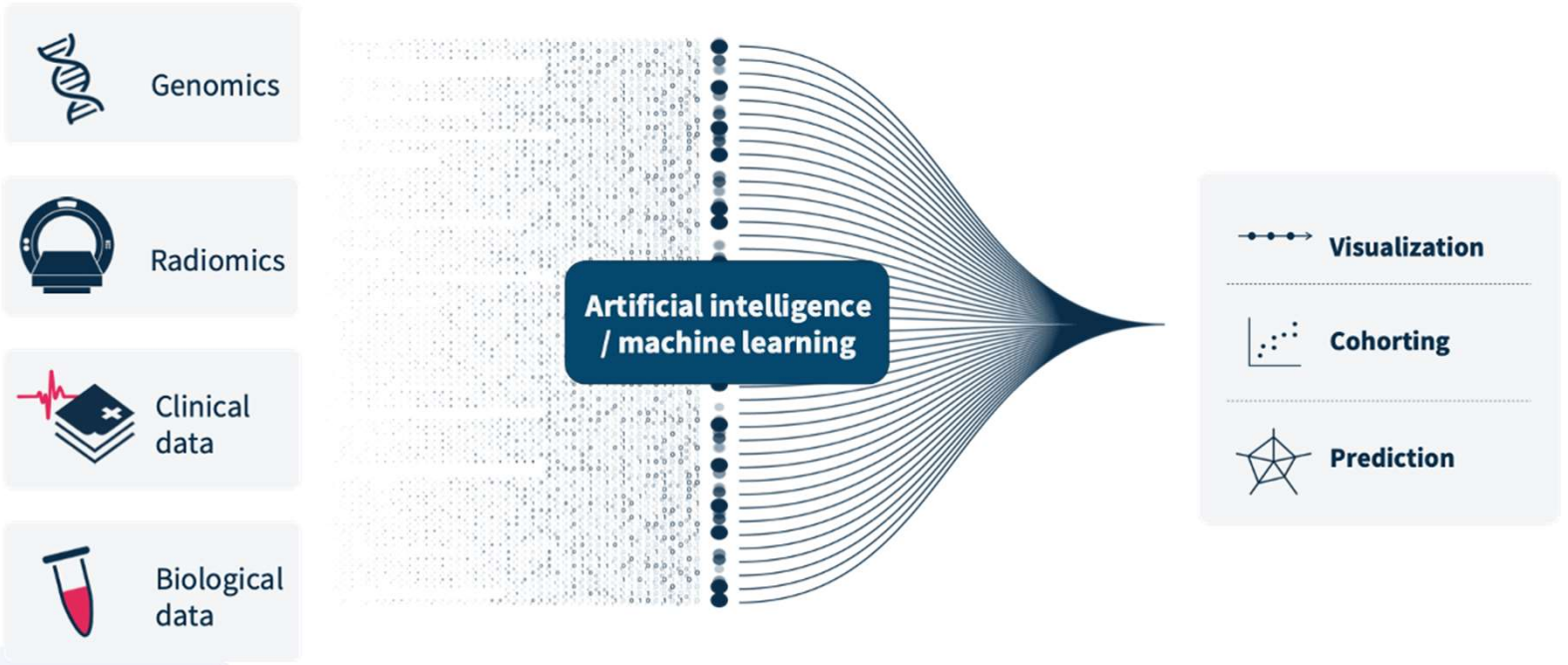


Lung Cancer is increasingly a collection of rare diseases



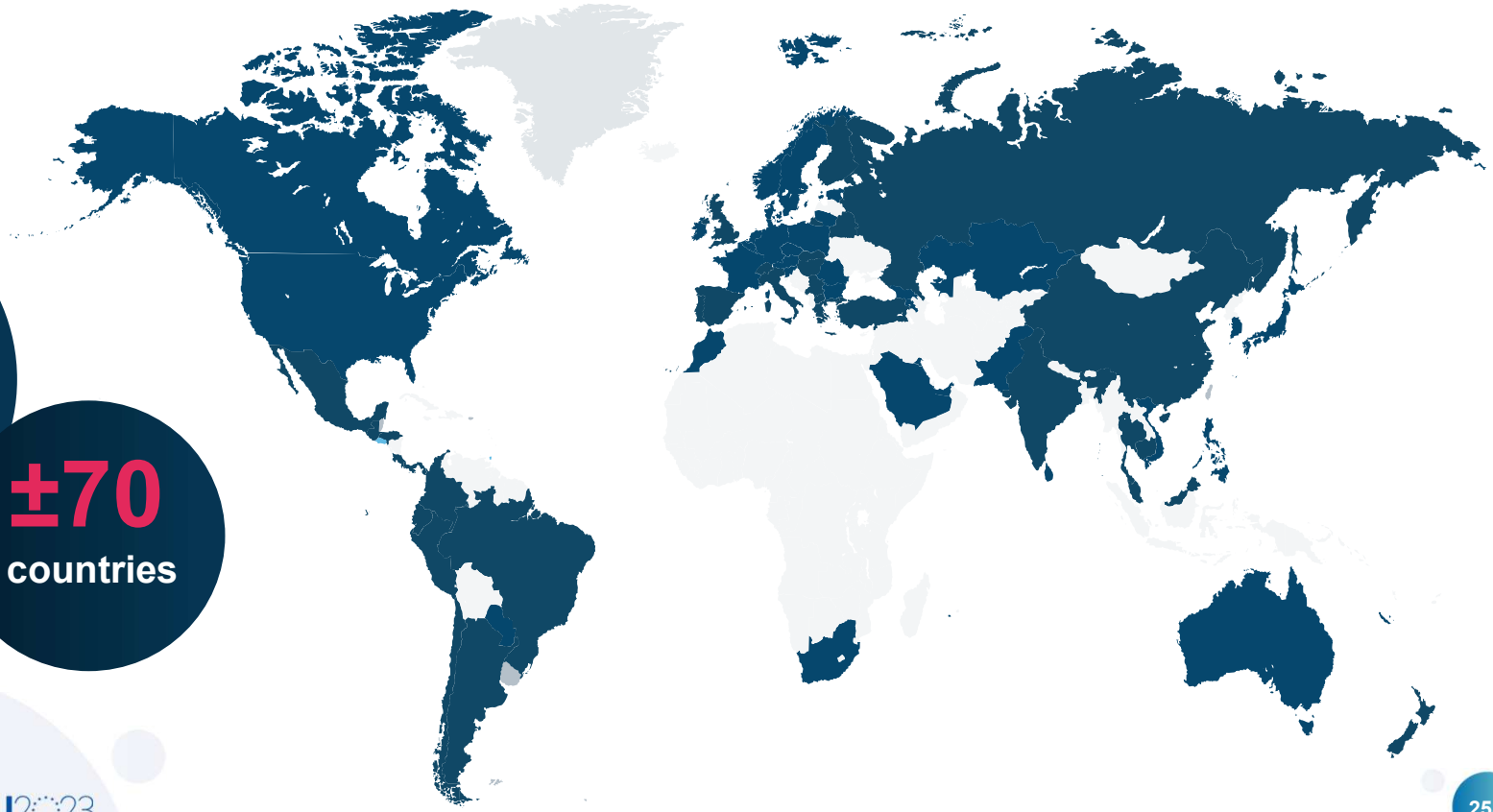
- **Specific variants** (e.g., KRAS G12C)
- **Co-mutations**
- **Tumor mutational fingerprint evolving over time**

Multimodality is further increasing the complexity



…and the rate of change

Globally Connected Devices



750+
connected healthcare institutions

±70
countries

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Adaptive devices need *adaptive* change management

- Focus on training & processes
- Continuous growth vs Discrete changes
- Careful monitoring & feedback

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THANK YOU

Melissa Finocchio

mfinocchio@sophiagenetics.com

European Commission | European Union

IMDRF International Medical Device Regulators Forum

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16:40 – 10:10

PMS for AI software

Lesley-Anne Farmer

Expert Advisor, Therapeutic Goods Administration

Haeung Lee

Director, Corelinesoft

European Commission | European Union

Post-Market Surveillance – considerations for artificial intelligence software

Lesley-Anne Farmer
Medical Devices and Product Quality Division
Therapeutic Goods Administration

Scope - 2 considerations

Consideration 1 - Monitoring devices with AI

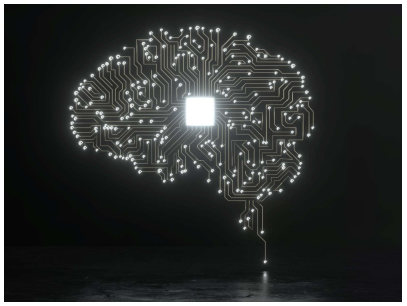
Criteria, methods, and strategies to monitor safety and performance: specific considerations for AI (ML)

Consideration 2 – Using AI data

Challenges and opportunities when collecting or generating data for digital medical devices

Consideration 1: Monitoring devices with AI

Regulatory requirements and what is acceptable are important and critical considerations to how and what is monitored

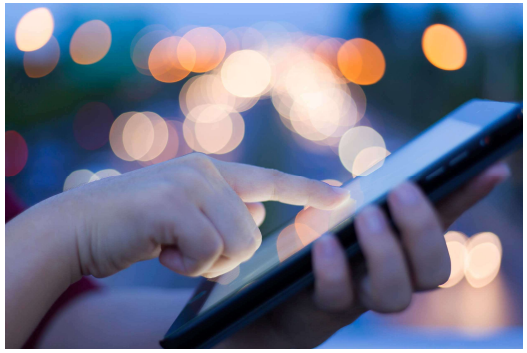


For AI software, some of the main areas under consideration for post-market surveillance include:

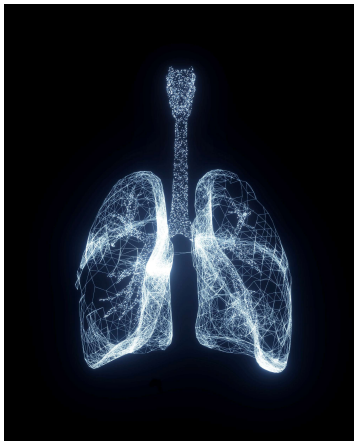
- Transparency
- Labelling
- How general software trends are applicable to AI
- Which medical specialisations are adopting AI most quickly
- How health professionals use AI products
- Signal evolution and design
- Governance of AI and data for adaptive systems
- Adverse event surveillance and what ‘manufacturer’ activities are undertaken

Some challenges

- New players do not have well-developed processes to support ongoing post market obligations
- Increasing sophistication/version updates not always factored into post market changes (especially if the changes do not require regulatory re-approval)
- Human factors – how people use software vs its design (intended purpose) and reporting of adverse events – do users KNOW it is an adverse event?
- Traceability of errors and their role in adverse events
- Some differences in classification of devices globally and post market obligations
- Using AI which may have bias and/or not be applicable to certain population cohorts – does this skew adverse event data?



Transparency and surveillance



Looking **inside** the product and using this information for surveillance

- Data AND model
- AI often sits inside a software “shell”
- What data is needed by regulator for post market issues that is specific to AI? e.g. logging and beyond

Using the product and what channels

- Human factors – consumers, patients, health professionals
- Understanding the purpose
- Scale of deployment

Signal evolution and design for AI products

- Clear leading medical specialisations – target surveillance design to these
- Digitalisation of pathology – significant changes in workflow and processes
- Keeping up with changes to theory/literature
- Target efforts
- For consumer products – speed of adoption
- Consider whole life cycle from design
- Still need to consider other software signals not just AI

Ongoing responsibilities post-approval

Building in good practices through the lifecycle

Governance, monitoring and surveillance systems are critical to:

- periodically verify that the product continue to work as intended
- detect if it develops any unintended bias or further performance drift

AI and software generally

- Focus on getting to market means AI/software living environment may not be adequately addressed
- Ecosystem compatibility maintenance
- Consumer facing devices, or self-management of a serious condition face further requirements to mitigate patient risks through its service life
- Updates or patches as ‘recall’ actions or notifications based on regulatory requirements

Adverse event surveillance

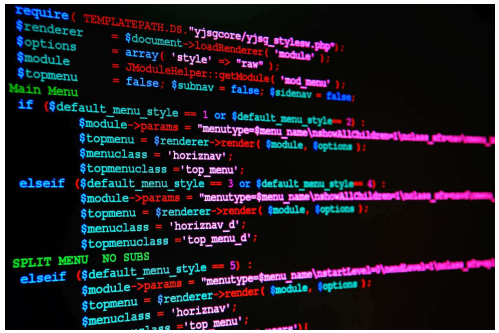
Planning for the unthinkable

- Ongoing surveillance and monitoring of complaints and adverse events regarding harm to a user or patient
- Software design should have data capture/ logs
- Manufacturer adequately resourcing the quality and post-market team
- Planning for timeframes and resourcing needed to investigate, respond, notify regulatory authorities and minimise risks from adverse events or issues
- Manufacturer needs channels to contact local agents or distributors for complaints and regulatory action, that are across different geographic regions
- Communication channels for updates, patches, recall actions to end users, or patients, or health providers

Consideration 2: Using AI data

Collecting or generating data

Regulatory requirements and what is acceptable for post market surveillance are important and critical considerations for manufacturers



- Clinical evidence guidance
- Real world evidence and real world data guidance
- Clear feedback to manufacturers by the regulator on what is expected

Real world evidence and real world data

Key points in relation to post-market surveillance:

- Real-world data collected from AI software in a proper study design can contribute to post-market clinical follow up
- Create real-world evidence for any applicable extension of intended purpose.
- Sources can include device output, sensors, patient entered data, EMRs, among others

Challenges

Post market challenges for use of data generated by AI

- Experience with other software shows that data may be difficult to get and timeliness becomes significant Monitoring for performance including development of bias and data drift – as for other AI
- Analysis of population segments and other sub-groups to check performance across spectrum of intended use including target population, equipment, user
- Monitoring for repeatability and reproducibility
- Variability of device output across use on same or similar patients/conditions, by same or different operators
- Opaque or black box models may introduce further risk and thus warrant higher stringency of monitoring
- Clinical reference standard may not be available for novel AI models

Opportunities

Post-market monitoring of data generated by AI can:

- Give further external validation of devices to support generalisability of model performance, i.e. ability to perform in a new use environment or new sample of patients.
- Track further clinical endpoints beyond model accuracy, for example mortality, rate of ICU admission, or other patient outcomes.
- Under a proper study design - create real-world evidence for subsequent pre-market decision making on indication expansion.
- Confidence in accuracy of generated data is paramount

Australian Government

Department of Health and Aged Care

Therapeutic Goods Administration

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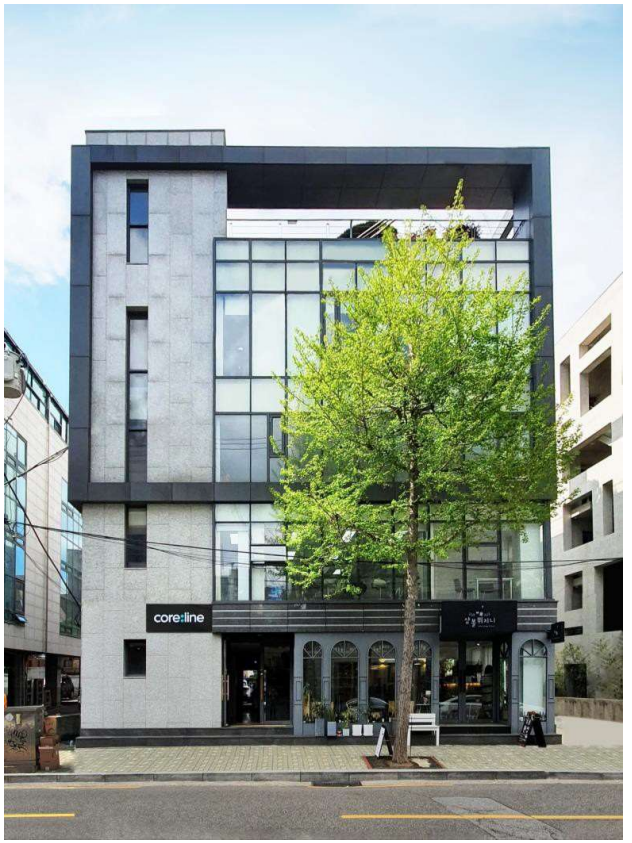
PMS for AI Medical Devices

Hae Ung Lee, Ph.D. Coreline Soft Co., Ltd.

OVERVIEW



Company Introduction

Leading large scale AI deployment

K-LUCAS
Korea

300 hospitals
(50 sites on Cloud based)

4 ITLR
EU, Nelson+

8 screening sites
in 5 countries
Full cloud operation

HANSE
Germany

3 Medical Center
Hybrid operation
(Cloud+ On-premise)

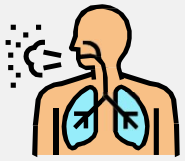
ILSP
Italy

8 IRCCS
4 Instituto Tumori
+6 University Hospitals
& Hospital Agencies

Product Overview – Clinical Products

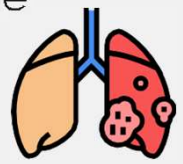
aview:LCS

aview:COPD



aview:CAC

aview: Lung Texture



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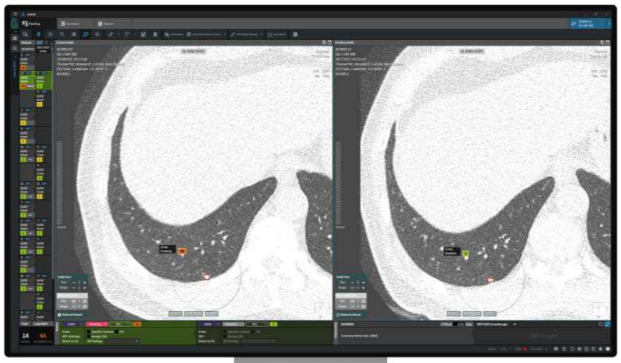
Clinical products I

aview:LCS



Key Features

1. Nodule CAD Sensitivity: 0.97, Specificity: 0.7644
2. F/up Mode(Automatic Nodule Matching)
3. Lung RADS(1.0/1.1)
4. Volumetric measurement & Volume Doubling Time(VDT)
5. Brock Score calculation
6. EUPS compliance

aview:COPD

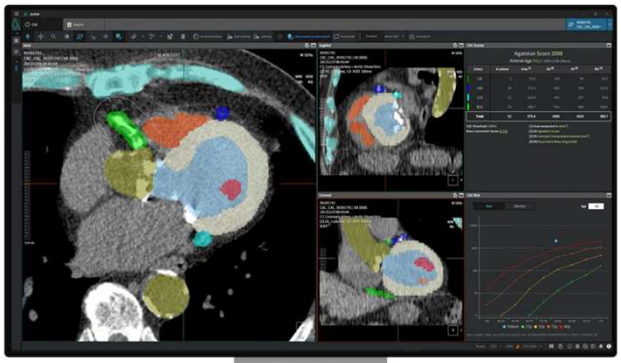
Key Features

1. Fully automated processing
2. Phenotyping
   - Emphysema
   - Fissure Integrity
   - Airway
   - Vessel

Clinical products II

aview:CAC

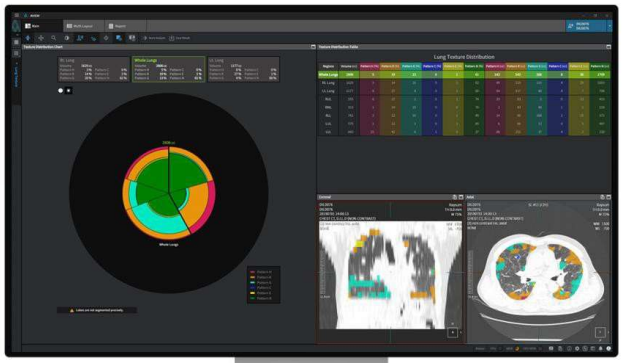
Non-Enhanced CTs



Key Features

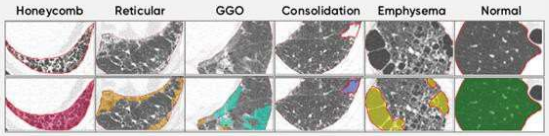
1. Fully Automated and Fast
2. Scores on each Vessel
3. Agatston, Volume and Mass Score

aview:Lung Texture



Key Features

1. Fully Automated using AI
2. Lung/Lobe segmentation based on AI
3. 6 Patterns Classification



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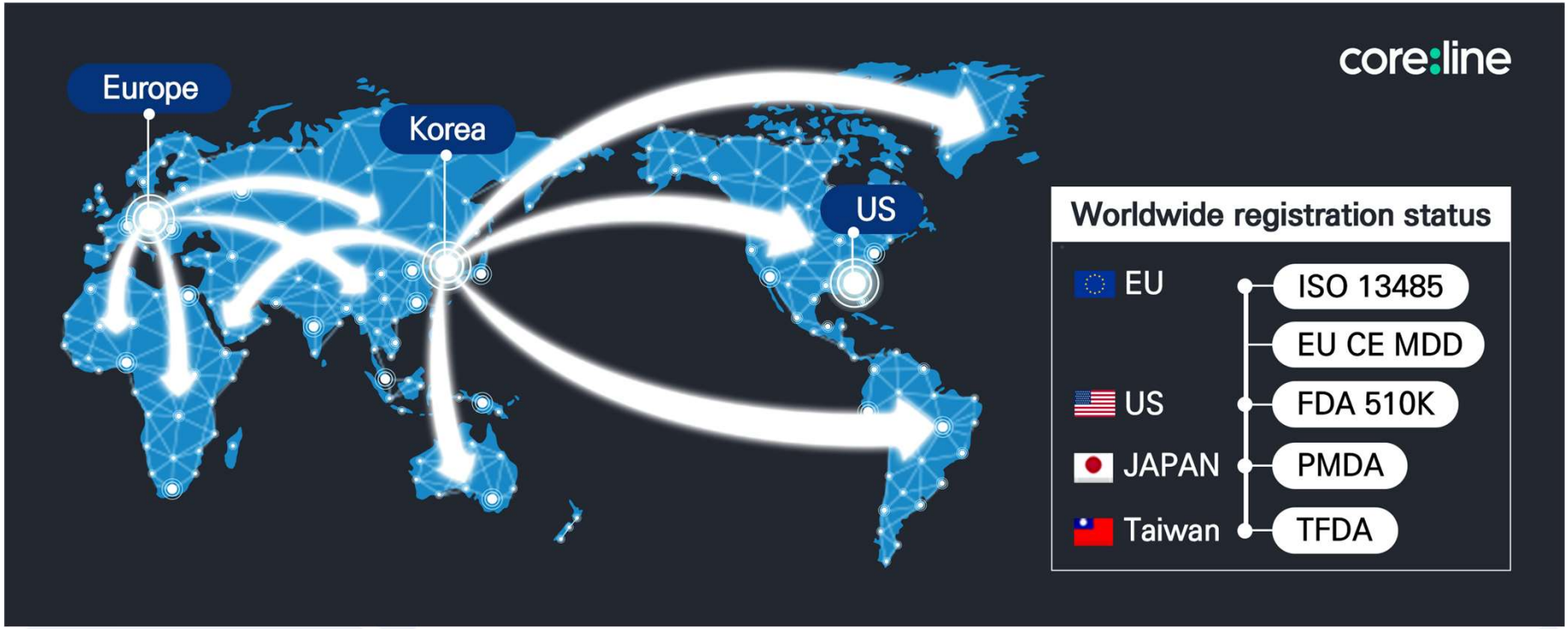
Company Introduction

Worldwide registration status



PMS for AI Medical Devices

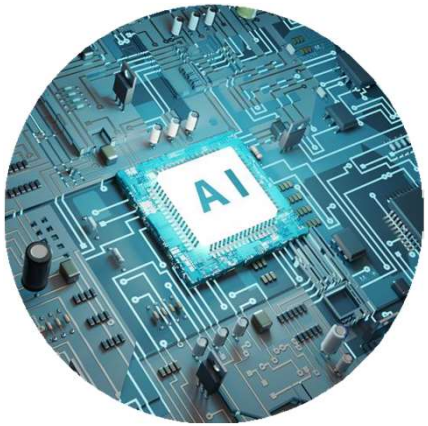
Key actions for PMS

- Vigilance Analysis
  - Real world Data analysis
    - Comply with regulatory requirements
    - Safety and effectiveness
- Literature search
- Cybersecurity information sharing networks searching

PMS for AI Medical Devices

How to conduct

01
Develop PMS plan



02
Implement the plan

03
Generate PMS report based on the findings

PMS for AI Medical Devices

PMS Plan

- Collecting and analyzing data
- Following up on collected complaint
- Communicating information to regulators and users
- Taking corrective actions on devices
- Producing a PMCF (Post-Market Clinical Following-up) plan or a rationale for why PMCF is not required

PMS for AI Medical Devices

Reporting

Region	Report Type	Details
US	Periodic Adverse Drug Experience Report (PADER/PAER)	Required by FDA
EU	Post-Market Surveillance Report (PMSR)	Required for low-risk Class I devices
	Periodic Safety Update Report (PSUR)	Required for Class IIa, Class IIb, and Class III devices
Korea	Report on production and export performance of medical devices	Reported annually
	Report on supply history of medical devices	Reported annually

AI Software

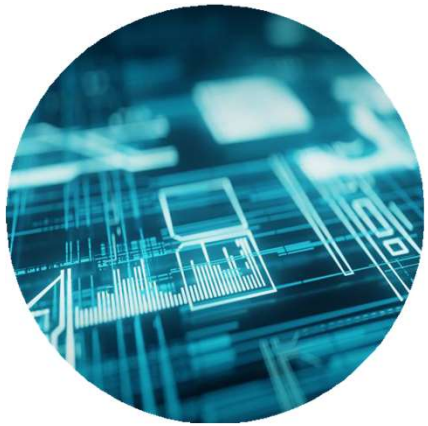
Continuous Learning Capabilities

Pre-market assessment is no longer sufficient

Control the learning process and respective changes

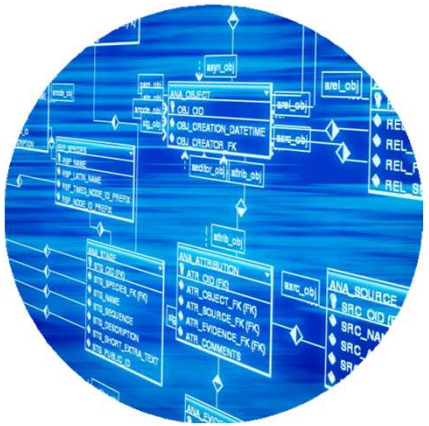
AI Software

Change Notification



Addition or reduction of input data type to generate the same output

Output results based on the approved input parameters (including changes for interpretation)



Approved workflow

AI Software

Change Notification related to a continuous learning algorithm

Exclusion/inclusion criteria for input data

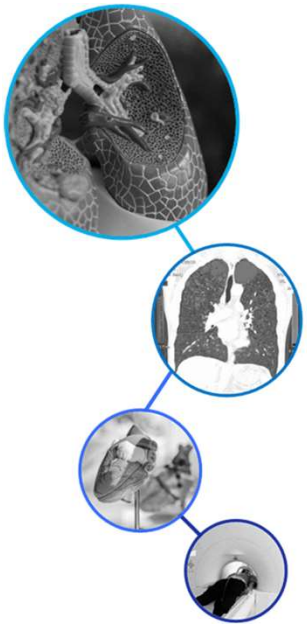
Defined boundaries

Baseline performance specifications

AI Software

Performance in Real World Setting

- High quality machine learning from private datasets
- But, limited learning data



- **NELSON** — Dutch-Belgian Lung Cancer Screening Trial
  - Lung Cancer Screeining
  - CT dataset
- **UKLS** — UK Lung Screening Trial
  - Lung Cancer Screening
  - CT dataset 3,000 cases
- **Russian LS** — Moscow Lung Screen Trial
  - Lung Cancer Screening
  - CT dataset 2,000 cases
- **SNUH** — 서울대학교병원, Collecting
  - 흉복부 전이암
  - CT dataset 12,200 cases
- **Russian LS** — (Korean Obstructive Lung Disease Cohort)
  - 17개 병원
  - 흉부 CT dataset 477 cases
- **ILD Project** — (10개 병원, Collecting)
  - 8개 병원
  - ILD CT dataset 762 cases
- **ROBINSCA** — (Risk Or Benefit IN Screening for Cardiovascular Diseases)
  - Coronary Artery Calcification
  - CT dataset (2,000 cases)
- **Dr. Answer** — (서울아산병원, 분당서울대병원, 신촌세브란스병원)
  - Coronary Artery Calcification
  - CT dataset (8,000 cases)
- **RT-ACS Project** — (신촌세브란스병원, 서울아산병원, Collecting)
  - 방사선종양치료계획 Multi-Contouring
  - CT dataset 800 cases (목표)

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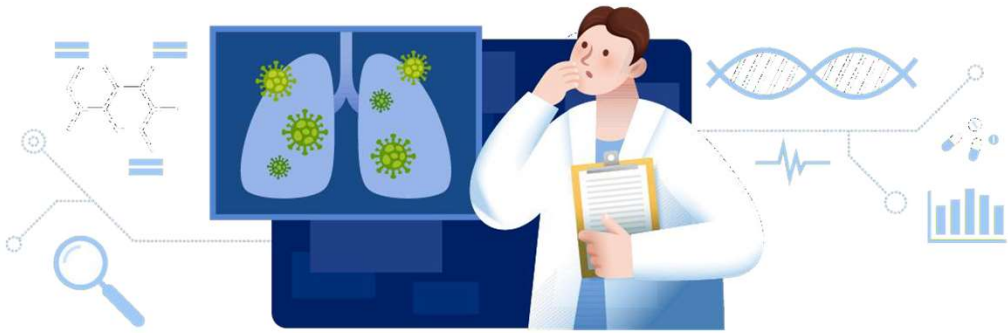
AI Software

Performance in Real World Setting

- Different setting from pre-market assessment
  - Different Data set
  - Uncontrolled clinical environment



→ Performance Evaluation for Real World Setting

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THANK YOU / QUESTIONS

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haeung.lee@corelinesoft.com

European Commission

European Union

IMDRF International Medical Device Regulators Forum

EU2023 EUROPEAN UNION Chair

17:00 – 17:25

Panel discussion

Similarities and differences in considerations for software and AI in the post-market phase

Matthias Neumann

Deputy Head Medical Devices Safety Unit, German Federal Ministry of Health (Moderator)

Jesús Rueda Rodríguez

Director General Strategies, Special Projects and International Affairs, MedTech Europe (Moderator)

European Commission | European Union