IMDRF International Medical Device Regulators Forum

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Specific Post-market Considerations for AI MDs

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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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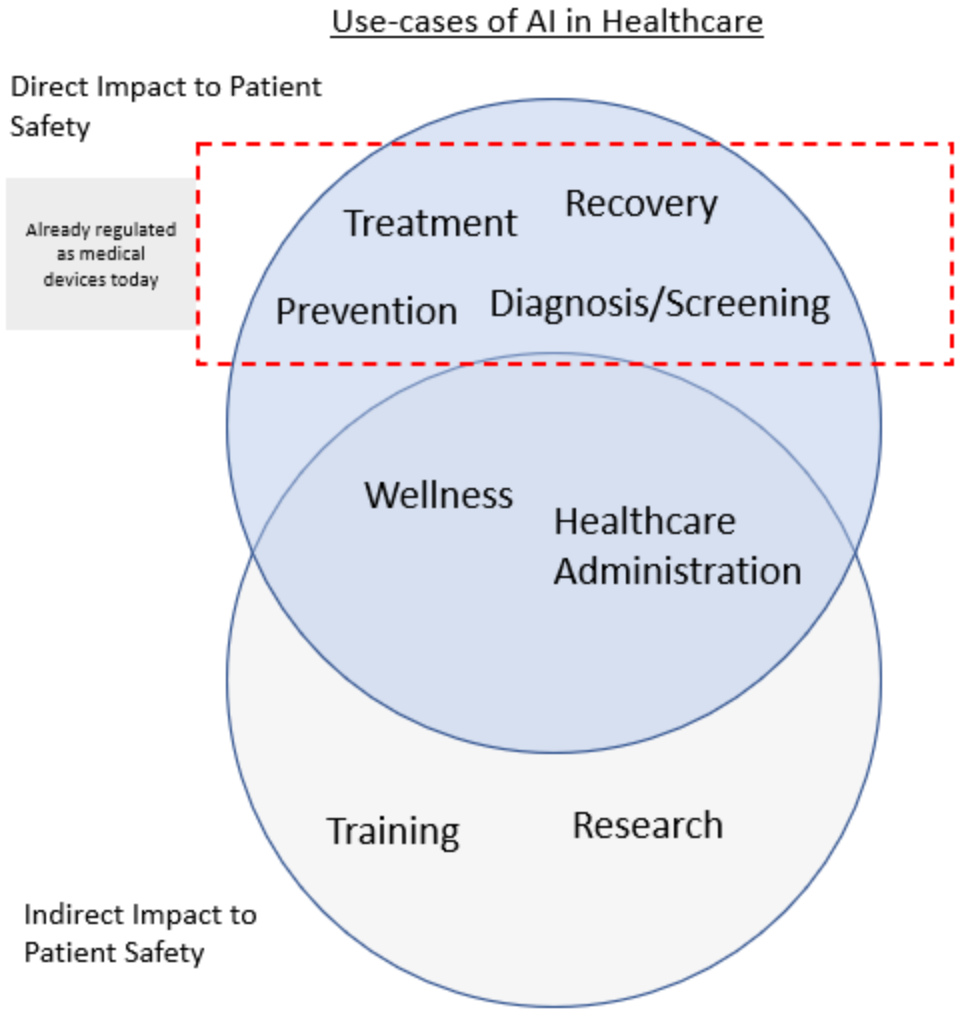
Artificial Intelligence based Medical Devices (AI-MD)



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

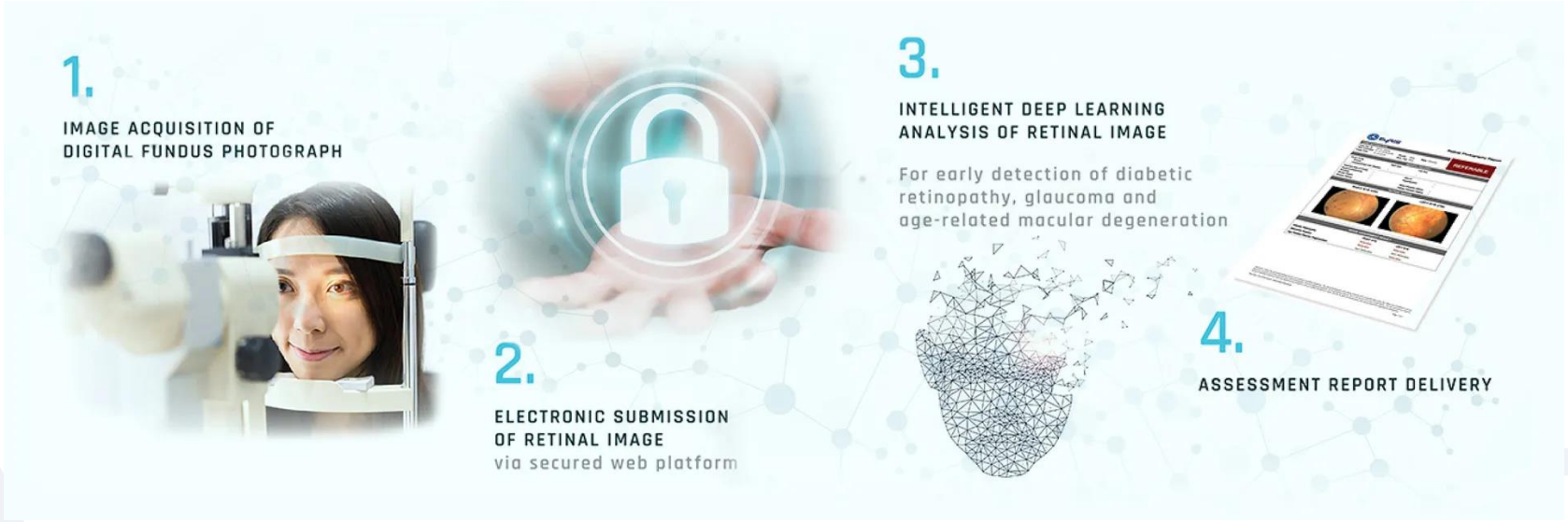
Legislative definition of "Medical Device" can be found in the First Schedule of the Health Products Act 2007: http://statutes.agc.gov.sg/

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

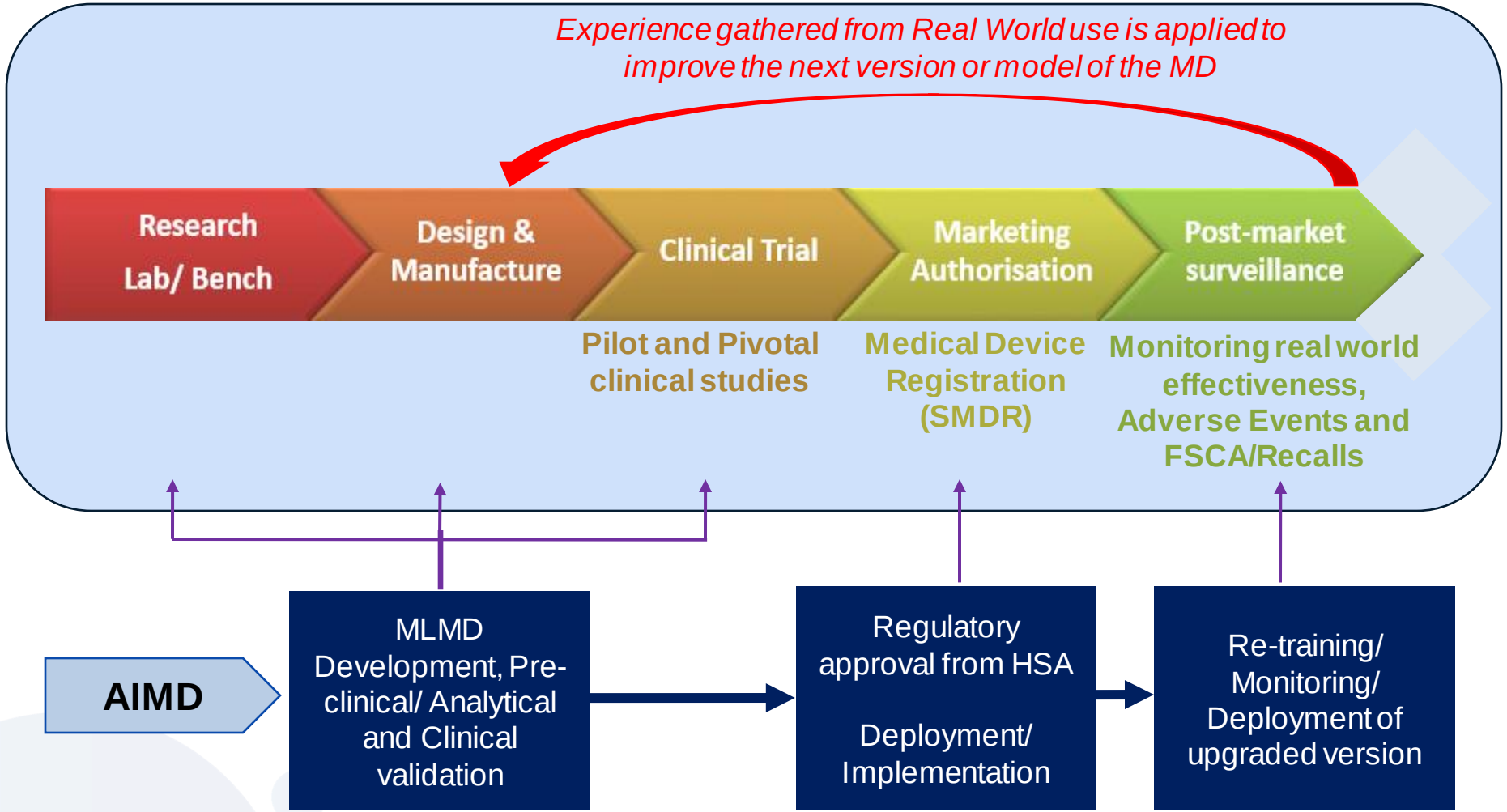
Risk Classification of AI-MDs

- 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

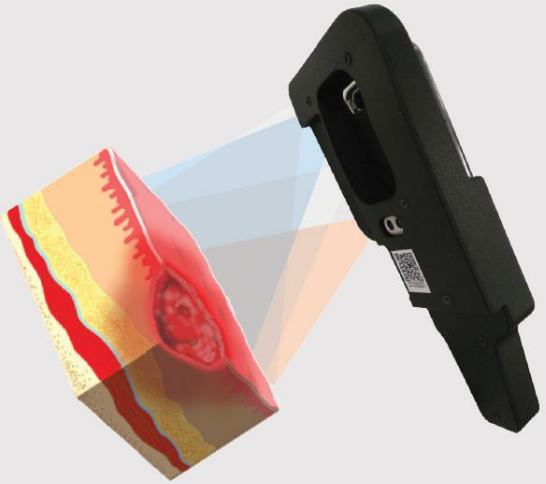
Change Management for AI-MDs - Examples

For locked and continuous learning algorithm based AI-MDs

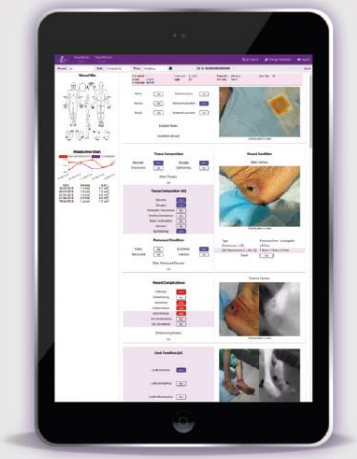
Examples of significant changes to AI-MDs subject to evaluation and approval by HSA (Technical Changes)

- 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

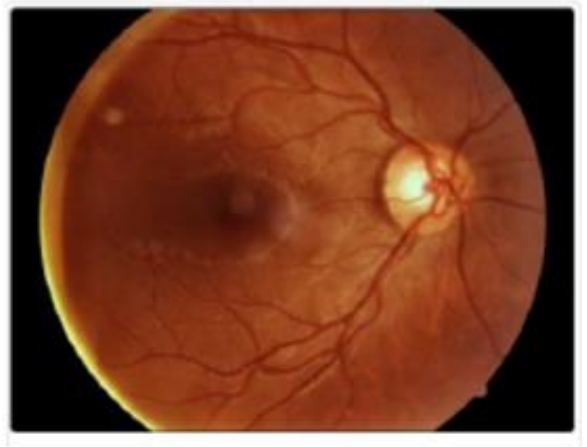
  Example – Removal of the review of the AI-MD's output results by a nurse and specialist from the workflow for deployment and use of the AI-MD.

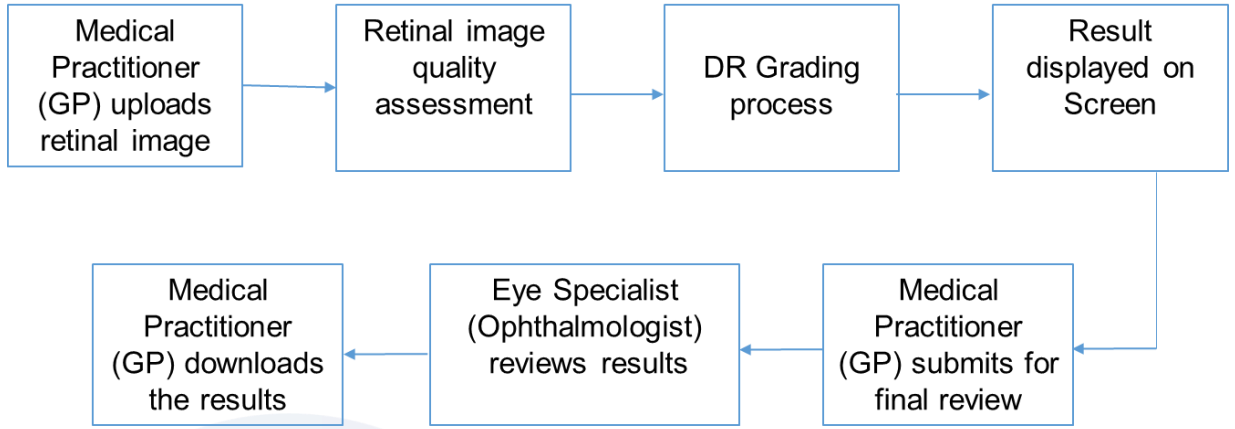
Change in the Workflow for deployment of AI-MD

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

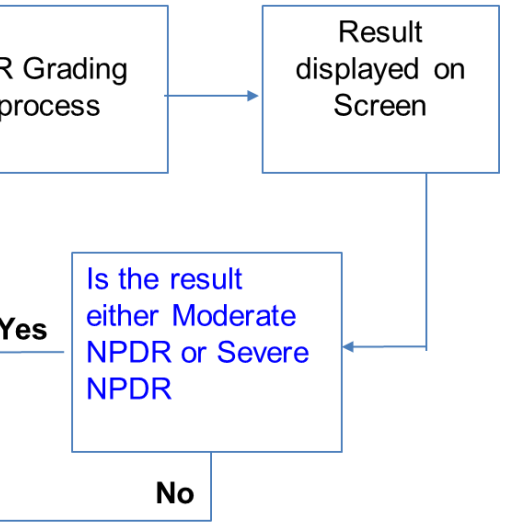
Disease
4. Moderate NPDR
5. Severe NPDR

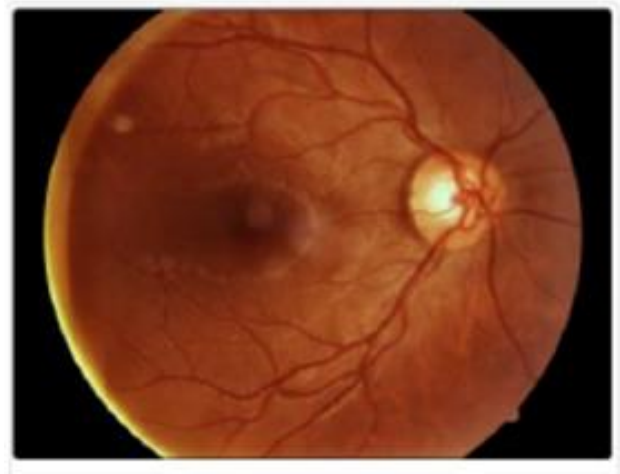
*American Academy of Ophthalmology

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

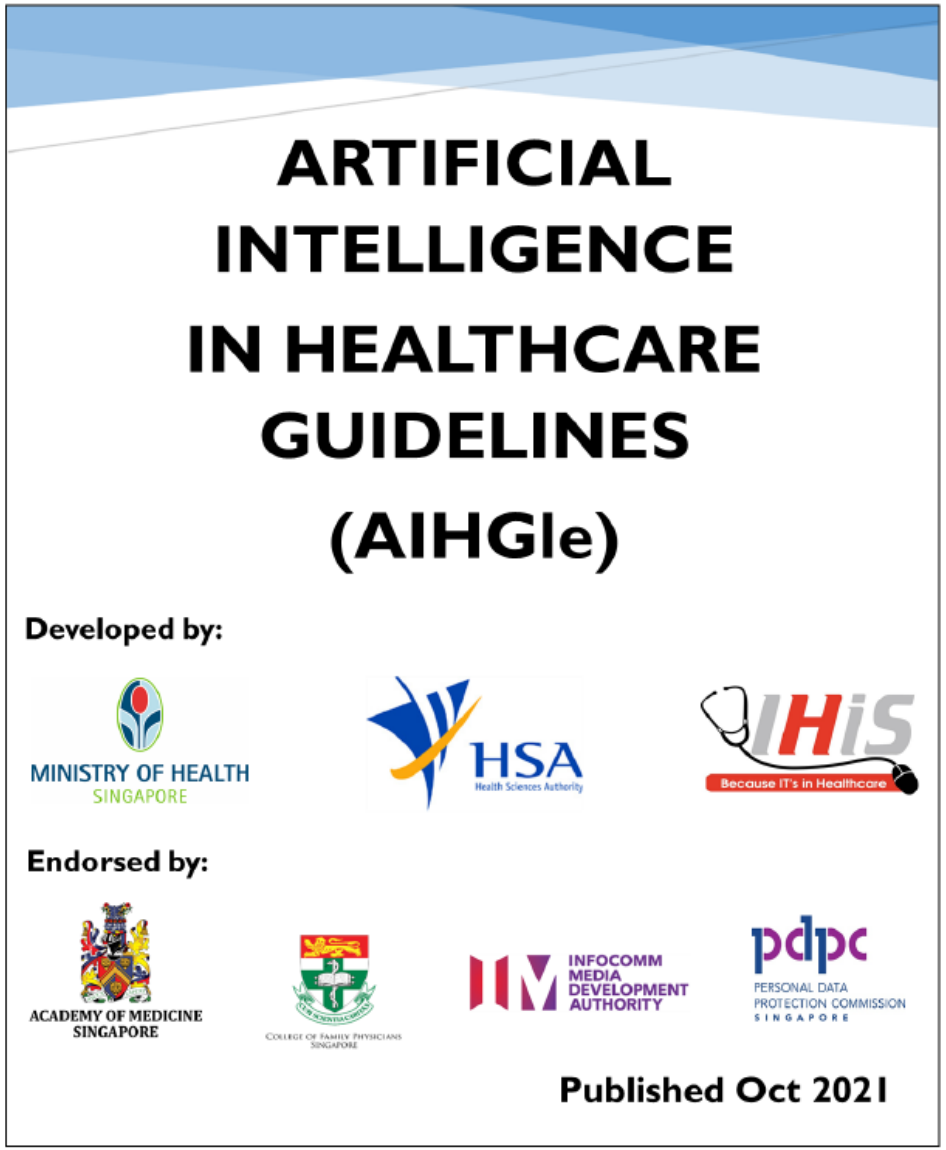
Guidelines for Implementation of AI-MDs in Healthcare

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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THANK YOU / QUESTIONS

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