



Federal Ministry
of Health



DITTA GLOBAL DIAGNOSTIC IMAGING,
HEALTHCARE IT & RADIATION THERAPY
TRADE ASSOCIATION



IMDRF International Medical
Device Regulators Forum

IMDRF /DITTA joint workshop on Artificial Intelligence in Healthcare

Regulatory challenges for AI – a European RA perspective

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16.09.2019



Agenda

1. Introduction
2. EU-regulation on „Medical Device Software“
3. Challenges caused by regulatory requirements on AI as MDSW
4. Other challenges



EU-Regulation on „Medical Software“

- New EU Regulation on Medical Devices (MDR-Medical Device Regulation) is setting new and modified requirements on software which might be considered as special challenges for AI.
- E.G. essential requirements:
- For devices that incorporate software or for software that are devices in themselves, the software shall be developed and manufactured in accordance with the state of the art taking into account the principles of development life cycle, risk management, including information security, verification and validation
- Devices that incorporate electronic programmable systems, including software, or software that are devices in themselves, shall be designed to ensure repeatability, reliability and performance in line with their intended use. In the event of a single fault condition, appropriate means shall be adopted to eliminate or reduce as far as possible consequent risks or impairment of performance.



EU-Regulation on „Medical Software“

- New EU Regulation on Medical Devices introduces for the majority of medical software (MDSW-Medical Device-Software) a stricter or modified conformity assessment procedure
- Majority of MDSW (including AI) will be upclassified from class I

		Significance of Information provided by the MDSW to a healthcare situation related to diagnosis/therapy		
		High Treat or diagnose ~ IMDRF 5.1.1	Medium Drives clinical management ~ IMDRF 5.1.2	Low Informs clinical management (everything else)
State of Healthcare situation or patient condition	Critical situation or patient condition ~ IMDRF 5.2.1	Class III Category IV.i	Class IIb Category III.i	Class IIa Category II.i
	Serious situation or patient condition ~ IMDRF 5.2.2	Class IIb Category III.ii	Class IIa Category II.ii	Class IIa Category I.ii
	Non-serious situation or patient condition (everything else)	Class IIa Category II.iii	Class IIa Category I.iii	Class IIa Category I.i



EU-Regulation on „Medical Software“

- Notified Body (NB) Involvement necessary
- NB has to certify the QMS and to perform at least one Technical Documentation Assessment
- The MDR is defining new processes as part of an QMS: e.g.
 - Clinical Evaluation including Post Market Clinical Follow-Up (lifecycle process, PMCF – real world evidence)
 - Post market surveillance system (planned systematic lifecycle process to proactively collect and review experience gained from devices placed on the market for the purpose of identifying any need to immediately apply any necessary corrective or preventive actions)
- The Technical documentation must include (beside others) :
 - software **verification and validation** (describing the software design and development process and evidence of the validation of the software, as used in the finished device.) This information shall typically include the summary results of all verification, validation and testing performed both in-house and in a simulated or actual user environment **prior to final release**.



Summary

- Relevant AI is regulated as Medical Device Software (MDSW) in the EU
- No special rules for AI
- Third Party review of the QMS and (in practice) Technical Documentation necessary
- Software validation and verification necessary
- reliability, repeatability also in case of single fault condition required
- Clinical Evaluation, demonstration of clinical benefit and clear description of the intended purpose/claims necessary



Regulatory perspectives for different kinds of AI

Artificial Intelligence:

1 : a branch of computer science dealing with the simulation of intelligent behavior in computers

2 : the capability of a machine to imitate intelligent human behavior

The theory and development of computer systems able to perform tasks normally requiring human intelligence, such as visual perception, speech recognition, **decision-making**, and translation between languages

Machine learning is an application of artificial intelligence (AI) that provides systems the ability to automatically learn and improve from experience without being explicitly programmed. **Machine learning** focuses on the development of computer programs that can access data and use it learn for themselves.

Deep learning is a subset of **machine learning in artificial intelligence (AI)** that has networks capable of **learning** unsupervised from data that is unstructured or unlabeled. Also known as **deep neural learning** or **deep neural network**

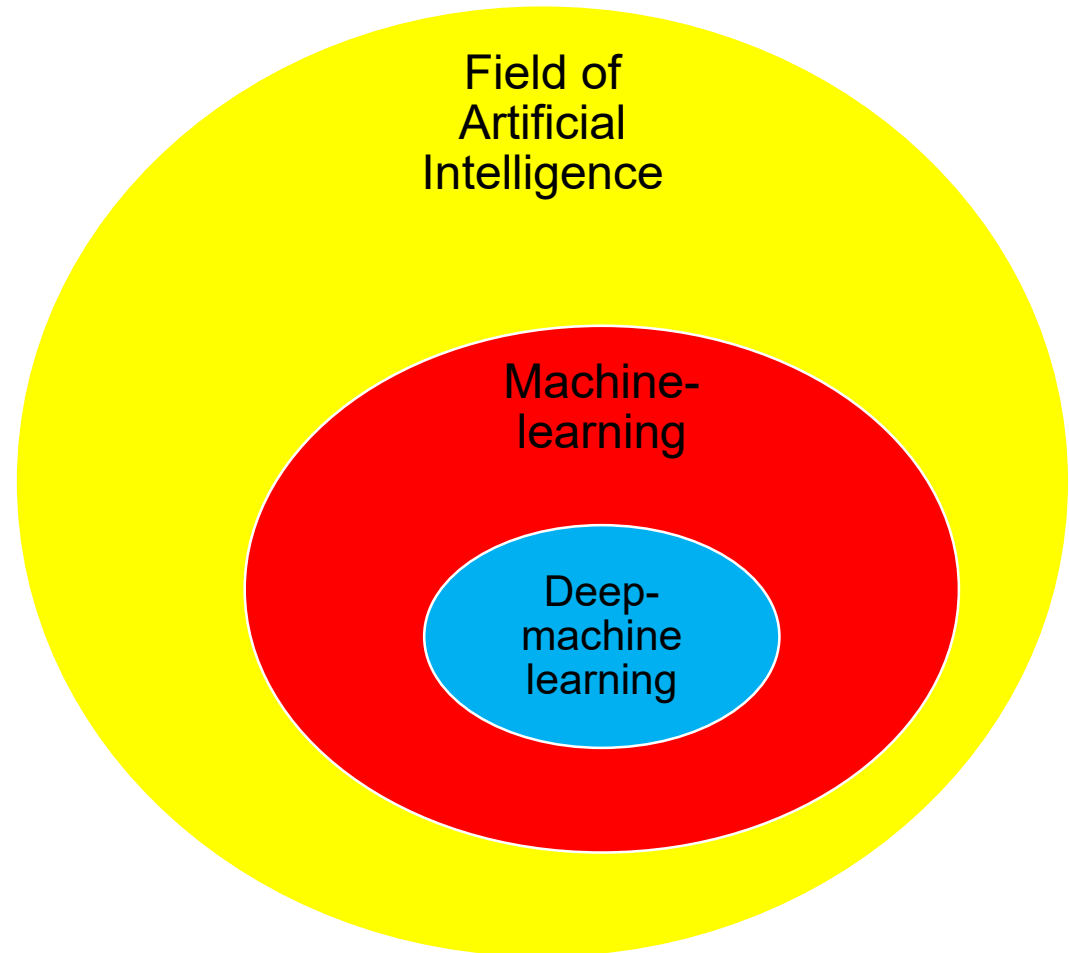


Regulatory perspectives for different kinds of AI

AI-1 Expert Systems
(based on rules)

AI-2 machine
learning
(supervised or
unsupervised learning)
finalised before approval

AI-3 (deep) machine
learning (continuous
learning in field,
generating source
code/knowledge,
additional claims)





Clinical Evaluation of AI

IMDRF and the EU MDR are requiring for the clinical evaluation:

- A SaMD manufacturer is expected to implement on-going lifecycle processes to thoroughly evaluate the product's performance in its intended market. As part of normal new product introduction processes, prior to product launch (pre-market) the manufacturer generates evidence of the product's accuracy, specificity, sensitivity, reliability, limitations, and scope of use in the intended use environment with the intended user,

Clinical Evaluation of AI

Challenges for all kinds of AI:

- at least 2 independent big pools of representative and assessed/validated data necessary for learning and validation/verification
- No specific regulatory requirements for specificity nor sensitivity available

- Solution (?):
- Establishment of national or international databases containing validated clinical information (e.g. records of medical findings together with e.g. X-ray records, physiological signals, MRT, genome sequences)

Clinical Evaluation of AI

Challenges for all kinds of AI:

- No specific regulatory requirements for specificity nor sensitivity available
- State of the art in medicine mostly not defined nor well known

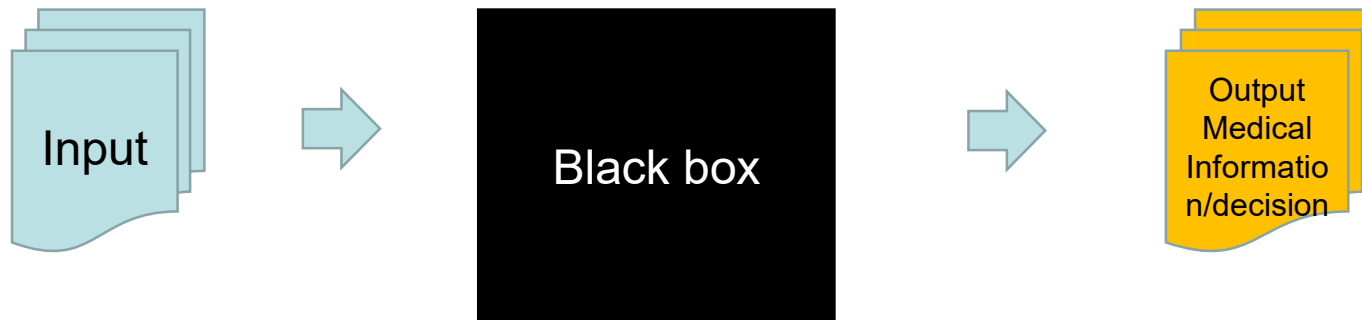


- Solution (?):
- Establishment of national or international databases containing **validated clinical information** (e.g. records of medical findings together with e.g. X-ray records, physiological signals, MRT, genome sequences)



Clinical Evaluation of AI

- **Clinical evaluation** is a systematic and planned process to continuously generate, collect, analyze, and assess the **clinical** data pertaining to a SaMD in order to generate **clinical** evidence verifying the **clinical** association and the performance metrics of a SaMD ...

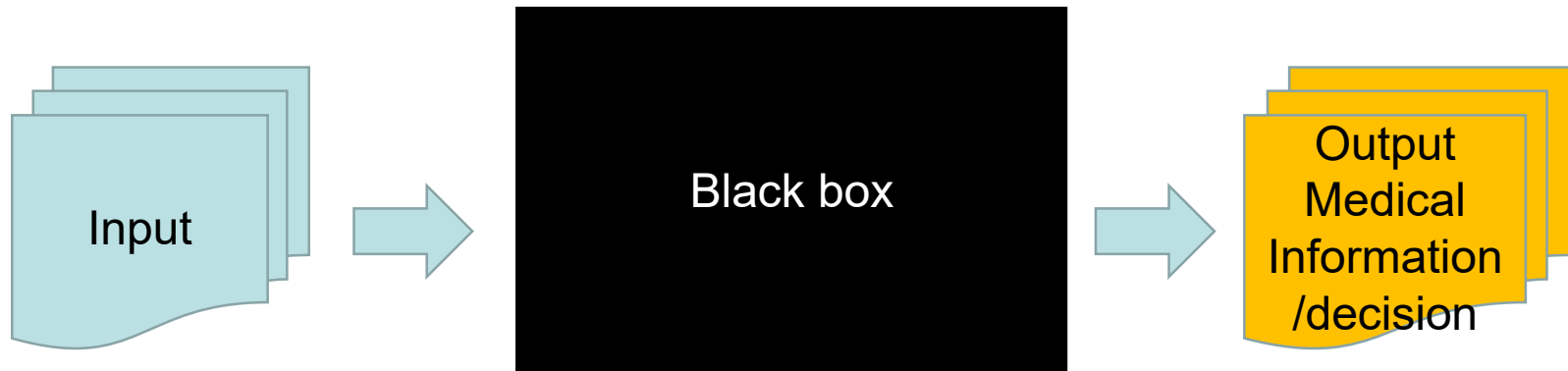


Solution (?):

- PMCF Post-market clinical follow up studies
- documentation (collection and regular analysis) of the processes/decisions in the black box for each output
- Explainable Artificial Intelligence XAI

Clinical Evaluation of AI

- Valid Clinical Association
- Is there a valid clinical association between your SaMD output and your SaMD's targeted clinical condition?



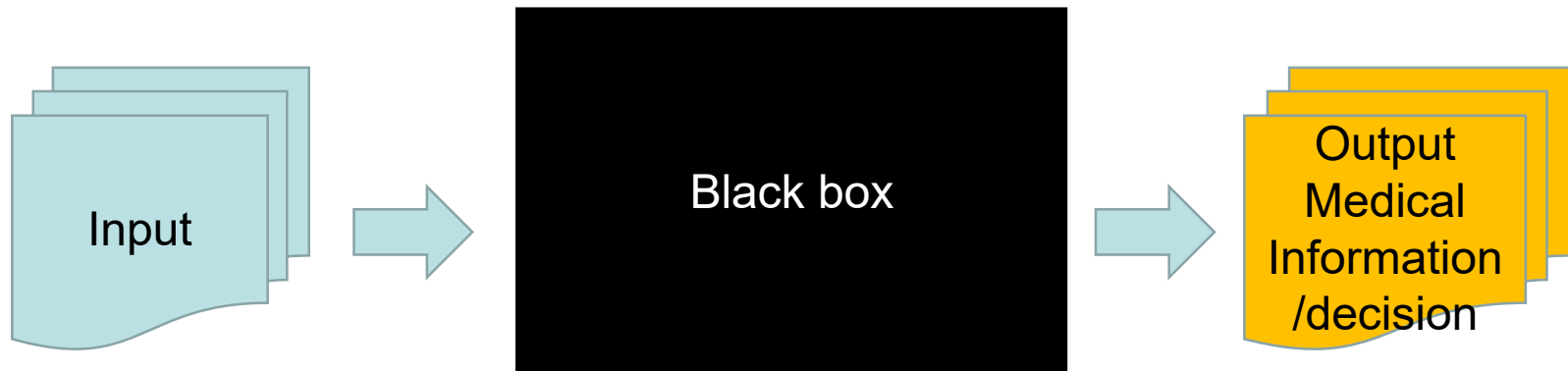
Solution (?):

- sophisticated testing against the state of the art in medicine
- Explainable Artificial Intelligence XAI



Clinical Evaluation of AI

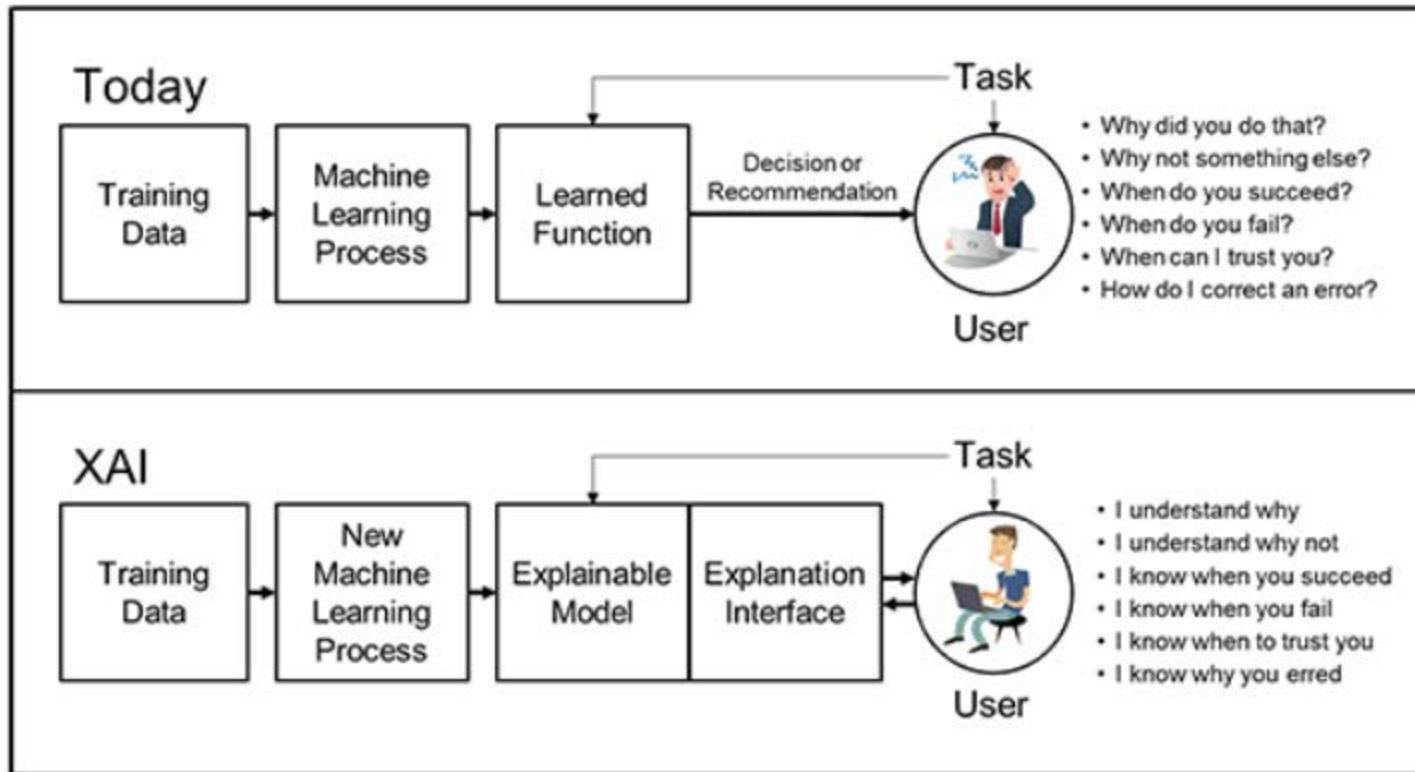
- **Analytical Validation**
- Does your SaMD correctly process input data to generate accurate, reliable, and precise output data?



- In case of rule based AI maybe not a problem, but in case of machine (self-) learning (AI-2. AI-3), as the processes inside the black box are not known.
- In case of continuous learning (AI-3): How to guaranty the reliability, accuracy etc.?
- Solution(?): Explainable AI



XAI- Explainable AI





Other challenges

- MDR requires clinical data to support – intended purpose or the claims
- If there is a change of the intended purpose (except some limitation of indications) a new conformity assessment including new clinical evaluation is necessary

- How should this be done in case of AI-3 (continuous learning in the field and creating new source code and knowledge etc.) ?
- Possible solution?:
- AI may continue to learn within set limits (original claims/intended purpose)
- AI is creating clinical data to be used for later re-assessment
- Additional claims may become operational only after re-assessment, re-validation, re-verification and if necessary recertification



Other challenges

The involved Notified Body shall assess

- The software **verification and validation** (describing the software design and development process and evidence of the validation of the software, as used in **the finished device**)
- How should this be done in case of AI-3 (continuous learning in the field and creating new source code and knowledge etc.)
- Possible solution?: AI may continue to learn within set limits (original claims/intended purpose) additional claims may become operational only after re-validation and re-verification



Other challenges

The involved Notified Body shall assess if the AI is

- designed to ensure repeatability, reliability and performance in line with their intended use. In the event of a single fault condition, appropriate means shall be adopted to eliminate or reduce as far as possible consequent risks or impairment of performance.
- How to implement or test single fault safety of AI ? (In particular if the AI-3 generates its own source code in the field)
- Software validation is state of the art and not software testing.
- How to ensure repeatability and reliability if the AI is not based on rules (AI-1)?



Other challenges

Art. 22 GDPR Automated individual decision-making, including profiling

- The data subject shall have the right not to be subject to a decision based solely on automated processing, ..., which significantly affects him or her.
-data controller shall implement suitable measures to safeguard the data subject's rights and freedoms and legitimate interests, at least the right to obtain human intervention on the part of the controller, to express his or her point of view and to contest the decision.



Summary

- European medical devices regulation doesn't properly address suitable regulatory requirements or pathways for AI-3 which is learning, source code/or knowledge generating in the field
- Progress in the area of regulatory science necessary
- Establishment of assessable big validated clinical/health data pools should be considered (preferable on international level)
- AI must ensure more transparency – Processes/decisions within the Black-Box must be recorded/documentated
- Further developments of the concept of Explainable AI might encourage regulators to consider necessary changes in the near future



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Thank you for the attention

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