leanRAQA

Is your state of affairs in MDR *state of the art*?

Michelle Lott, RAC
Principal & Founder, leanRAQA

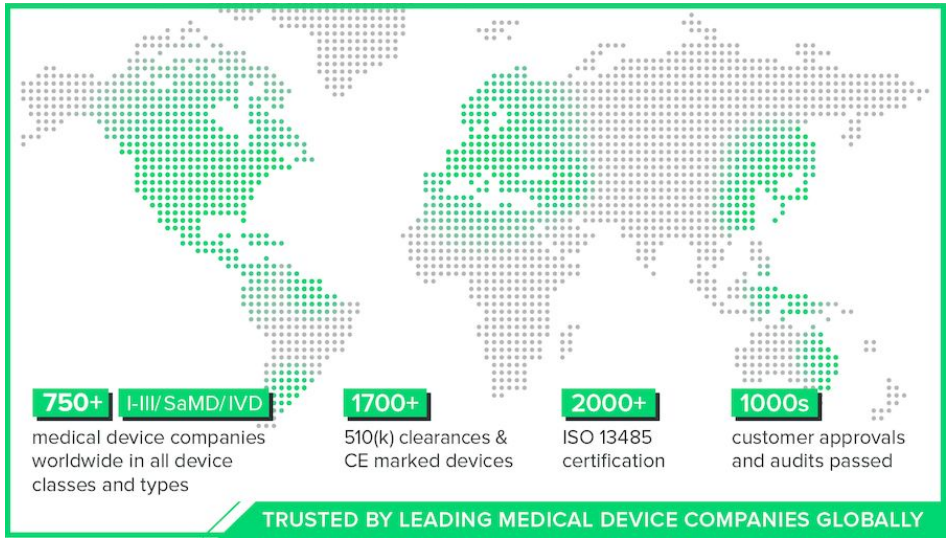
MEDICAL DEVICE QUALITY IS ALL WE DO, AND WE'RE ALWAYS AHEAD OF THE GAME.

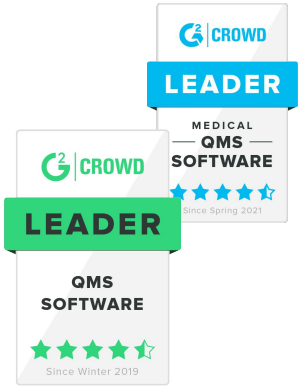
1.5M
years industry experience

522k
podcast listeners

182k+
look to us for the latest in quality

#1
blog and podcast in the industry





"Best eQMS I have ever used..."

This is the easiest eQMS I have used in the 20 years I have been in the Medical Device Industry. ***It is simple, intuitive and easy to use...*** We are successfully implementing a Quality Culture.

- Director of Regulatory Affairs & Quality Assurance

"Modern QMS Software and Outstanding Customer Service."

★★★★★

"Demystifying QMS and Regulatory Requirements"

★★★★★

"Makes your QMS Simple and Effective"

★★★★★

greenlight guru

About leanRAQA

- Expert in RAQA for ~ 20 years
- Advisor on FDA GMP Advisory Committee
- Master Grief Counselor

Michelle Lott
Principal and Founder

Morty
Chief Entertainment Officer

Chopper
Chief Fun Officer

Lucy
Chief Therapy Officer

State of the Art (SOTA)
vs.
Standard of Care (SOC)

More than semantics?

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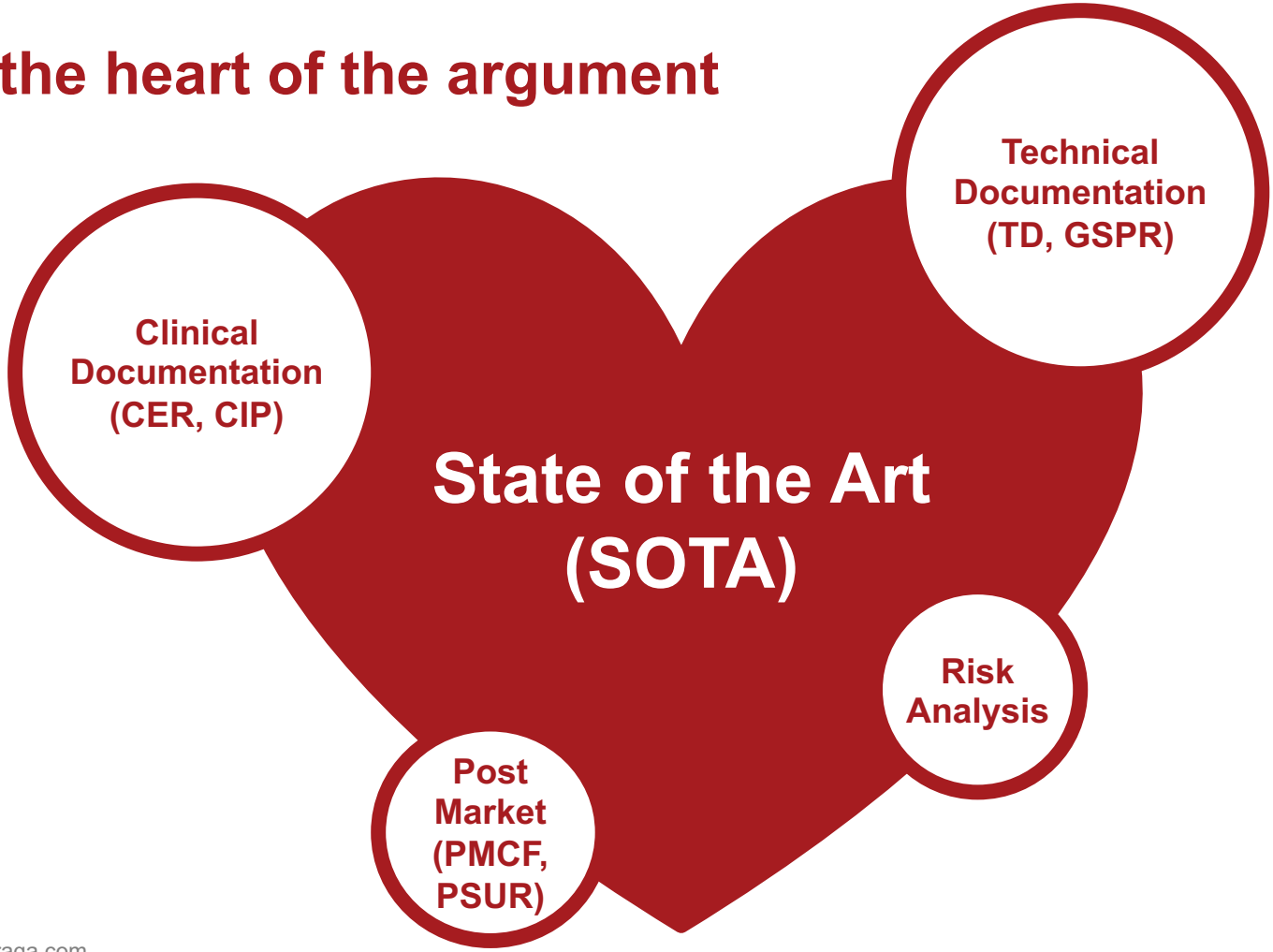
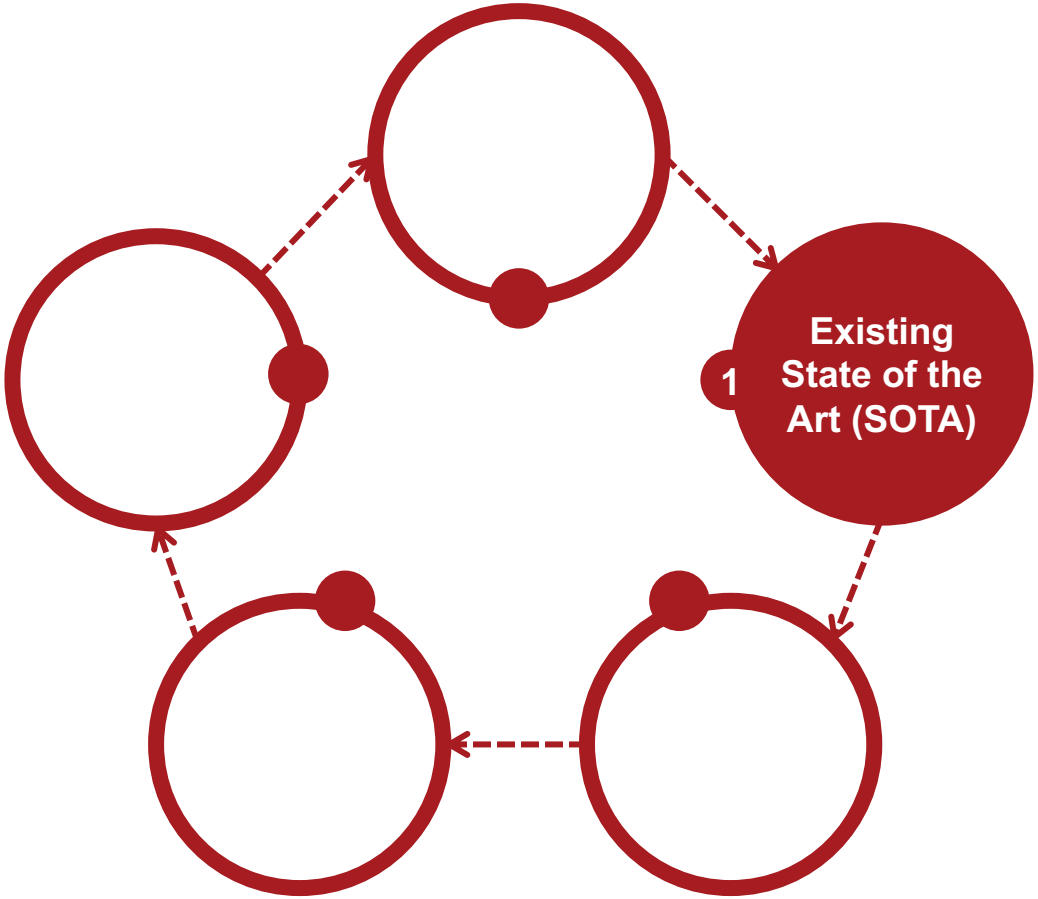
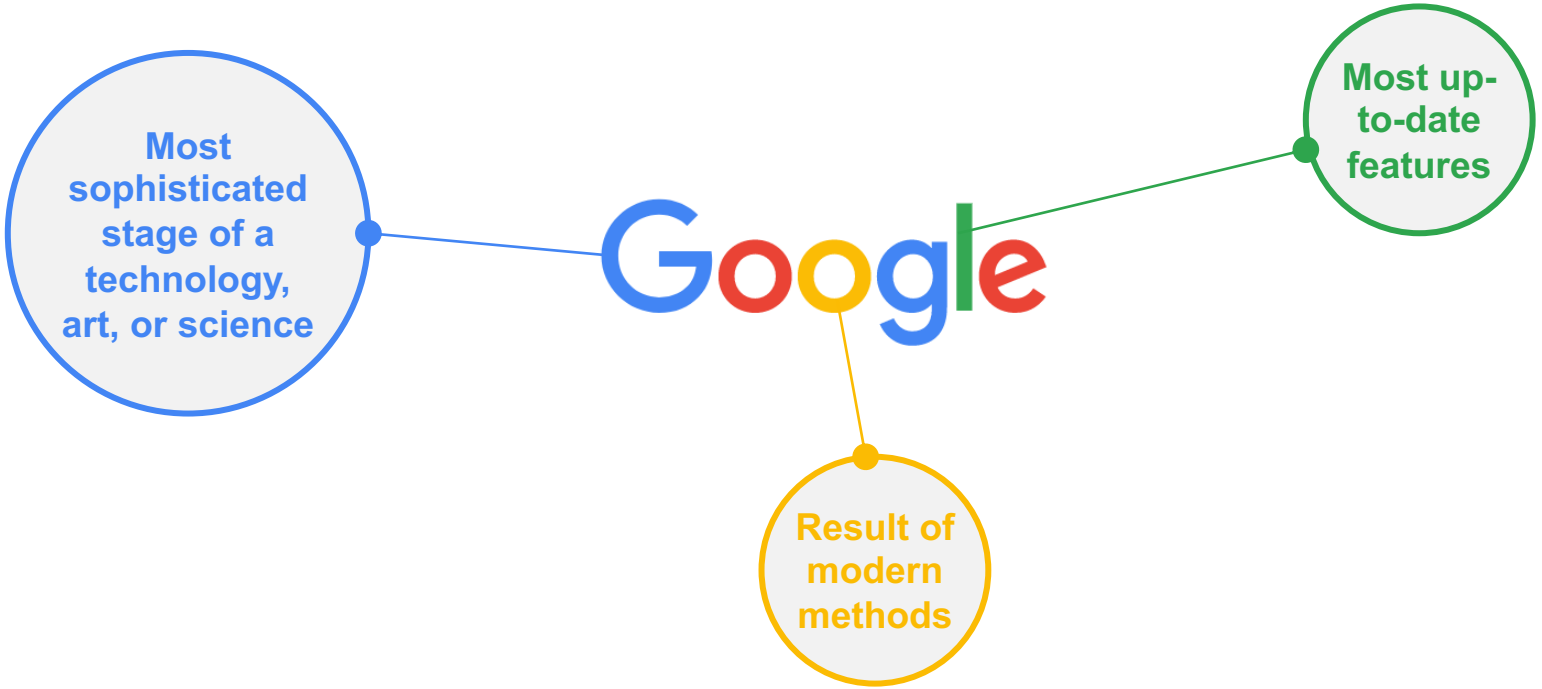
At the heart of the argument



Lifecycle of State of the Art



SOTA according to…



What say you, Mister ISO 14971:2019?

ISO 14971:2019 says… [Definition]

1st time in history

State of the Art: Developed stage of technical capability […] as regards products, processes and services, based on the relevant consolidated findings of science, technology and experience.

- Currently and generally accepted as good practice in technology and medicine
- Does not imply the most technologically advanced solution

Mentioned 15 times

ISO 14971:2019 says… [Pre-market]

The manufacturer takes into account the generally acknowledged *state of the art*, in order to determine the suitability of a medical device to be placed on the market for its *intended use*.

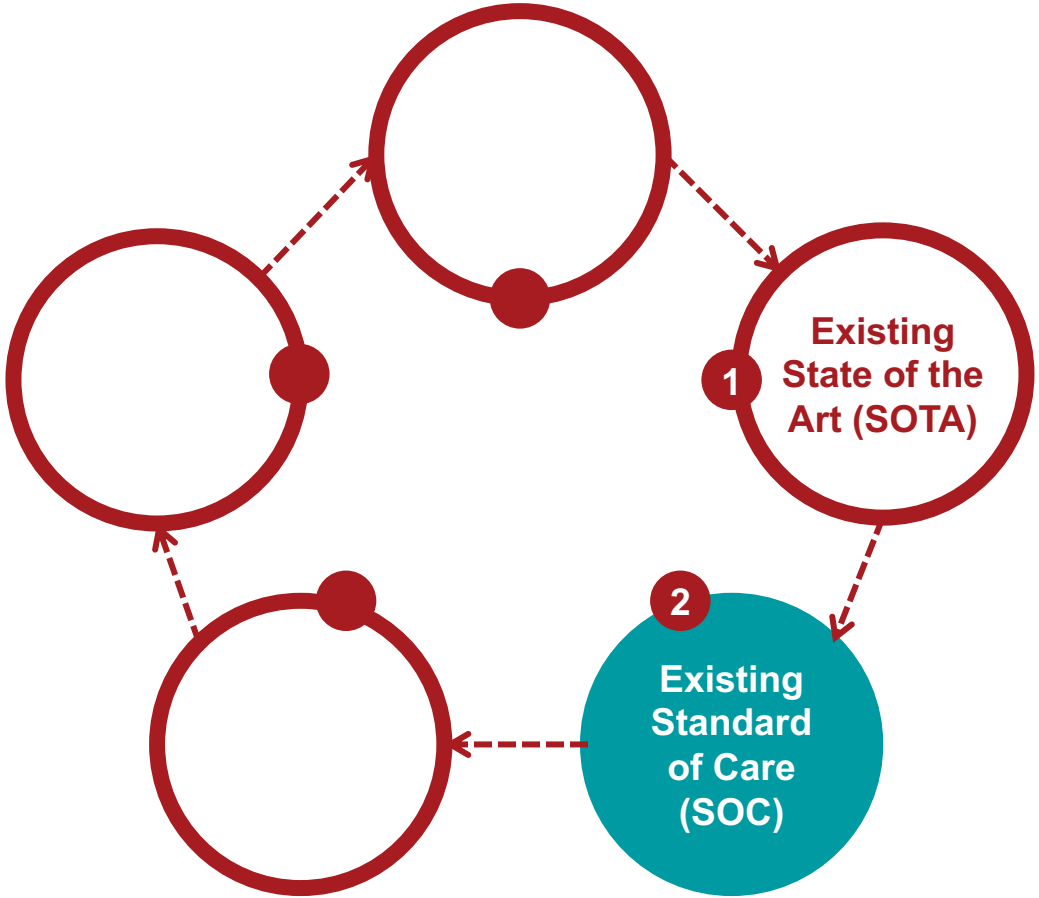
Information related to the generally acknowledged *state of the art* can include new or revised standards, published validated data specific to the application of the medical device under consideration, the availability of alternative medical devices and/or therapies, and other information **(10.2)**

ISO 14971:2019 says… [Post-market]

The manufacturer should also take into account considerations of the generally acknowledged *state of the art*, including new or revised standards. **A 2.10**

The conditions under which follow-up actions need to be considered, are extended with changes in the *state of the art* that can be relevant to safety, such as alternative medical devices and/or therapies becoming available on the market, as well as changes in risk perception or risk acceptability. **A 2.10**

Lifecycle of State of the Art



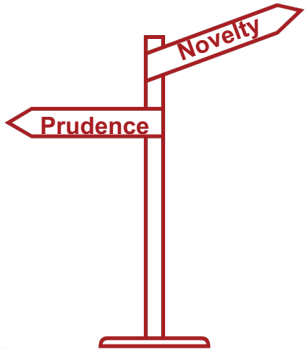
SOC according to…

Appropriate treatment based on scientific evidence and collaboration between professionals

Google

What a minimally competent physician in the same field would do in the same situation, with the same resources

Level at which the average, prudent provider in a given community would practice



Wherefore art thou, Standard of Care?

What say you, Mister MDR?

MDR says…

Medical Devices Regulation
EU MDR

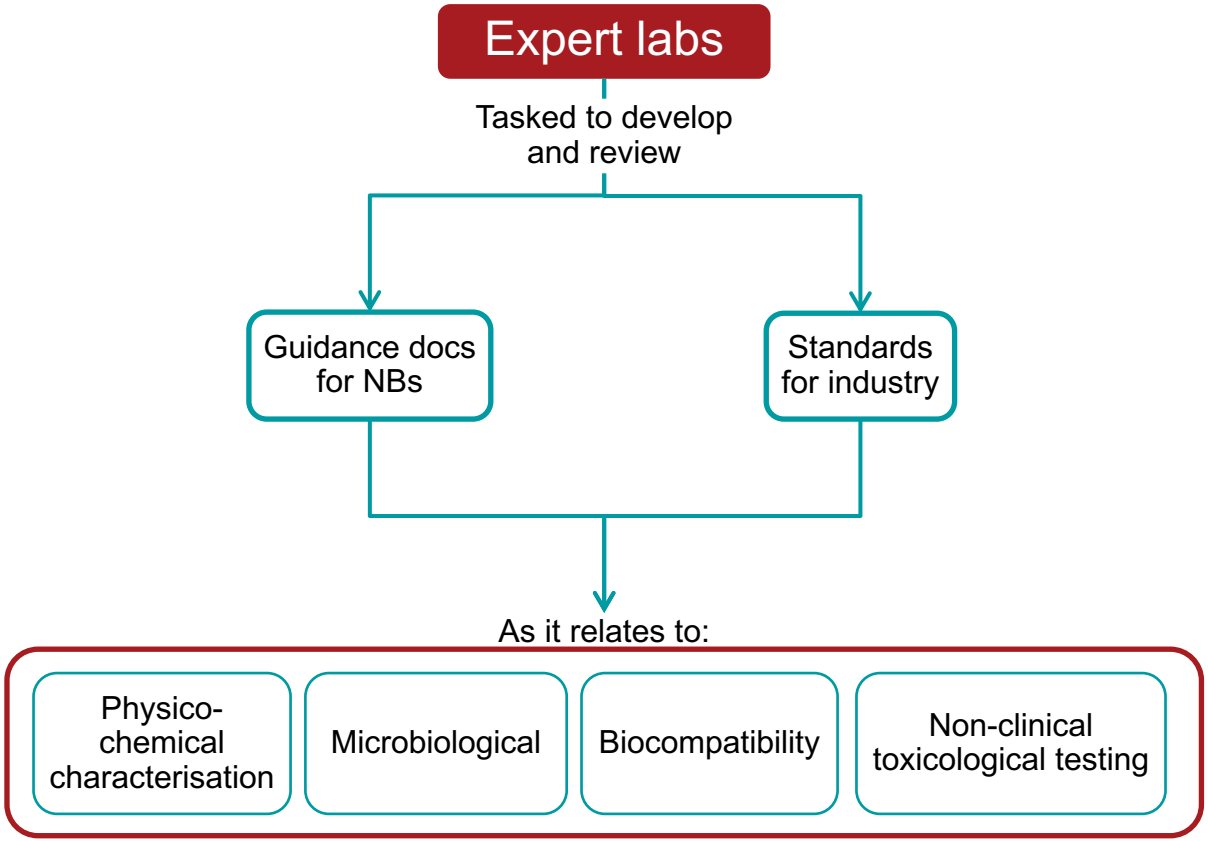
70 new definitions

Does **NOT** define:

- State of the Art
- Standard of Care

Mentioned SOTA 11 times

What MDR does say – Ch. VIII Cooperation w/ expert labs



What MDR does say – Annex 1 General Safety and Performance

- Devices shall achieve the performance intended that… they are **suitable for their intended purpose**. They shall be safe and effective … provided that any risks which may be associated with their use **constitute acceptable risks** when weighed against the benefits … **taking into account the generally acknowledged *state of the art***.

- **Risk control measures** … for the design and manufacture of the devices shall **conform to safety principles**, taking account of the **generally acknowledged *state of the art***….

What MDR does say – Annex XIV Clinical Eval. and PMCF

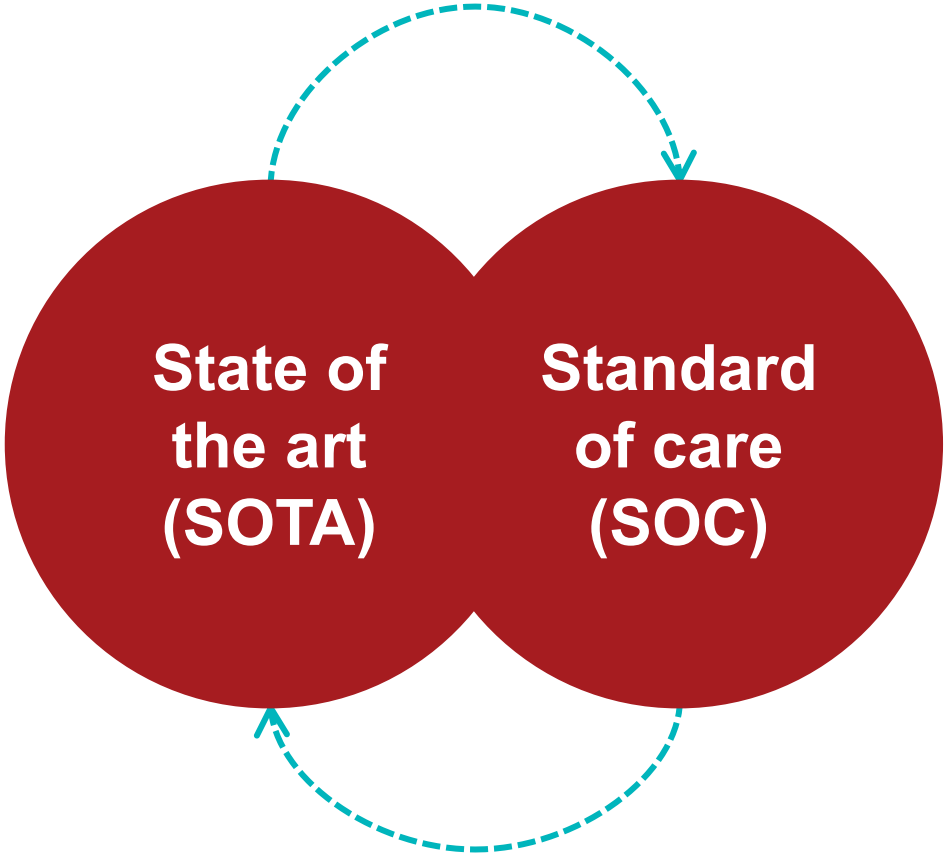
- To plan, **continuously conduct** and document a clinical evaluation, manufacturers shall establish and update a clinical evaluation plan which shall include at least:

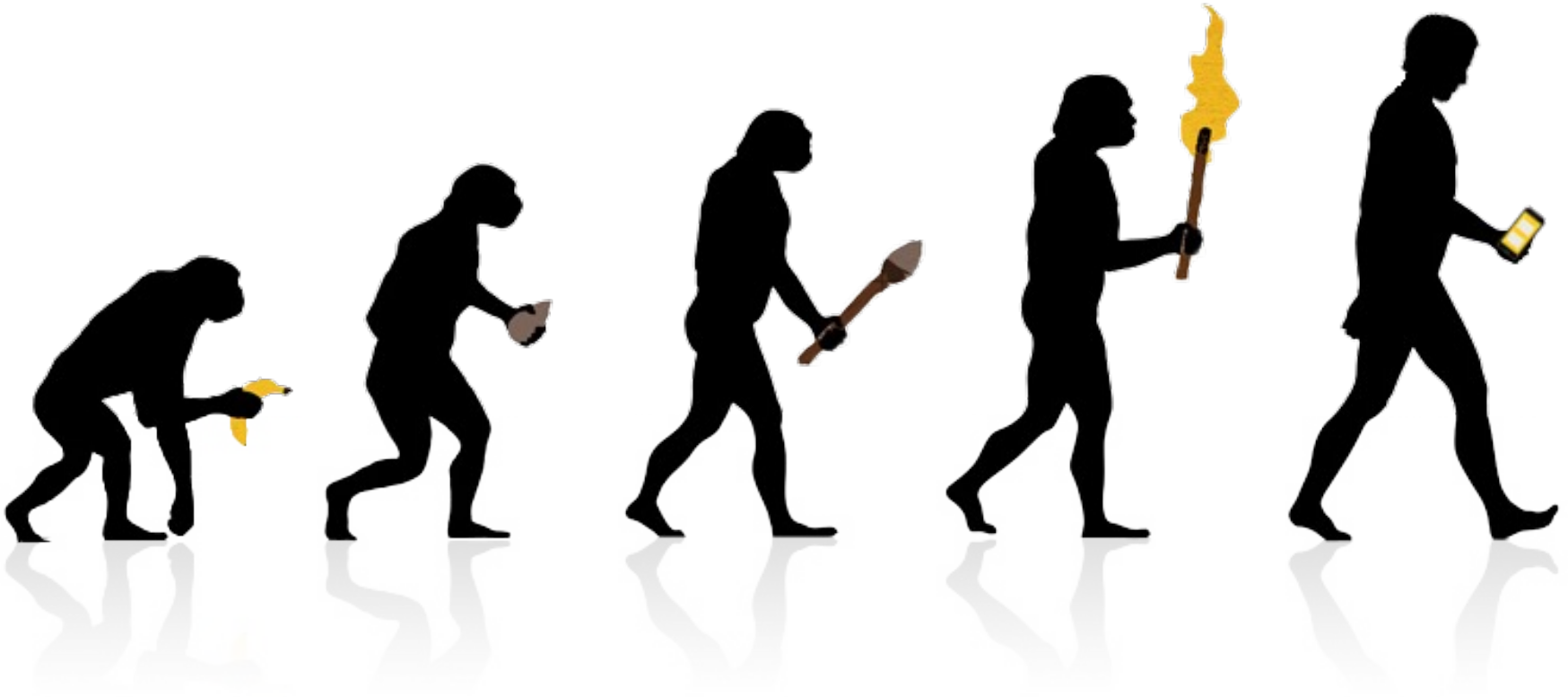
  – An indicative list and specification of parameters to be used to determine, based on the ***state of the art*** **in medicine**, the **acceptability of the benefit-risk ratio**;

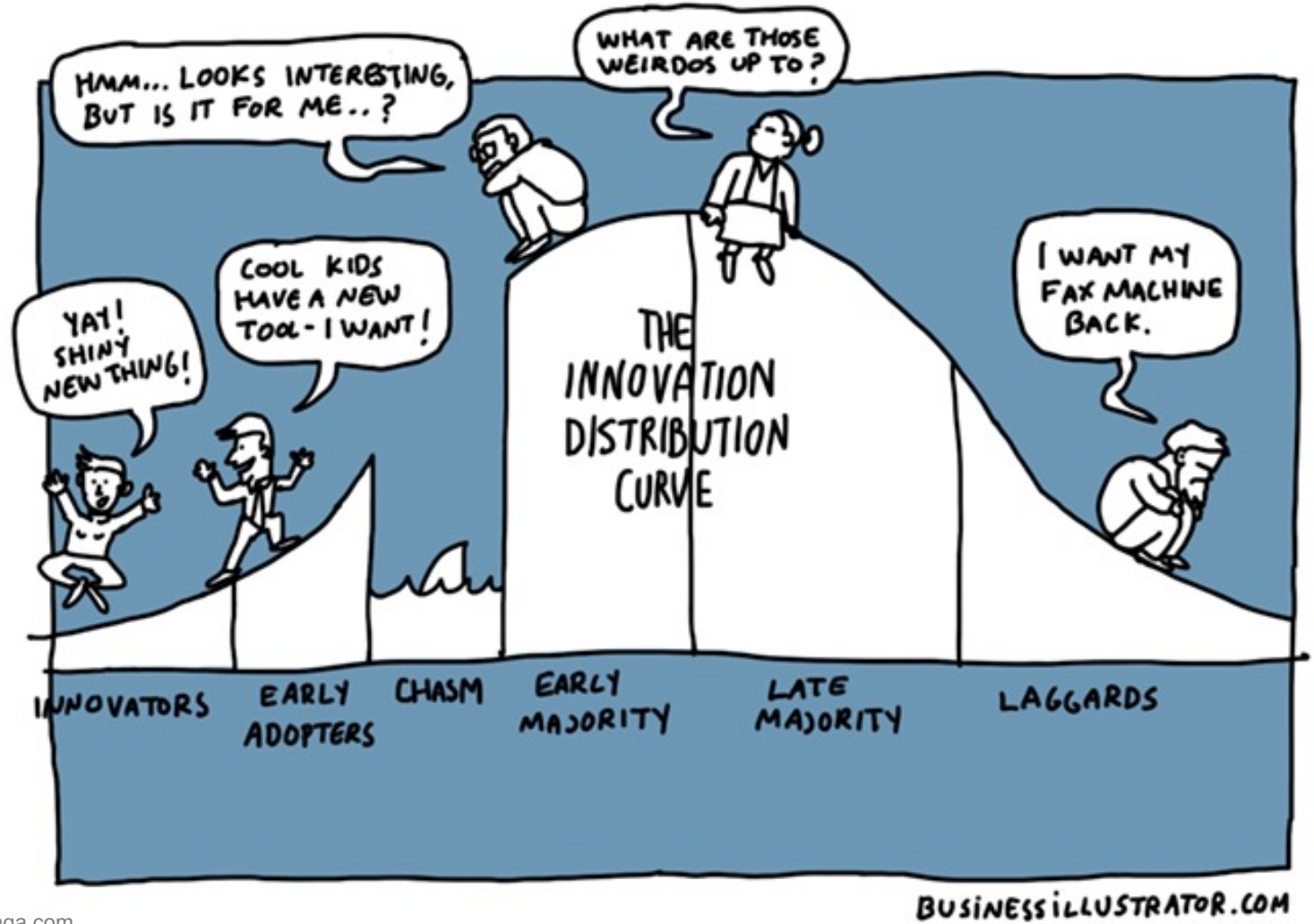
What MDR does say – Annex XV Clinical Investigations

- The clinical investigation plan (CIP) shall set out …
  - The **current *state of the art* in clinical care** in the relevant field of application and the proposed benefits of the new device.
  - Description of the relevance of the clinical investigation **in the context of the *state of the art* of clinical practice**.
- The Sponsor shall prepare a clinical investigation report which includes the following:
  - Discussion and overall conclusions covering safety and performance results, assessment of risks and clinical benefits, discussion of **clinical relevance in accordance with clinical *state of the art***….

Interchangeable concepts?







michelle@leanraqa.com

What say you, Mister MEDDEV 2.7.1/4?

Clinical Evaluation: A guide for manufacturers and notified bodies under Directives 93/42/EEC and 90/385/EEC

MEDDEV 2.7.1/4 says…

Medical Devices Guidance
MEDDEV

Does **NOT** define:
- State of the Art
- Standard of Care

Mentioned SOTA 39 times

General principles of clinical evaluation (1 of 4)

- … Determination of the benefit/risk … **acceptability of that profile based on current knowledge / the state of the art in the medical fields concerned**.

- Verify…a high level of protection of health and safety and acceptable according to current knowledge / the ***state of the art***

General principles of clinical evaluation (2 of 4)

- Definition of scope
  - The current knowledge / ***state of the art*** **in the corresponding medical field**, such as applicable **standards** and **guidance** documents, **information relating to the medical condition managed** with the device and its natural course, **benchmark** devices, **other devices and medical alternatives** available to the target population.

- Data on the safety and performance **of other devices and alternative therapies**, including benchmark devices and equivalent devices, should be **used to define the *state of the art* or identify hazards** due to substances and technologies.

General principles of clinical evaluation (3 of 4)

- Expert documents … are important for assessment of current knowledge / **the *state of the art*, including clinical practice guidelines** and consensus statements.

- Importance of literature review to risk management process. The literature review will provide data on **current interventions** for the intended patient population **(*state of the art*)** in order to give input to the **assessments of acceptable benefit/risk profiles**, what is currently considered as providing a high level of protection of health and safety and what are considered acceptable side-effects.

General principles of clinical evaluation (4 of 4)

- Evaluate if the clinical data on **benefits and risks are acceptable** for all medical conditions and target populations covered by the intended purpose when **compared with the current state of the art** **in the corresponding medical field** and whether limitations need to be considered for some populations and/or medical conditions.

MDCG 2020-6

Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC. A guide for manufacturers and notified bodies

MDCG 2020-6 says…

MDCG 2020-6 Guidance

8 new definitions

DOES define:
- State of the Art

Does **NOT** define:
- Standard of Care

Mentioned SOTA 20 times

Mentioned SOC 4 times

MDCG 2020-6

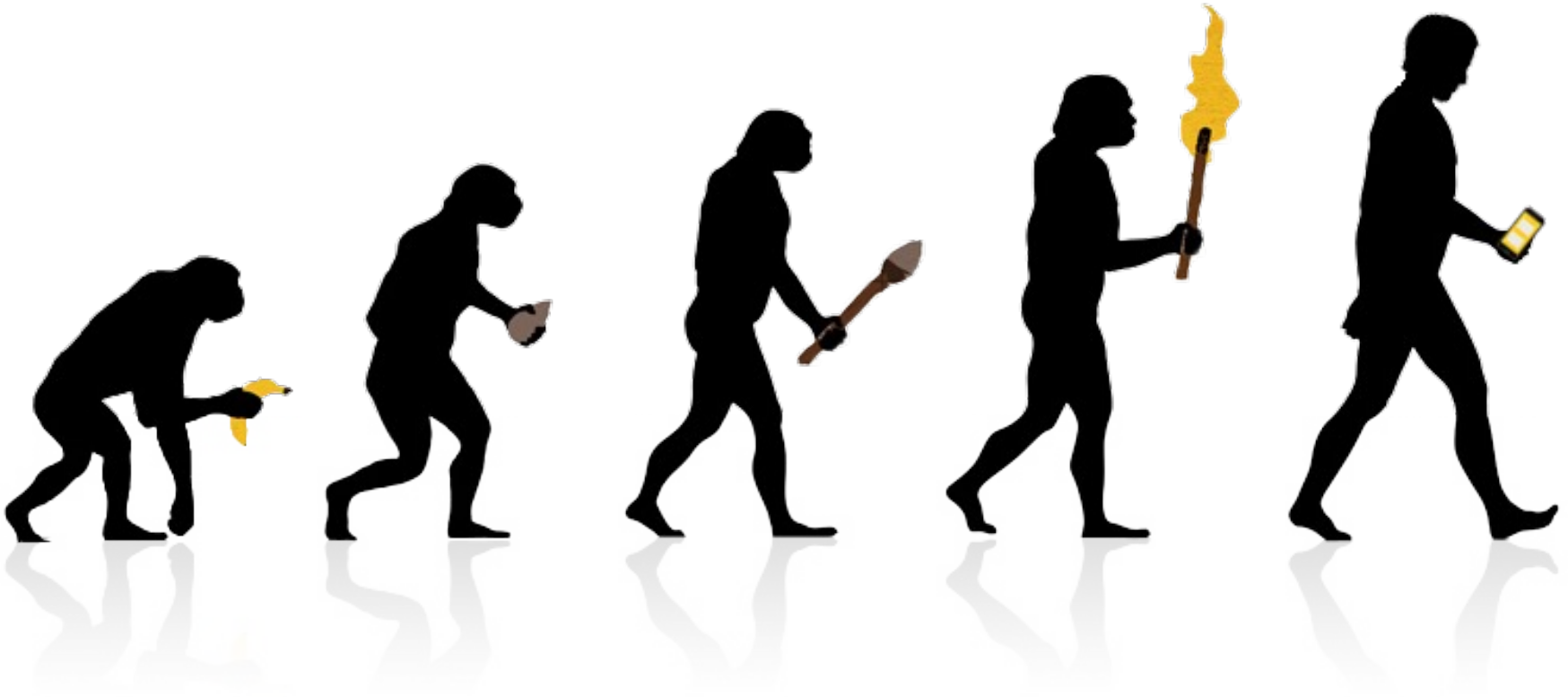
- **IMDRF/GRRP WG/N47 provides the following definition:**
  - Developed stage of **current technical capability and/or accepted clinical practice** in regard to products, processes and patient management, based on the relevant **consolidated findings of science, technology and experience**.
  - Note: The state-of-the-art embodies what is **currently and generally accepted as good practice** in **technology and medicine**. **The state-of-the-art does not necessarily imply the most technologically advanced solution.**

MDCG 2020-6

- **The common features of the devices which are "well- established technologies" (WET) are that they all have:**
  - relatively simple, common and stable **designs with little evolution**;
  - their generic device group has **well-known safety** and has not been associated with safety issues in the past;
  - **well-known clinical performance** characteristics and their generic device group are **standard of care** devices where there is **little evolution in indications and the state of the art**;
  - a long history on the market.

MDCG 2020-6

- … for low risk **standard of care** devices where there is **little evolution in the state of the art**, it **may be possible to demonstrate conformity with the relevant GSPRs with a more limited clinical data set.**



MDCG 2020-6

- … in practise the data collected may not meet MDR criteria, if the devices were considered **standard of care** and were not associated with safety concerns. Stable, **(WET)** that perform as intended and are **not associated with safety concerns**, and where there **has been no innovation**, are less likely to be the subject of research, and therefore literature data may be limited or non-existent. … **may be necessary …to undertake PMCF** … prior to certification under the MDR, **even if they are (WET) and have been on the market for several decades,** to enable an evaluation of their safety and clinical performance in relation to **an *evolving* state of the art.**

MDCG 2020-6

- In ***exceptional*** cases, particularly for **low risk standard of care devices** where there is **little evolution in the state of the art**, and the device is identified as belonging to the group of 'well-established technologies' … **a lower level of clinical evidence may be justified to be sufficient for the confirmation of conformity with relevant GSPRs.**

MDCG 2020-6

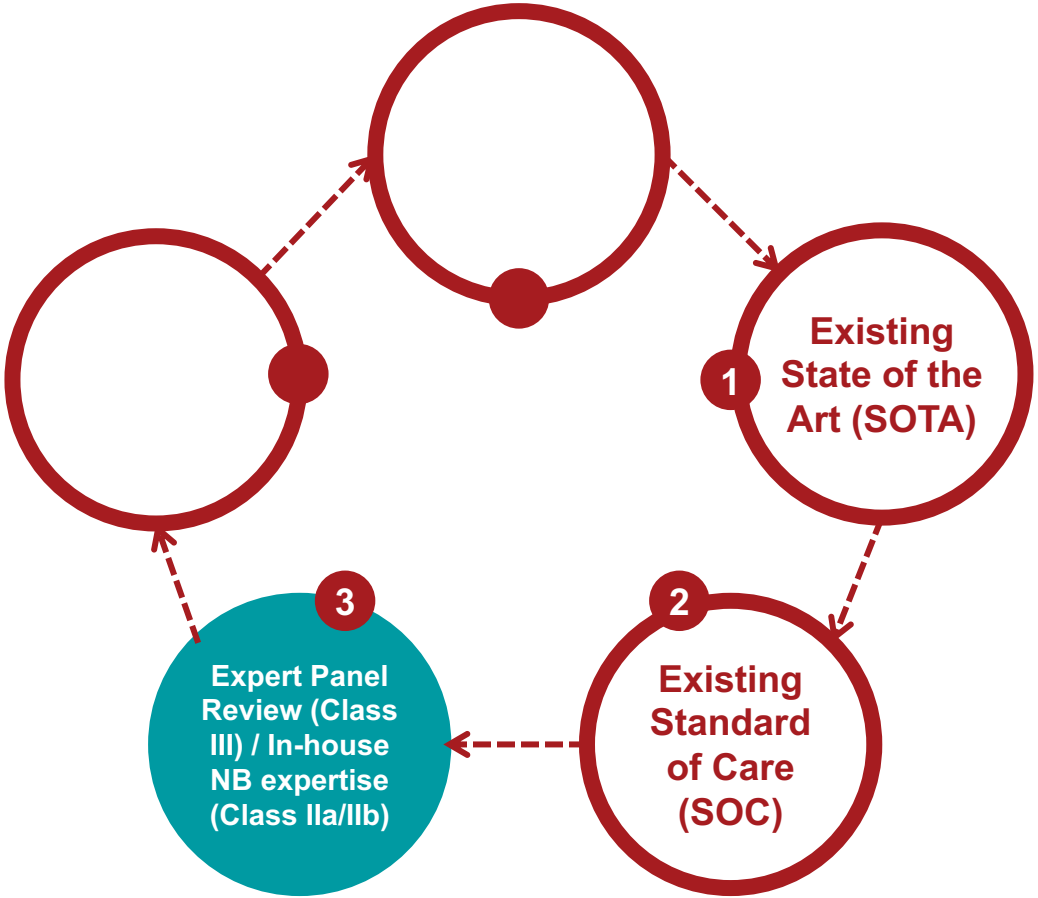
- Clinical State of the Art v Technical State of the Art

Clinical SOTA:
Relating to evaluation of clinical data

Technical SOTA:
Relating to current technological capability

How do I establish New State of the Art and Standard of Care?

Step 1


1
Existing State of the Art (SOTA)
2
Existing Standard of Care (SOC)
3
Expert Panel Review (Class III) / In-house NB expertise (Class IIa/IIb)

What to expect from the CECP or expert panels?

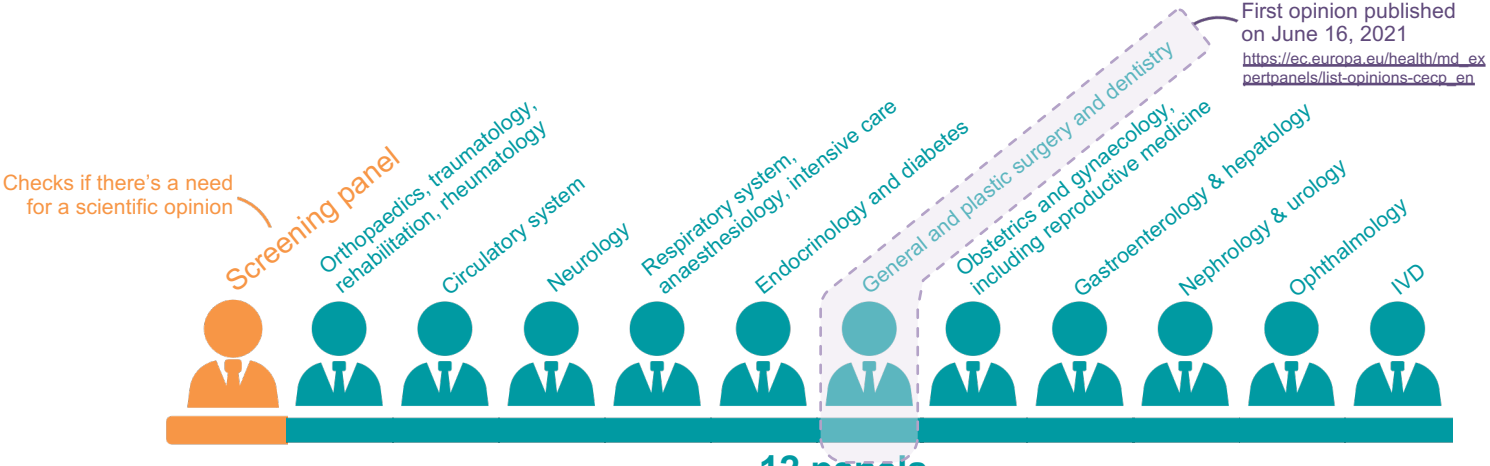
Who are they? CVs and DoIs:
https://ec.europa.eu/health/md_expert panels/experts/expert_panels_en

European Commission

Created by EC to support scientific assessment, deliver opinions and provide ad hoc advice

Appointed for 3 years, with possibility of renewal

First opinion published on June 16, 2021
https://ec.europa.eu/health/md_expertpanels/list-opinions-cecp_en



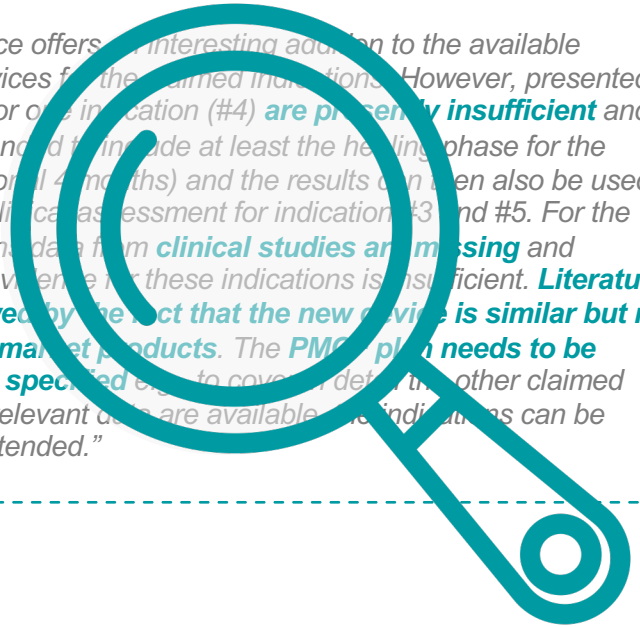
12 panels

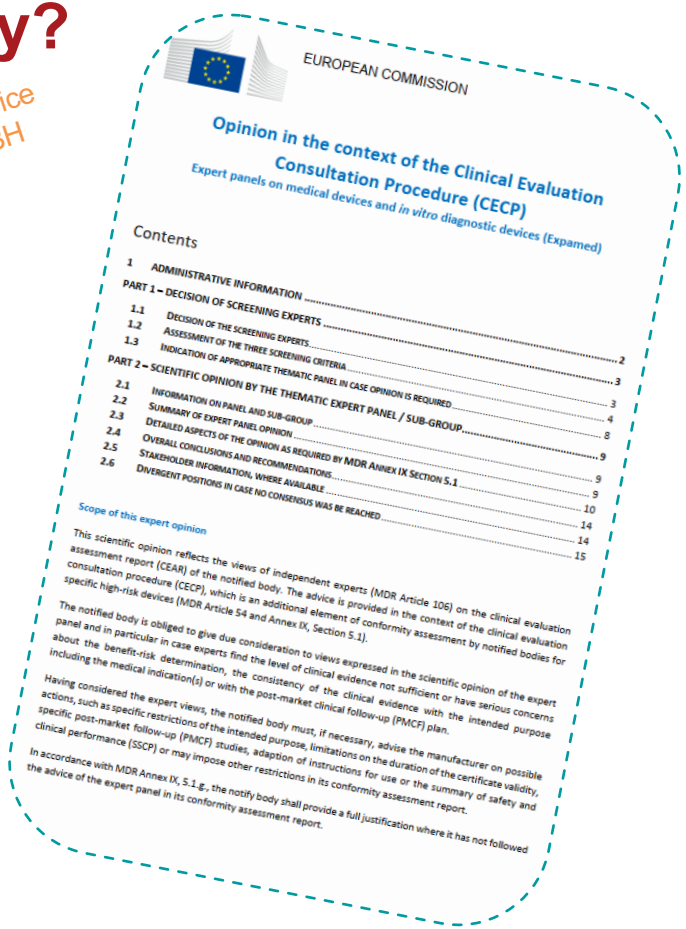
First opinion – More transparency?

- **NB0483, Ivory Graft Ltd, 2021-000201_NB0483_opinion:**
  - *Following a request from the notified body the opinion has been temporarily removed.*

MDC Medical Device Certification GMBH

*"The new device offers an interesting addition to the available portfolio of devices for the claimed indications. However, presented **clinical data** for one indication (#4) **are presently insufficient** and should be extended to include at least the healing phase for the implant (additional 4 months) and the results can then also be used for a positive clinical assessment for indication #3 and #5. For the other indications data from **clinical studies are missing** and therefore the evidence for these indications is insufficient. **Literature survey is flawed by the fact that the new device is similar but not equivalent to market products**. The **PMCF plan needs to be extended and specified** e.g. to cover / detect the other claimed indications. If relevant data are available, the indications can be accordingly extended."*





EUROPEAN COMMISSION

Opinion in the context of the Clinical Evaluation Consultation Procedure (CECP)

Expert panels on medical devices and in vitro diagnostic devices (Expamed)

Contents

Scope of this expert opinion

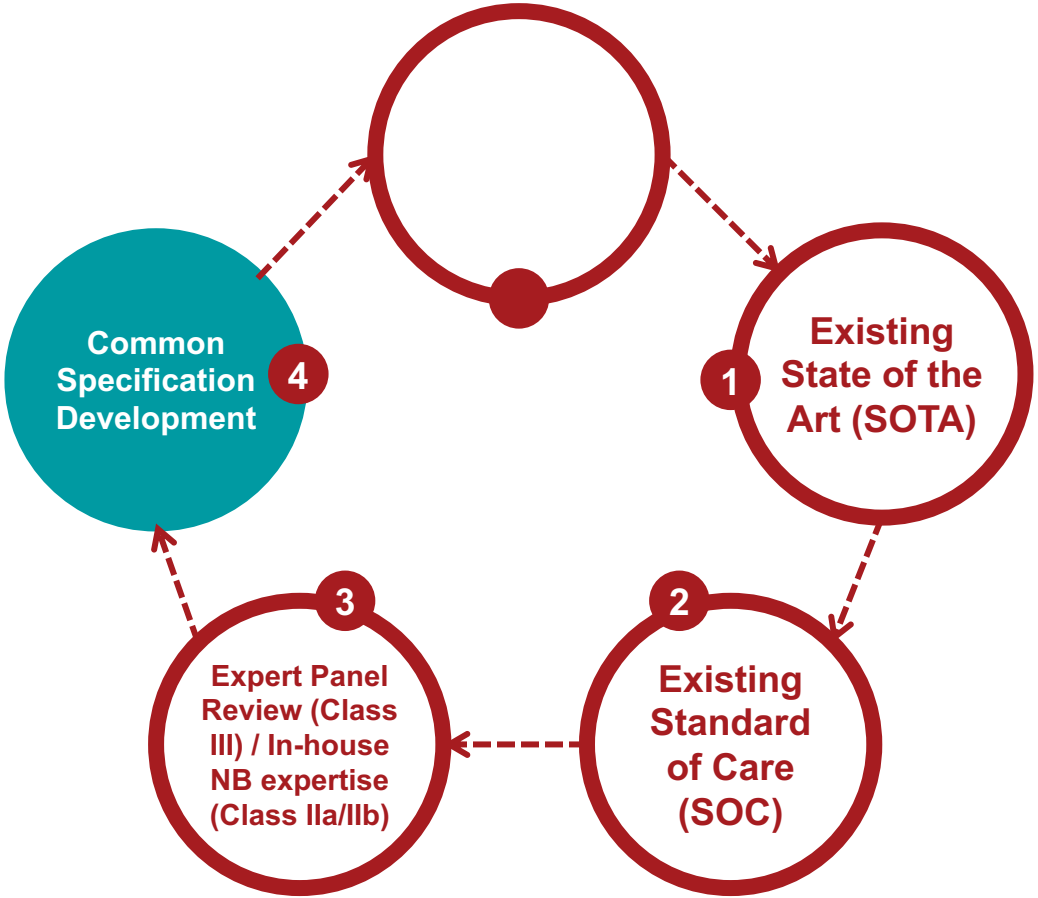
This scientific opinion reflects the views of independent experts (MDR Article 106) on the clinical evaluation assessment report (CEAR) of the notified body. The advice is provided in the context of the clinical evaluation consultation procedure (CECP), which is an additional element of conformity assessment by notified bodies for specific high-risk devices (MDR Article 54 and Annex IX, Section 5.1).

The notified body is obliged to give due consideration to views expressed in the scientific opinion of the expert panel and in particular in case experts find the level of clinical evidence not sufficient or have serious concerns about the benefit-risk determination, the consistency of the clinical evidence with the intended purpose including the medical indication(s) or with the post-market clinical follow-up (PMCF) plan.

Having considered the expert views, the notified body must, if necessary, advise the manufacturer on possible actions, such as specific restrictions of the intended purpose, limitations on the duration of the certificate validity, specific post-market follow-up (PMCF) studies, adaption of instructions for use or the summary of safety and clinical performance (SSCP) or may impose other restrictions in its conformity assessment report.

In accordance with MDR Annex IX, 5.1.g., the notify body shall provide a full justification where it has not followed the advice of the expert panel in its conformity assessment report.

Step 2


Common Specification Development
4
1
Existing State of the Art (SOTA)
2
Existing Standard of Care (SOC)
3
Expert Panel Review (Class III) / In-house NB expertise (Class IIa/IIb)

What is a Common Specification (CS)?

Common Specification
MDR

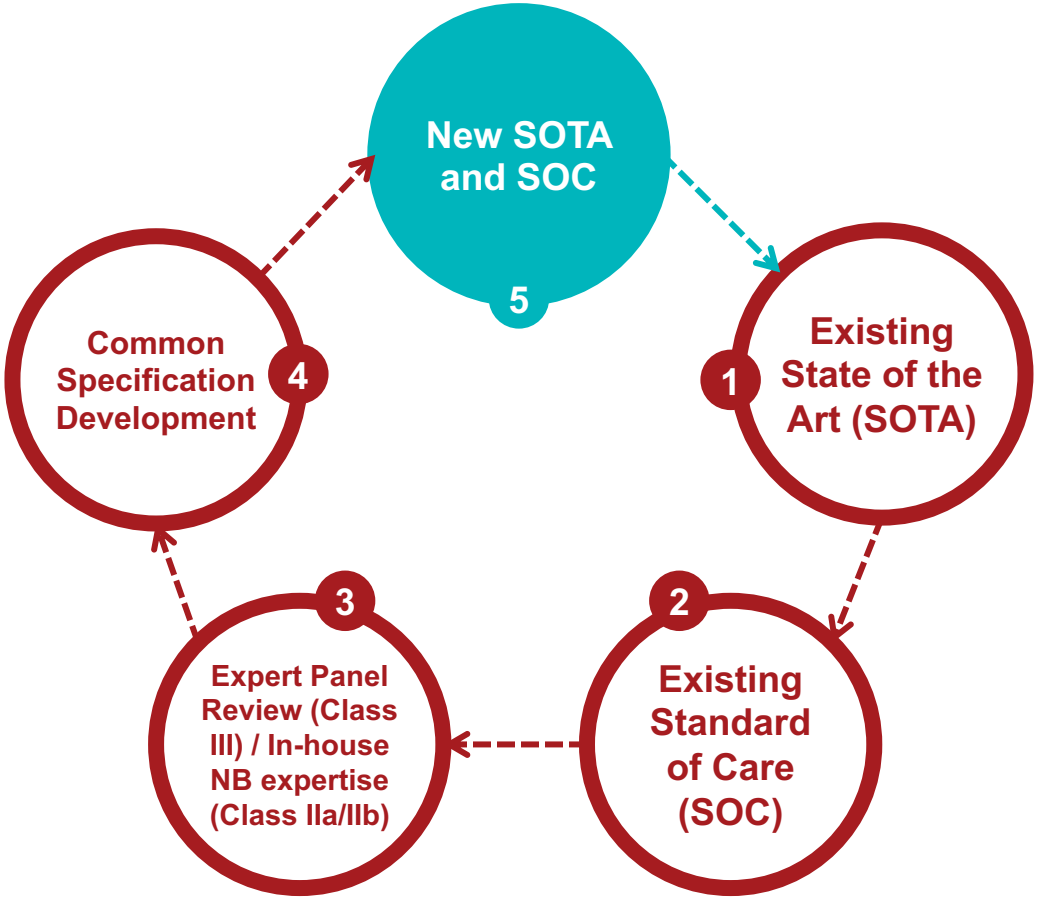
Set of technical and/or clinical requirements – other than a standard – that provide a means of complying with the legal obligations.

Applicable to a device, process, or system when no harmonized standards exist, when relevant harmonized standards are not sufficient, or when there is a need to address public health concerns.

MM 202X?

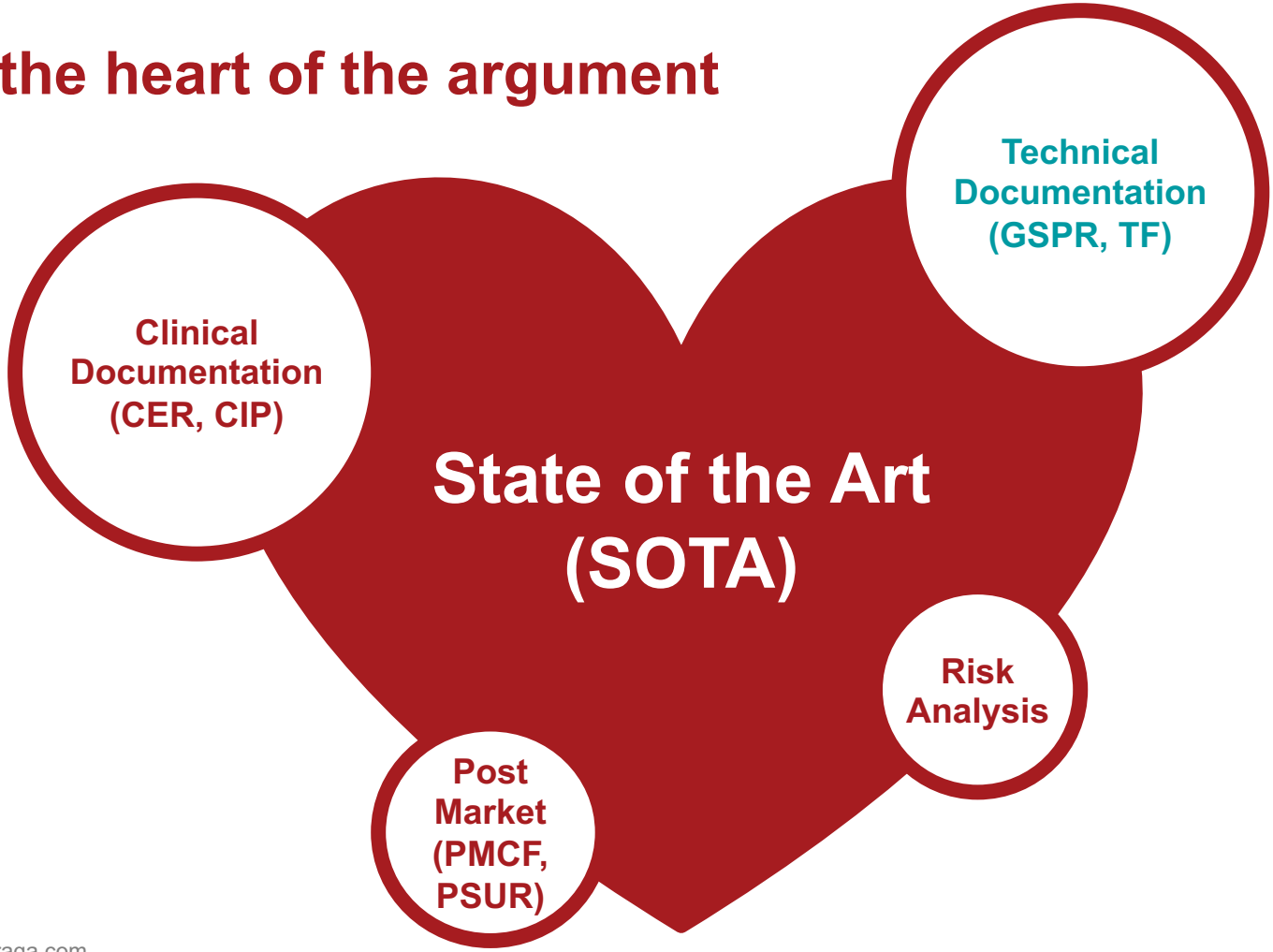
Are we there yet?

Lifecycle starts over



Back to the heart of the argument

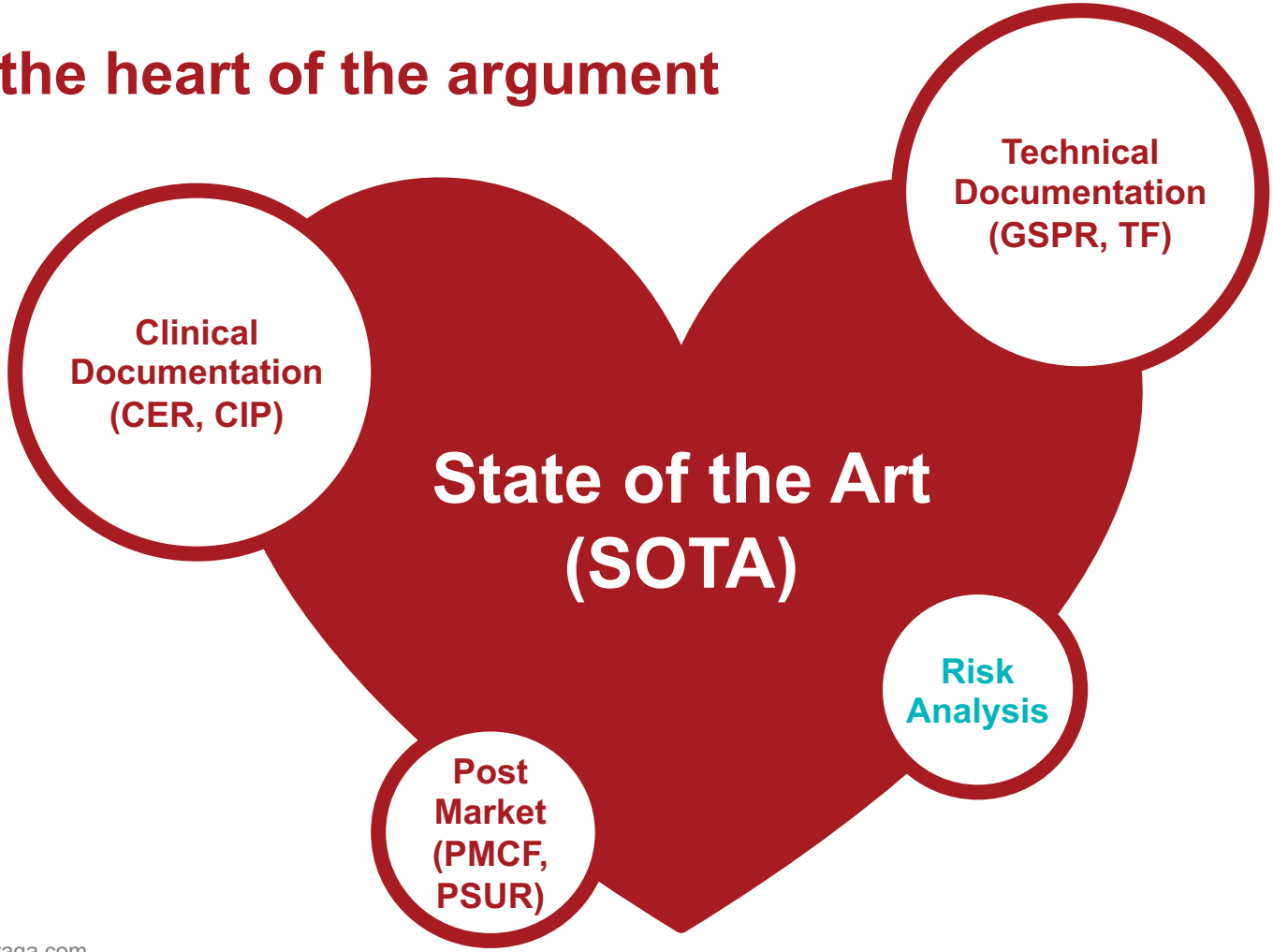
At the heart of the argument



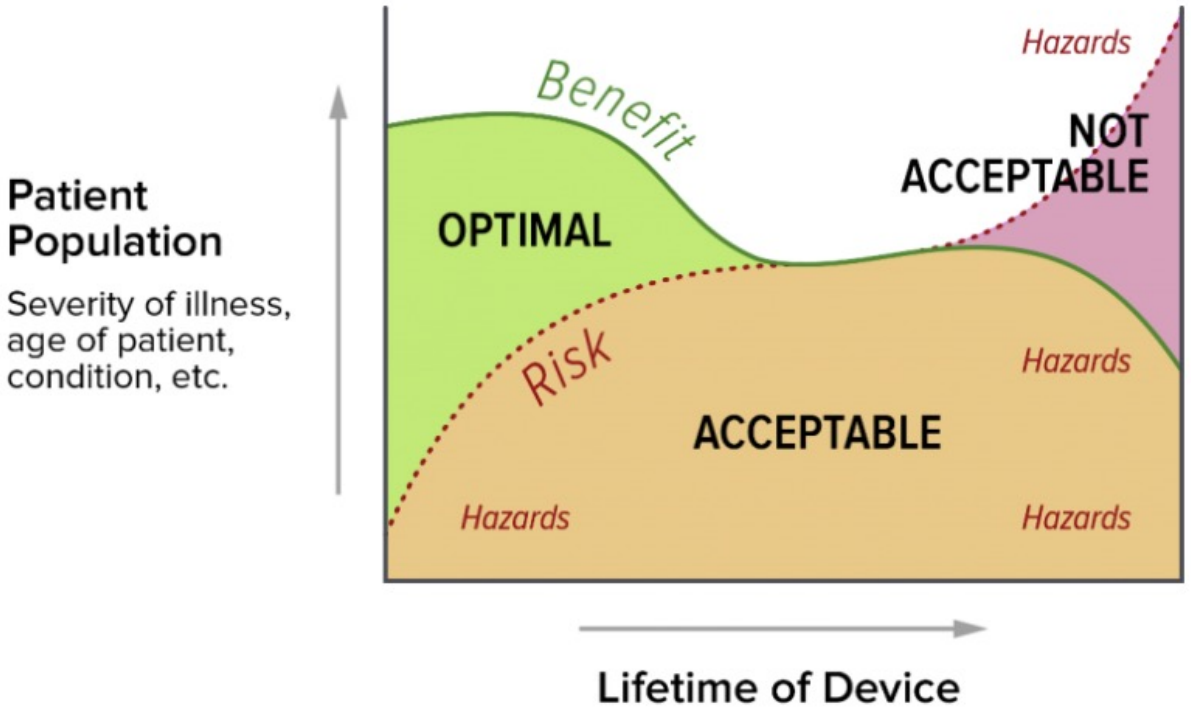
SOTA and your Technical Documentation

- MDD v MDR Technical Documentation Requirements – significant additional requirements (particularly for clinical evaluation process)

At the heart of the argument

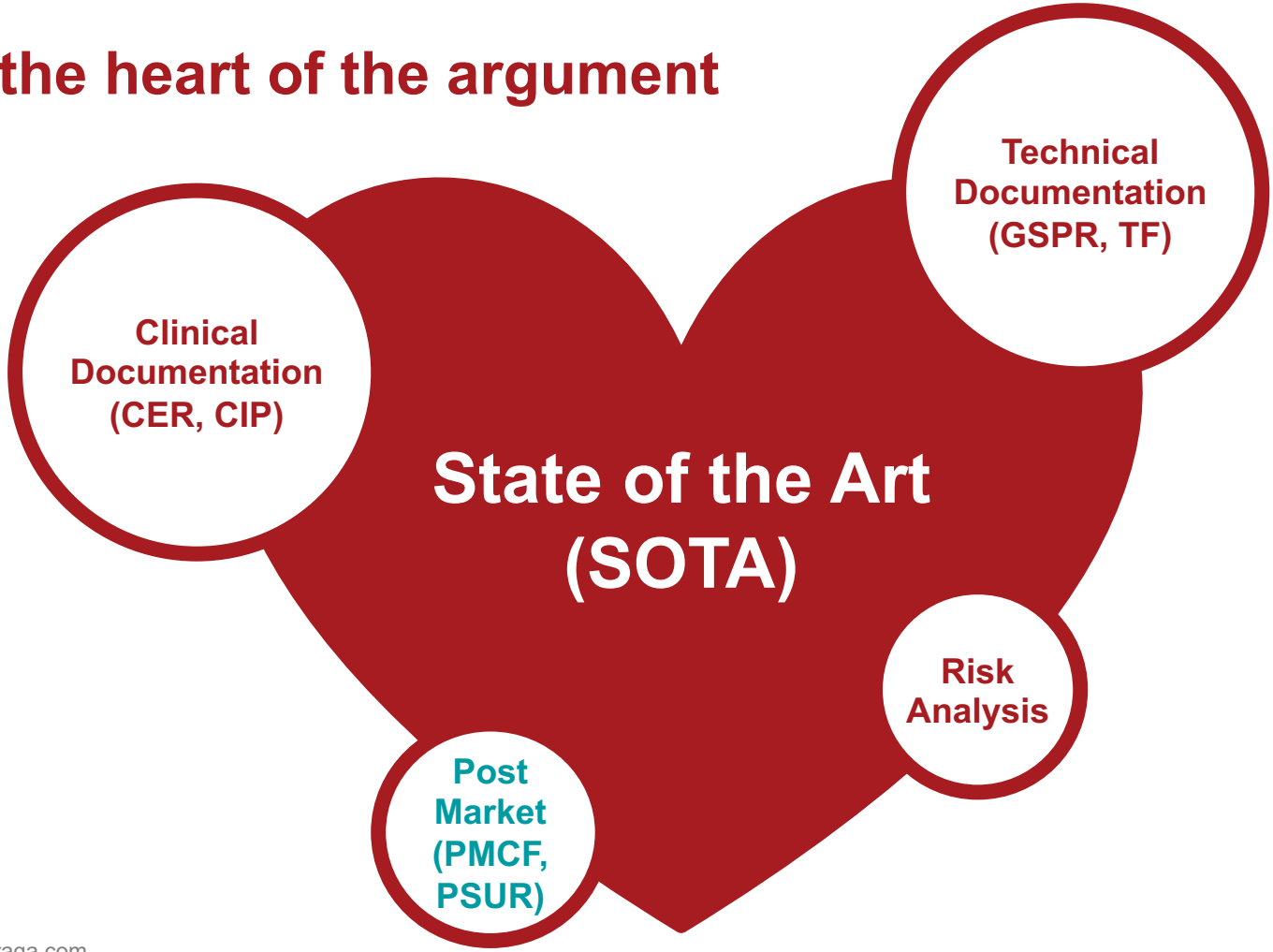


SOTA and your Risk Analysis



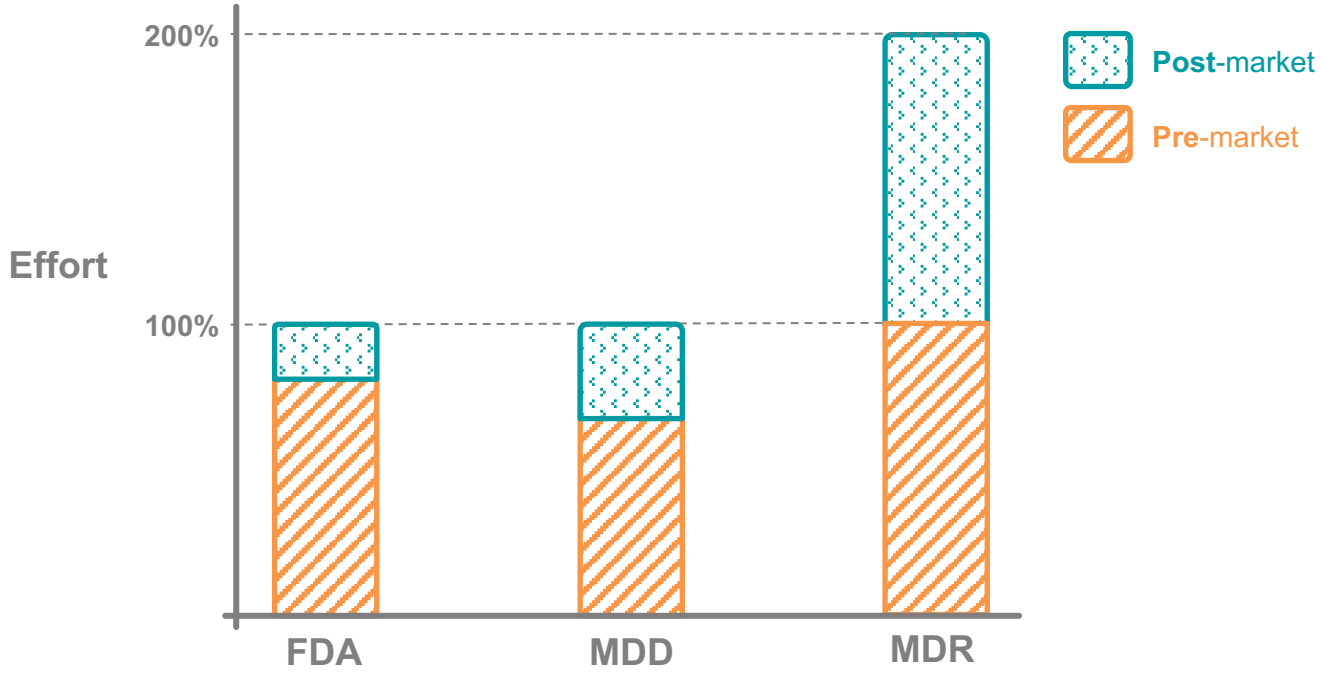
Source: https://www.orielstat.com/blog/eu-mdr-state-of-the-art/

At the heart of the argument

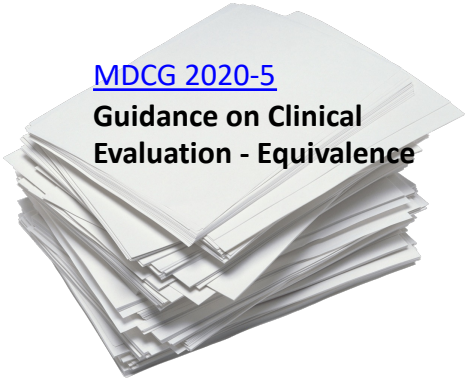


SOTA and your Post Market Surveillance

- Requirement of PMS activities to show your device is still based on SOTA or whether it has changed.

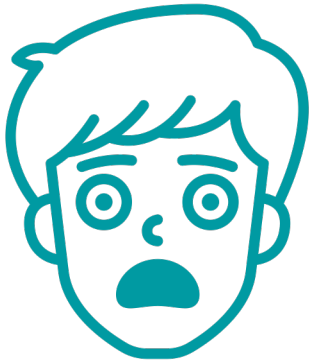


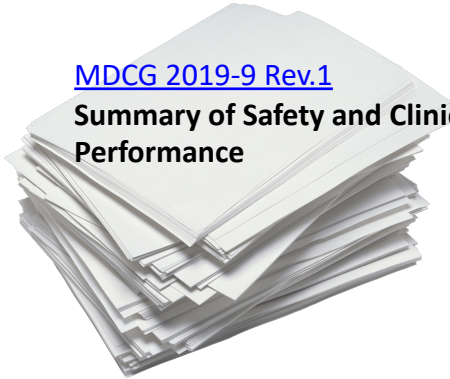
New Post-Market Surveillance Requirements



MDCG 2020-5

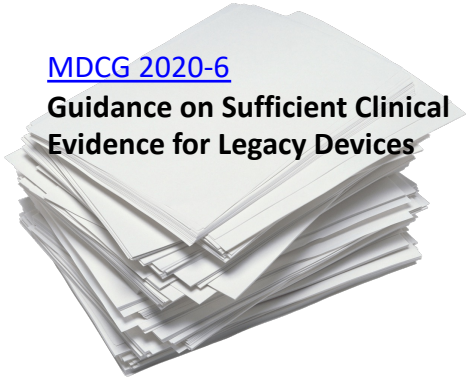
Guidance on Clinical Evaluation - Equivalence





MDCG 2019-9 Rev.1

Summary of Safety and Clinical Performance

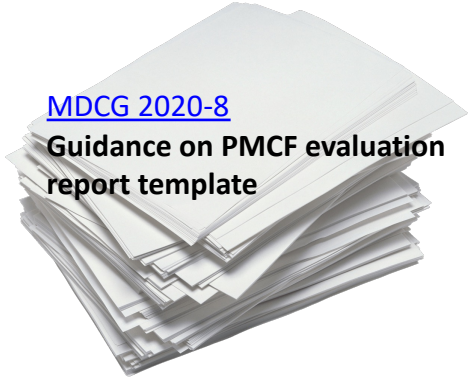


MDCG 2020-6

Guidance on Sufficient Clinical Evidence for Legacy Devices

MDCG 2020-7

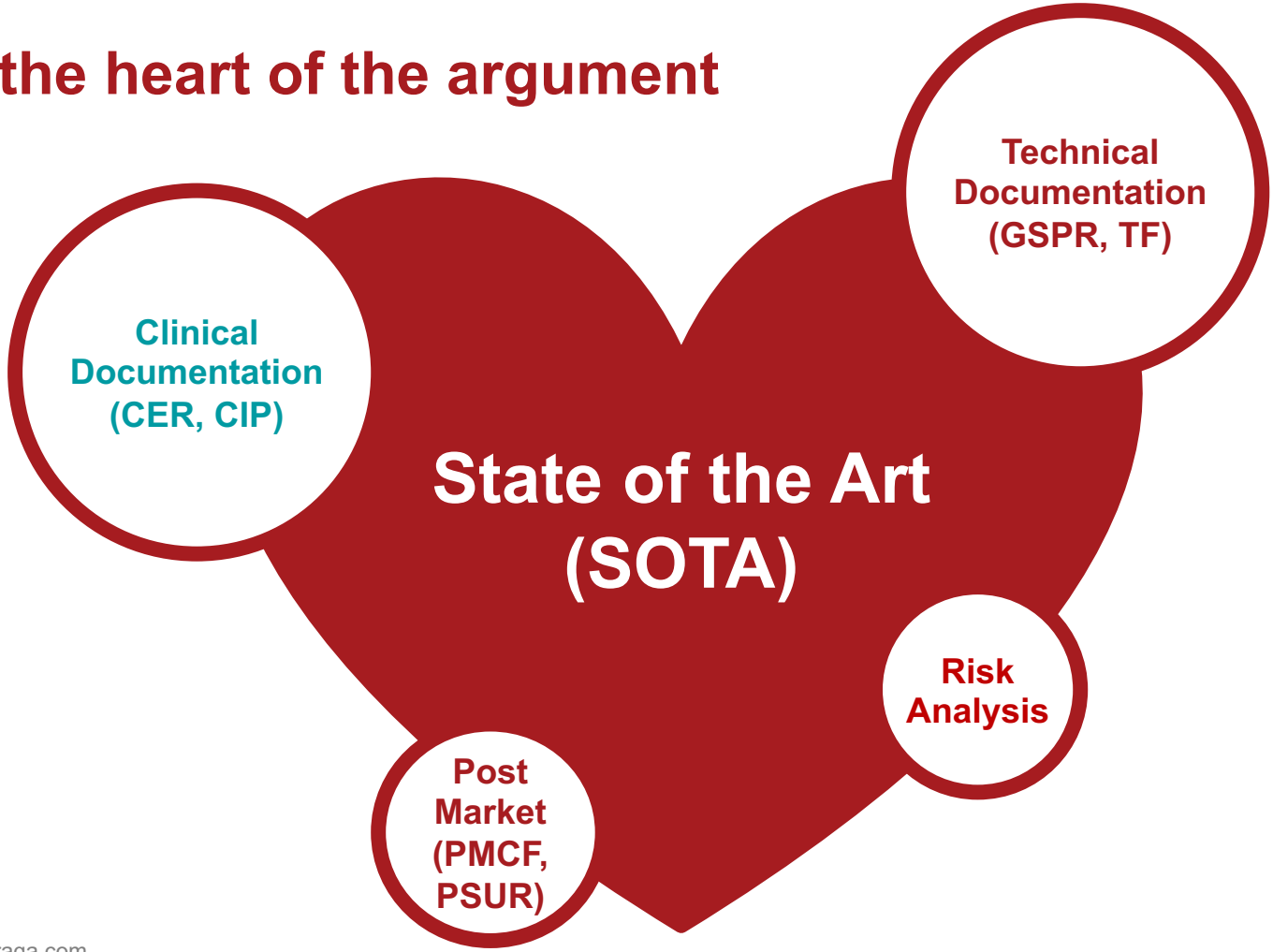
Guidance on PMCF plan template



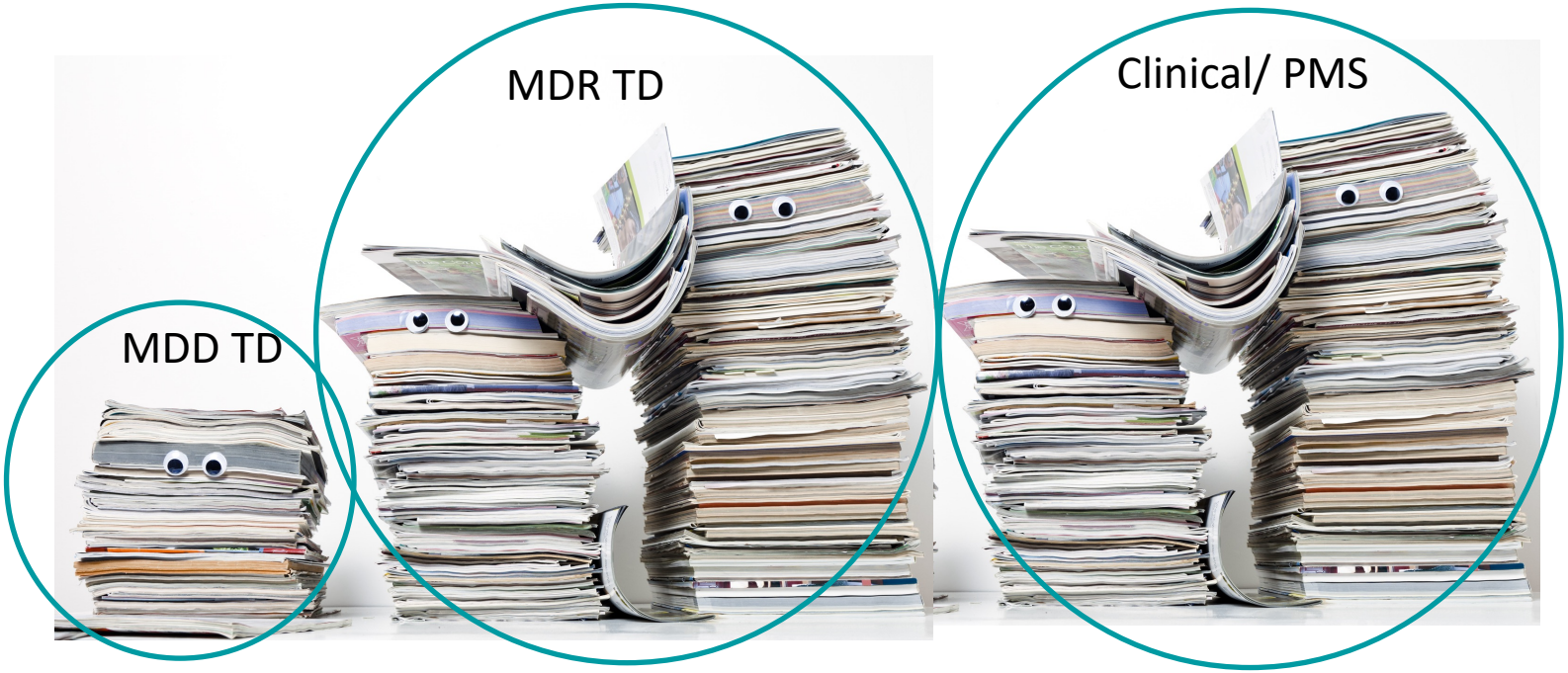
MDCG 2020-8

Guidance on PMCF evaluation report template

At the heart of the argument

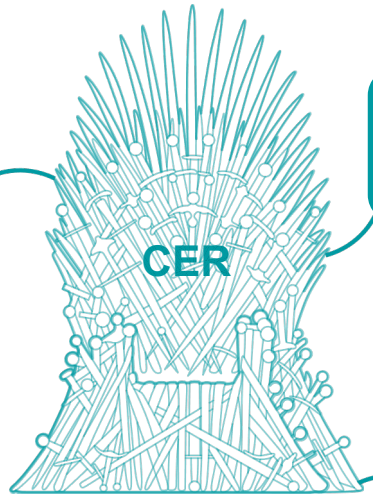


Clinical documentation supersedes TD



SOTA and your Clinical Evaluation: CER is king

$XX - $XXX endeavor (**>200-300h**)



Takes **primacy** on all individual assessments

Redundant items:
- CEP↔CER: **53** repeated items
- PMCF↔CEP/CER: **5** repeated subsections
- TD↔CEP/CER: **14** repeated subsections

Corner stone of TD but also the **most subjective** part of it

In a CER-centric system, the easiest CERs are the ones with the **most clinical evidence**

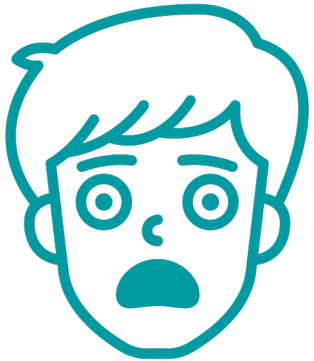
For **low-risk** or '**boring**' products that nobody is ever going to publish about, it's paradoxically going to be more difficult to write and rationalize the CER

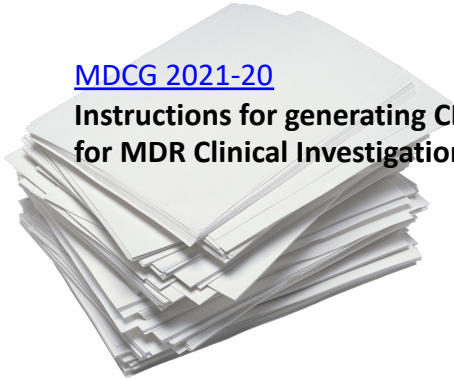
The ones with the **most clinical evidence** are the ones with either:
- Higher class device (typically large manufacturers) with registry data for last decade
- Extremely novel device with a lot of supporting literature data and device specific studies

New Clinical Requirements

MDCG 2021-28

Substantial modification of clinical investigation under Medical Device Regulation





MDCG 2021-20

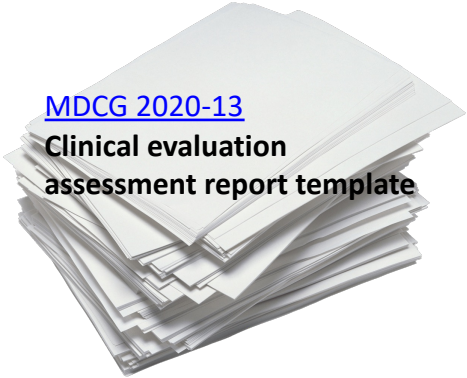
Instructions for generating CIV-ID for MDR Clinical Investigations

MDCG 2021-8

Clinical investigation application/notification documents

MDCG 2020-7

Regulation (EU) 2017/745 – Questions & Answers regarding clinical investigation



MDCG 2020-13

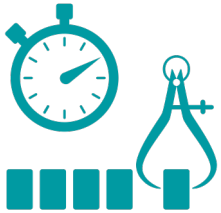
Clinical evaluation assessment report template

New Technologies Guidance

MDCG Infographic:
Is Your Software a Medical Device?

MDCG 2020-1
Guidance on clinical evaluation (MDR) / Performance evaluation (IVDR) of medical device software

MDCG 2019-16 Rev.1
Guidance on cybersecurity for medical devices



MDCG 2021-5
Guidance on standardization of medical devices

MDCG 2019-11
Qualification and classification of software

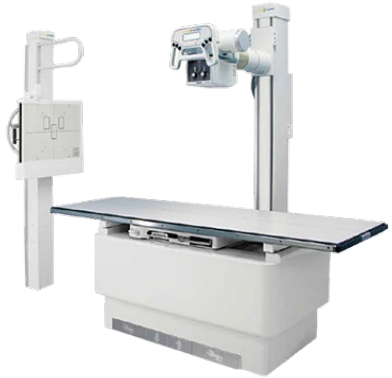
Example: SOTA Digital Imaging System

- Note: “state of the art” refers only to products that are developed and approved for sale in the marketplace.

- Difference between a new state-of-the-art digital imaging system that is undergoing trials and one that already has CE Marking.
  - For EU medical device regulators, the latter is considered state of the art, but the former is not until it has CE Marking.

X-Ray Machine

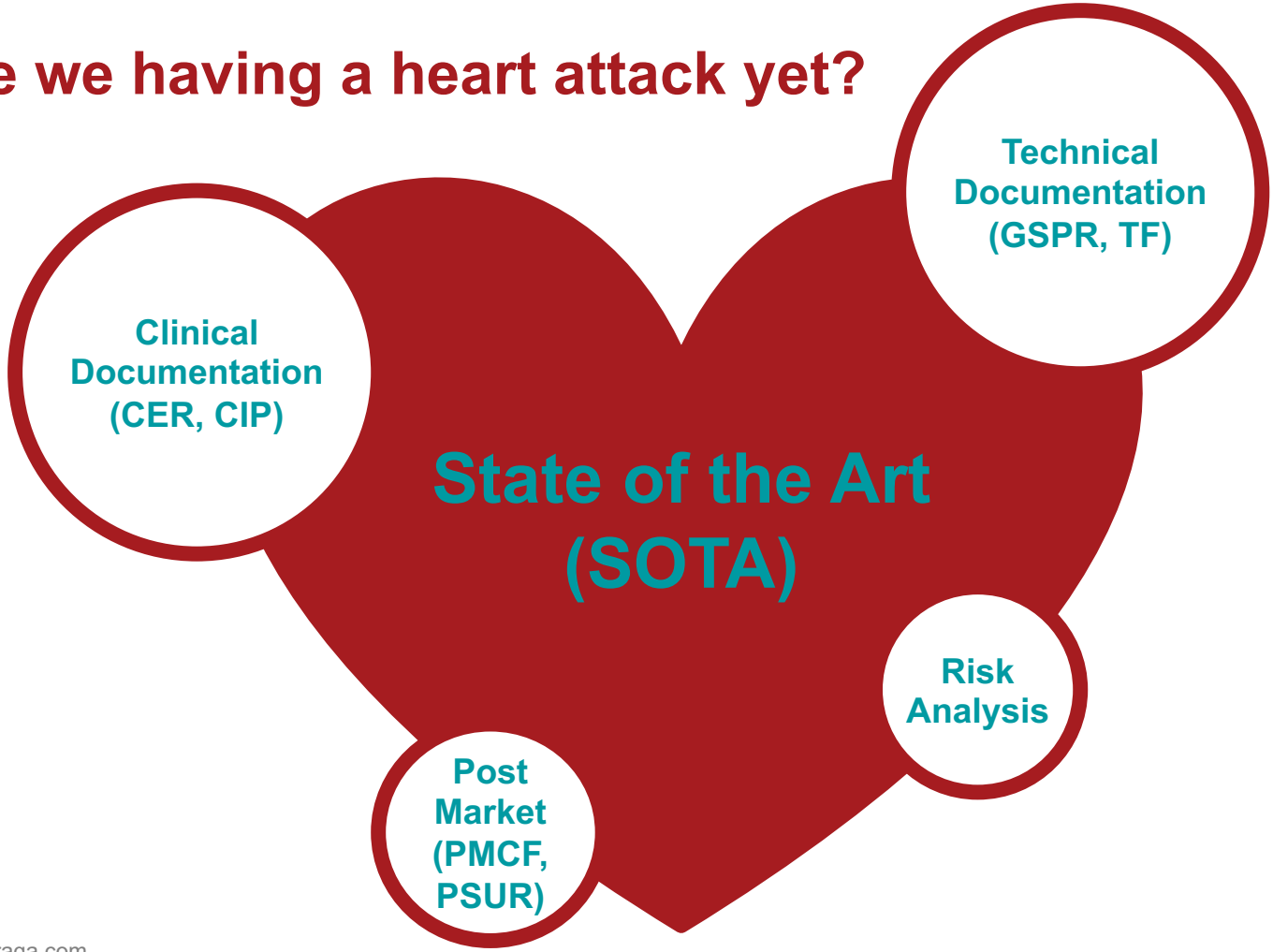
Considered state-of-the-art



X-Ray Machine with Remote Monitoring Features (under review, not approved yet)

What does this mean for you?

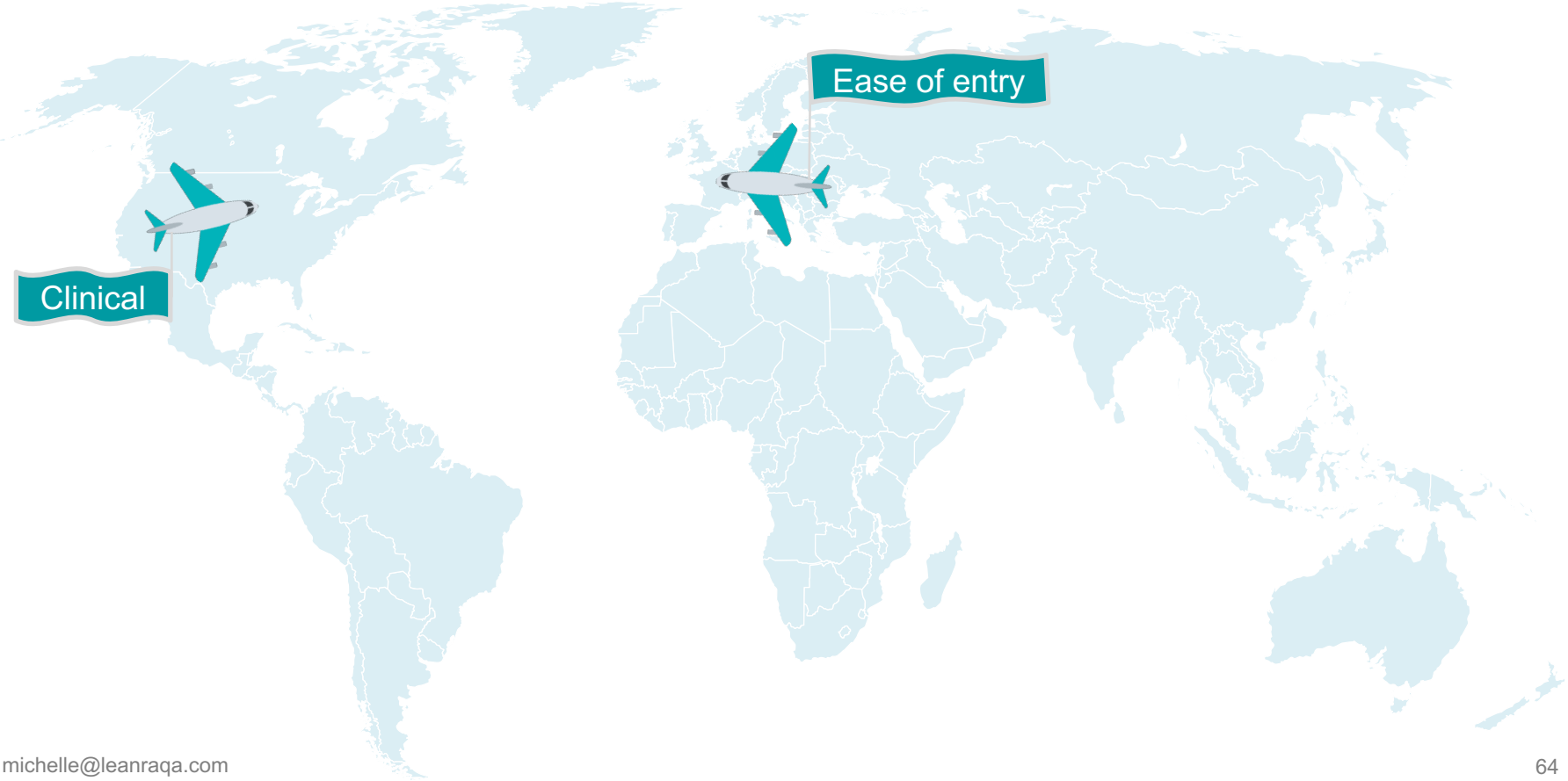
Are we having a heart attack yet?



Are we having a heart attack yet?

- Perform an in-depth assessment of **alternative treatment methods**
- State of the art is critical in assessing the **benefit-risk ratio of the device**, and you need to address it in your **clinical evaluation report (CER).**
- If your device has been on the market for decades and there are **competitive devices** that are **technically superior and present lower risk** than yours, they reduce the benefit of your device and increase the risk side of your benefit-risk equation.

Paradigm shift in go-to-market strategy



FDA's strategy to be first

- **Received by a customer:**
  - "I am contacting submitters of Q-Subs … to measure CDRH's performance in meeting one of its 2018-2020 strategic priorities:

    "By December 31, 2020, more than 50% of manufacturers of novel technologies for the U.S. market intend to bring their devices to the U.S. first or in parallel with other major markets."

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Result

62% of novel technology manufacturers intend to bring their devices to the United States

Based on an 87% response rate from companies contacted about novel technology devices between 2018 and 2020, 62% of companies intended to bring their devices to the United States first or in parallel with other major markets by December 31, 2020.

Source: CDRH 2018-2020 Strategic Priorities Accomplishments

Free download

- Regulatory Pathway Assessment (RPA)
- Business Market Assessment (BMA)

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Your audit management

Your due diligence

Your technical support

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	food
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