qarad
European Regulatory Services

EU IVDR SOTA & SDC

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European Regulatory Services

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QBL
QUALITY BY DESIGN

The leading EU consulting/CRO company specialized in IVDs

our 4 key business areas

Why SOTA is important ?

State Of The Art is quoted 20 times in the IVD-R // it needs to be formalized in a document as per a defined process!

- **Annex XIII, Part A, 1.1 (PEP):**
  - **a description of the state of the art, including an identification of existing relevant standards, CS, guidance or best practices documents**
- **Annex XIII, Part A, 1.3.2 (PER):**
  - **the clinical evidence as the acceptable performances against the state of the art in medicine;**

Need to document SOTA

- **Because the IVDR requires a formal description of the STATE OF THE ART for the device in question then it must be formally documented**
  - a QMS procedure on how to document / **who(*)?** / when? is recommended
  - but before writing a procedure you need to have a proper understanding of what SOTA is for IVDs in the context of the IVDR.

(*)Not RAQA !!

Unfortunately SOTA is not defined by the IVDR

"State of the art" – EN ISO 14971:2012

- Means what is currently and generally accepted as good practice.
- Various methods can be used to determine "state of the art" for a particular medical device. Examples are:
  - standards used for the same or similar devices;
  - best practices as used in other devices of the same or similar type;
  - results of accepted scientific research.
- Does not necessarily mean the most technologically advanced solution.

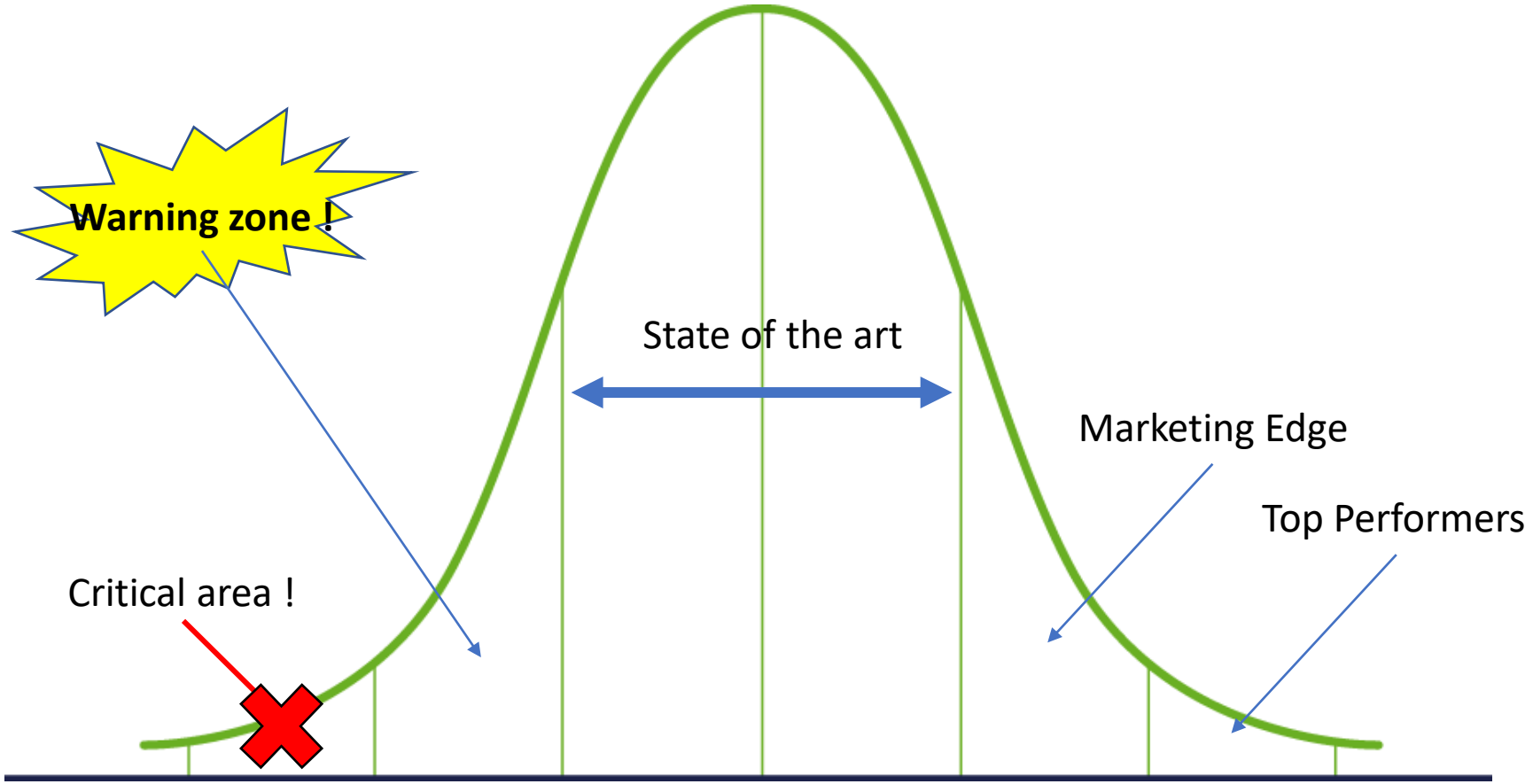
EU Commission Guideline on COVID-19 n. C(2020) 2391 published 2020-04-15

"State of the art" does not mean that the device has to be the best in its class. However, the device may not fall behind what can reasonably be achieved and is achieved by a majority of devices(13).

MDCG 2006: 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.

Annex XIII Performance Evaluation mentions: "**Acceptable performance against the state of the art**… "

the Gaussian curve



This is where you don't want to be!

HOW TO DOCUMENT 'SOTA'

SOTA should be evaluated and documented at two levels:

- **Clinical practice**: what is the current clinical practice for the detection of a clinical condition; which parameter, which technology is current practice? Which device is typically used in this clinical situation ?

- **Performance specifications**: what is the expected performance of the assay?

HOW TO DOCUMENT 'SOTA' contd.

Clinical practice

- Sources for relevant information:
- ECDC, CDC, WHO,
- National health authorities: Sciensano-BE, INSERM-FR, RKI-DE etc.
- International associations for specific diseases
- SVR reports and accompanying literature list

Evaluation of clinical practice should preferably be done by medical experts.

HOW TO DOCUMENT 'SOTA' contd.

Performance specifications

This second part of SOTA can be written by exploring the following sources of information:

- Common specifications - standards
- Other specifications (FDA, WHO, …)
- Comparative assays with the same technology.

Selection criteria for comparative assays:

- CE marked
- Currently on the market / best sellers
- Performance characteristics published (IFU, FDA reports, WHO reports, …)

HOW TO DOCUMENT 'SOTA' contd.

SOTA is required in the PEP, to determine the acceptability of benefit/risk ratio once you have evaluated the performance of your device

A practical approach is to:

- **Refer to a vertical standard preferably an EU Harmonized Standard or an international one or to national standards/guidelines like the CLSI ones.**
- **Refer to Market Surveillance studies published by the EU Authorities**
- **Refer to a Common Technical Specification / Common Specification**
- **Summarize the analytical/clinical performance of 5 "like" assays currently on the EU market.**
  - **ideally pick the best sellers in the targeted geography**

Never forget that SOTA needs to be periodically monitored via your PMS

The IVDD last minute rush

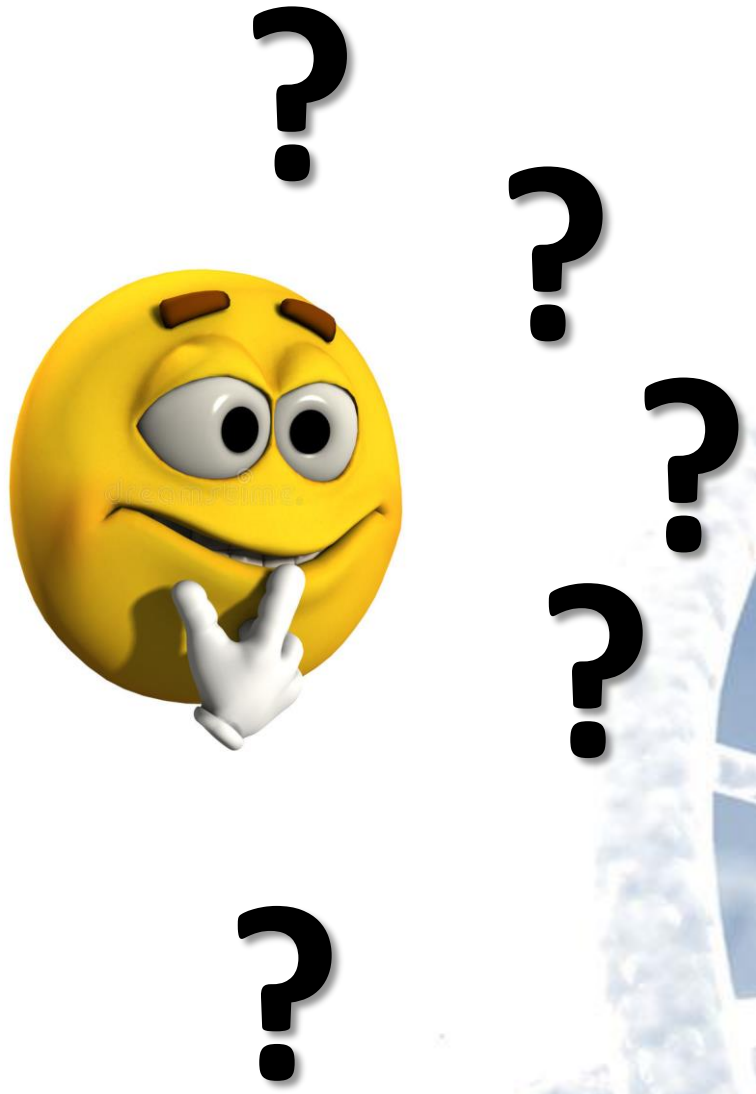
Phew !

I've just managed to notify my IVDD device on time.

But…

Can I change it w/out going for full IVDR approval ?

What does it mean "Significant Design Change ?



Thou shall NOT change your IVDD if it SDCs !

So what is considered an SDC ?

And what is not ?

These are likely to be SDCs !

SDC is a change in the design or Intended Purpose Extension of IP

- additions to what's detected/measured
- a new function (screening, monitoring, etc.)
- addition/change of a specimen type
- change of intended user (professional -> NPT)
- from automatic to manual or vice-versa
- change of core technology (ELISA to chemioluminescence)

These are likely to be SDCs !

- change of IFU to announce reduced sensitivity based on PMS observed data
- changed primers for PCR
- changed capture Abs for ELISA
- different detection marker
- SW: new architecture / database structure / algorithm / new database
- Substitution of a chemical substance to comply with REACH if it negatively impacts performance
- Change sterilization method or changes in packaging that negatively affect the sterility

These are NOT likely to be SDCs !

- Different manufacturer's name/address (mergers/acquisitions)
- Different EU-AR
- Different supplier (if w/no impact on specs)
- Change to external packaging (provided it doesn't impact sterility)
- Changes due to FSCA assessed & approved by CAs
- Updates to IFUs if required by law or are clarifications w/out affecting performance
- Limitation of the IP (restricting target population, specimen type)

These are NOT likely to be SDCs !

- New instrument platform (previously approved on instrument A, now on A and B w/out any design change in the reagents)
- New incubation times & temperatures (w/ no impact on performance)
- New processing steps (w/ no impact)
- Use of new PCR cycler / adding new PCR cyclers
- extension / reduction of shelf life (if non sterile)
- Change from 2to8C to room temp
- Change of IFU to refer to better device performance based on PMS data or adding new interferences
- Adding IFU clarifications

These are NOT likely to be SDCs !

- Appearance
- Operating efficiencies
- Changes to enhance user interface
- Changes of ingredients/materials not essential for the operating principle (preservative, new buffer, different chemical substance)
- Change of sterilization cycle parameters
- Change of the shelf life by validated protocols NB approved

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Thank you