Medicines & Healthcare products Regulatory Agency

MHRA
Regulating Medicines and Medical Devices

The new EU IVD regulation: overview and expectation for the regulation of companion diagnostics

Official Journal of the European Union

L 117

English edition

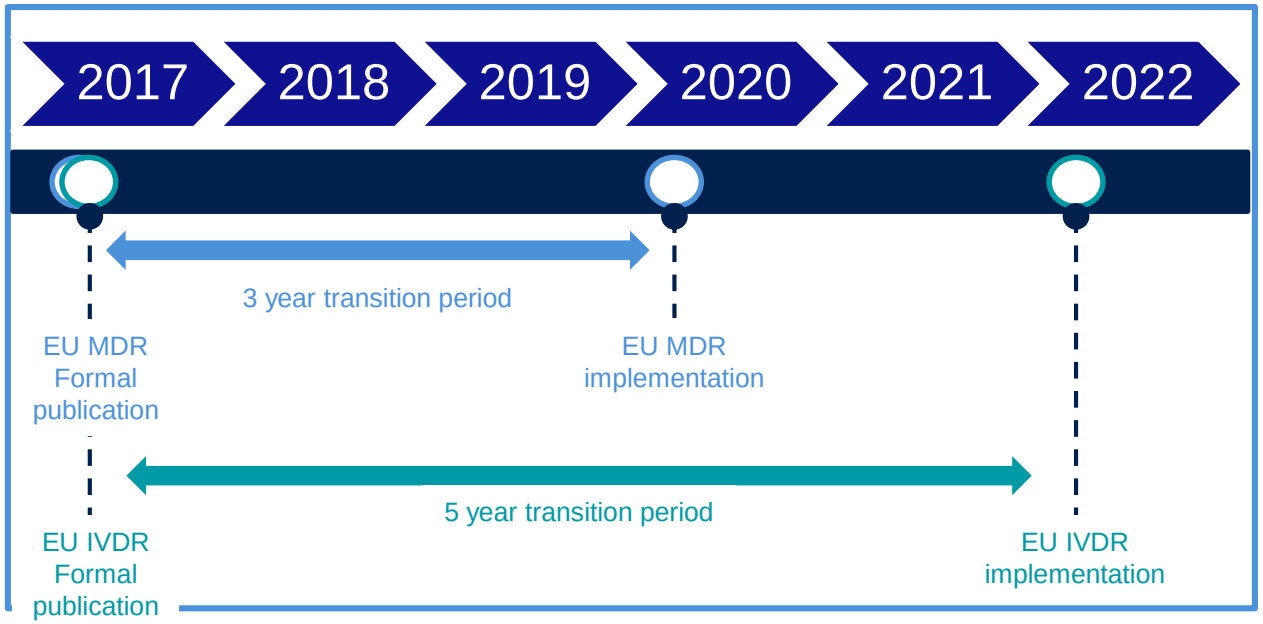
Legislation

Volume 60

5 May 2017

Contents

http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=OJ:L:2017:117:TOC



The Regulations entered into force on 25th May 2017.

However, most requirements will not fully apply until 26th May 2020 for Medical Devices, and 26th May 2022 for In Vitro Diagnostic Medical Devices.

Highlights of the new Regulations

New rules based risk classification (80:20)

Cementing the strength of Notified Bodies

Introducing reference labs and expert panels

Economic Operators (MAIDs) and persons responsible

Performance evidence and documentation requirements

Traceability via UDI

Market Surveillance/Post Market Surveillance

Requirements for devices that are put into service but not placed on the market

New definition and conformity assessment route for companion diagnostics

'companion diagnostic'

a device which is **essential** for the **safe and effective** use of a **corresponding medicinal product** to:

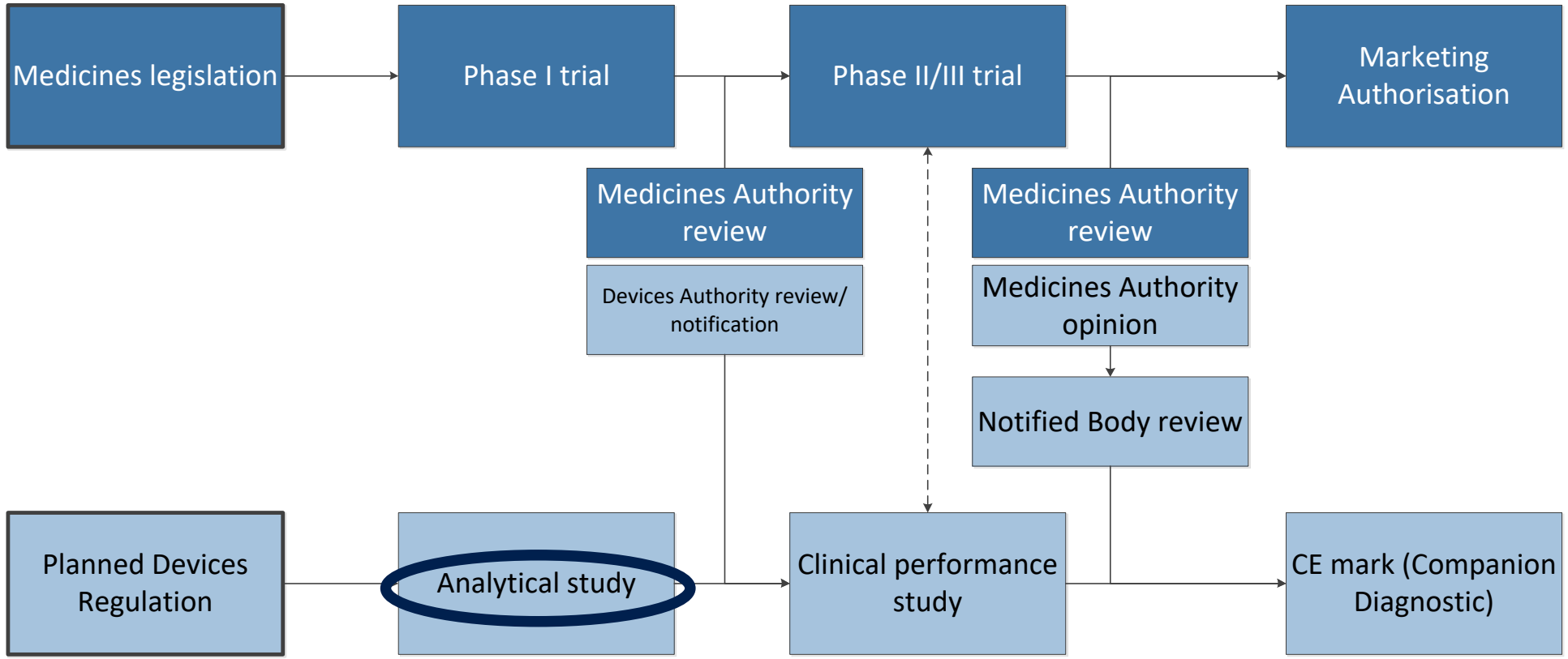
- identify, before and/or during treatment, patients who are most likely to **benefit** from the corresponding medicinal product; or
- identify, before and/or during treatment, patients likely to be at increased **risk** of serious adverse reactions as a result of treatment with the corresponding medicinal product

**This includes devices used in clinical trials to stratify patients for inclusion/exclusion in the trial or stratified to a cohort within a trial.*

Health Warning!

These views on the interpretation of the Regulations represent my own best judgement based on the information currently available and MHRA would always advise you to seek the views of your own professional advisers.

Companion Diagnostics: conformity assessment



General requirements for all IVD performance studies

- the health and safety of patients, users and other subjects
- the circumstances of the study
- rights, safety, dignity and well-being of the subjects in the study
- studies involving left over samples
- data generated by the study

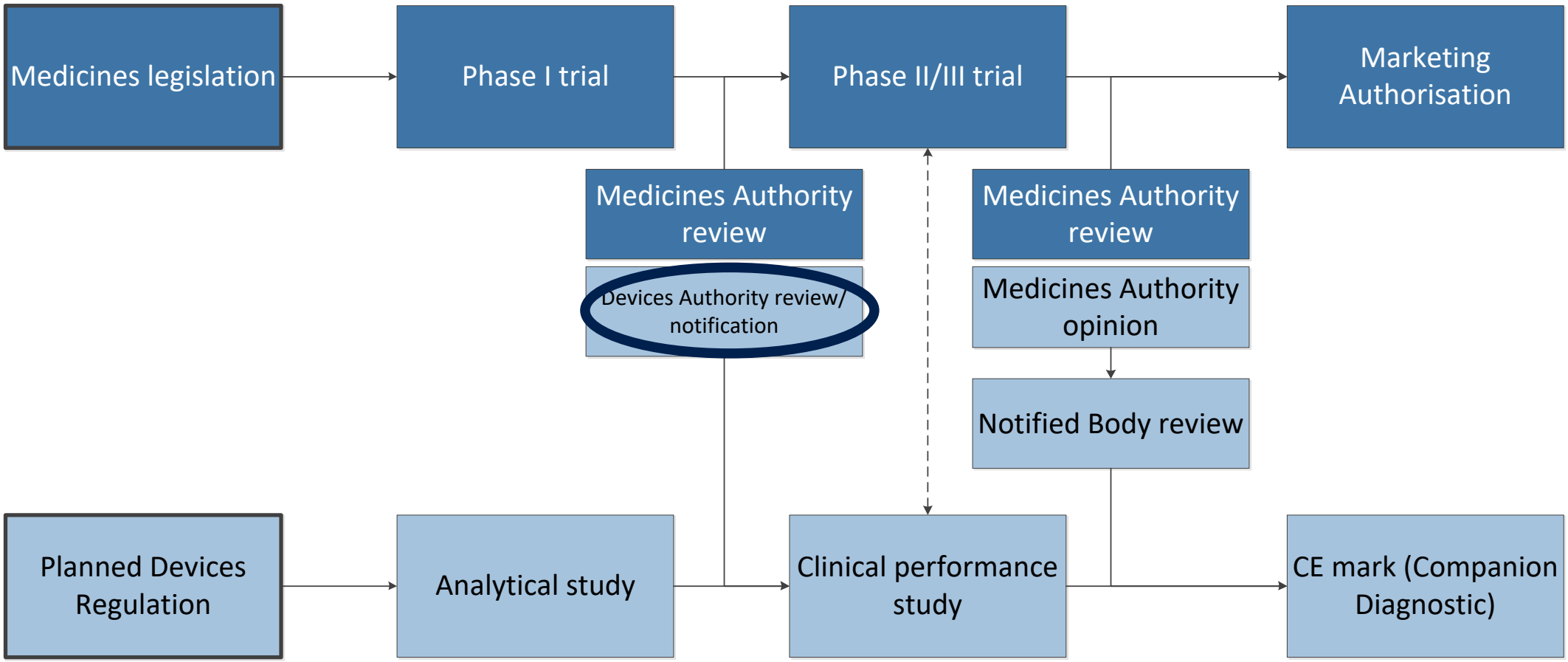
data generated are going to be scientifically valid, reliable and robust

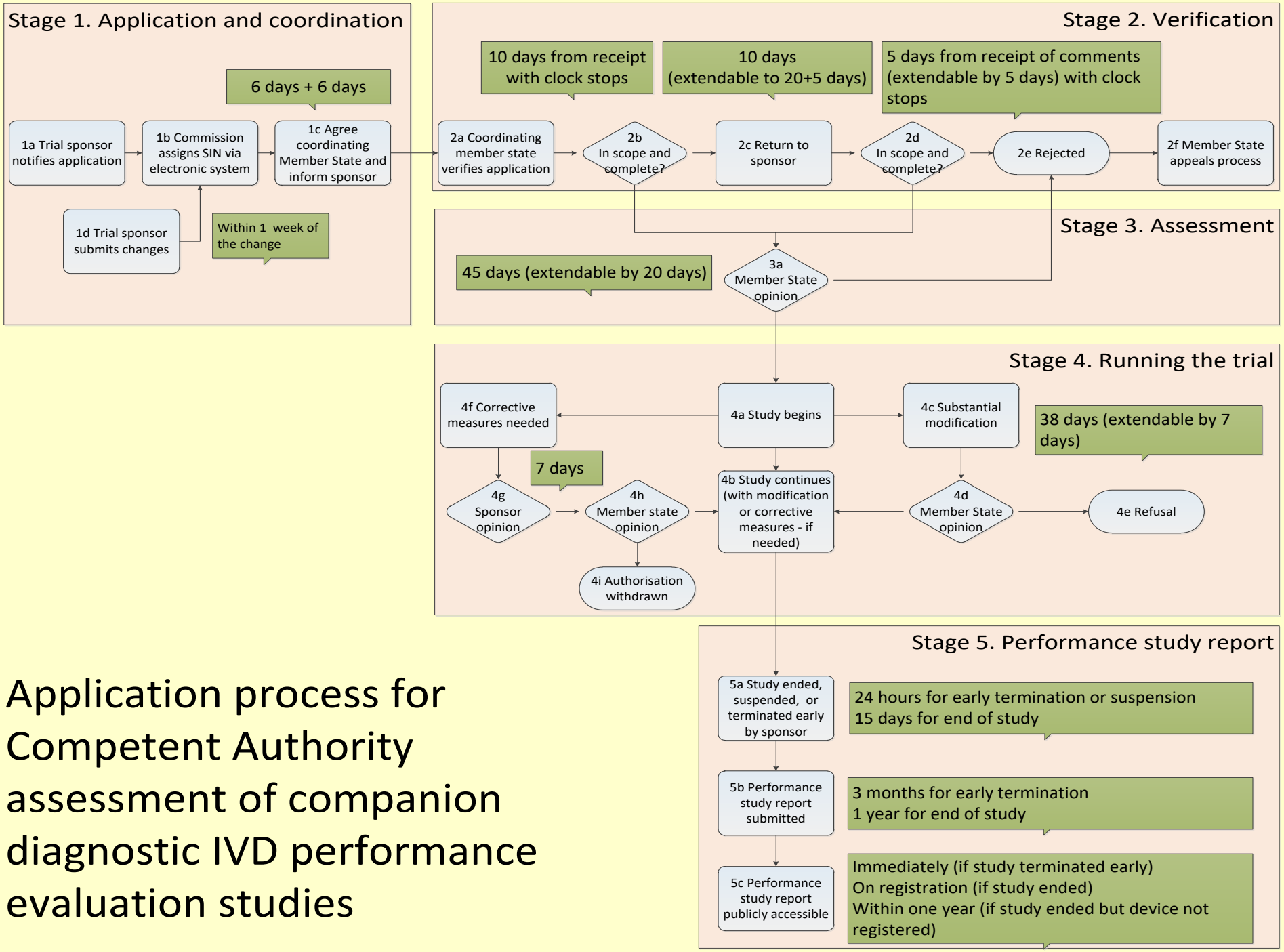
Additional requirements may apply

- Surgically invasive samples
- Interventional studies
- Additional risks to subjects
- Companion diagnostic IVDs
- Studies that involve people from specific groups
- Emergency situations

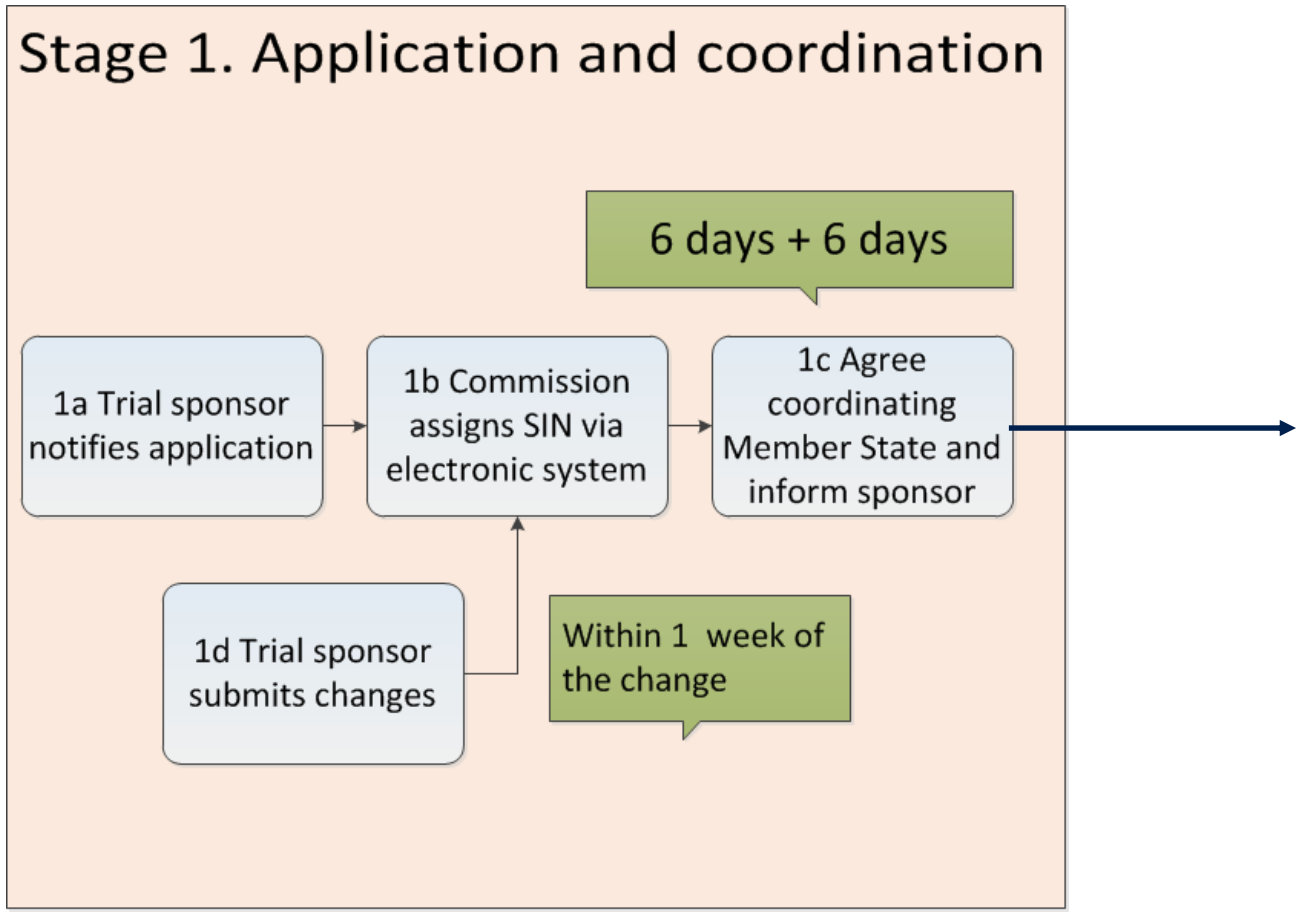
What are the additional requirements?

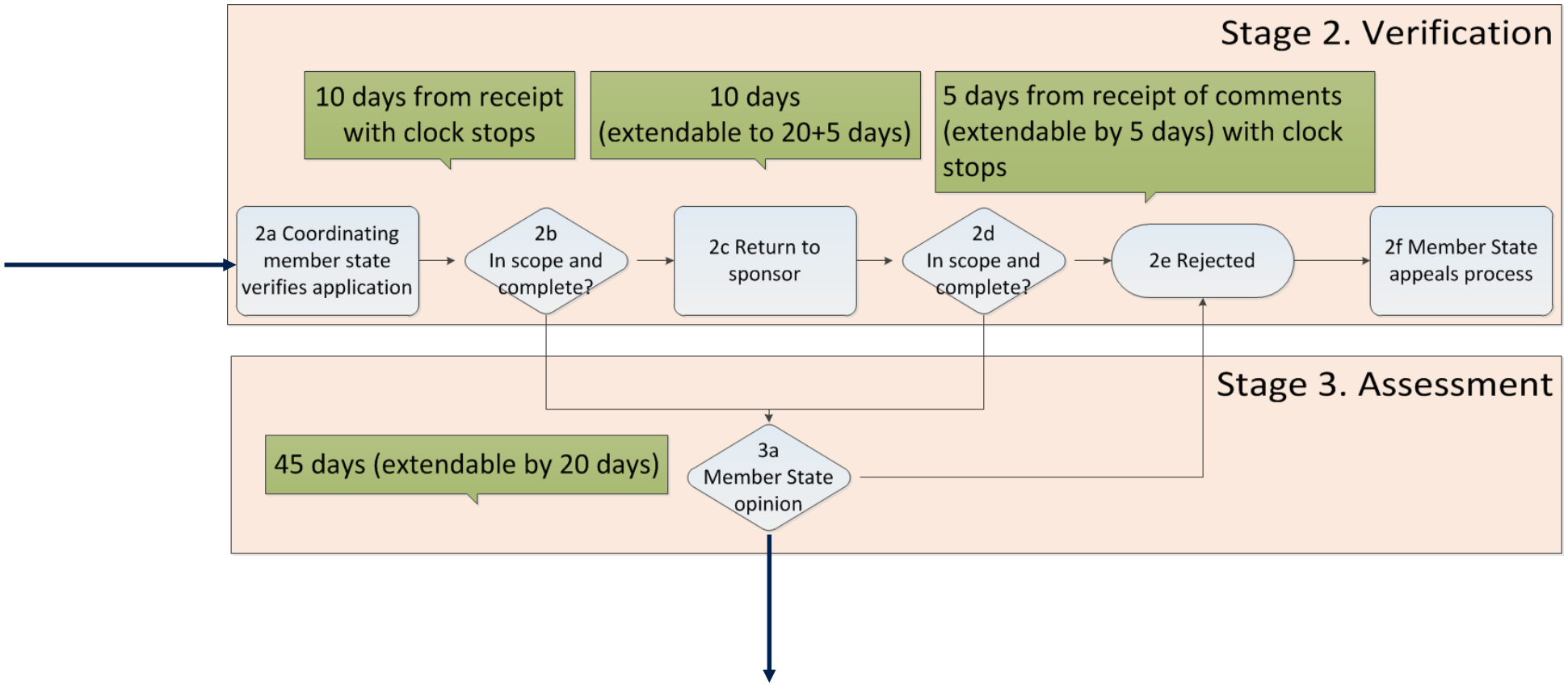
- Prior authorisation by a Member State(s)
- Review by an independent ethics committee
- Protection of vulnerable subjects
- Management of risks and benefits to the subject
- Informed consent and not exerting undue influence
- Demonstrating analytical performance and scientific validity
- Qualifications of those involved in the study
- Study facilities


Medicines legislation
Phase I trial
Phase II/III trial
Marketing Authorisation
Medicines Authority review
Devices Authority review/ notification
Medicines Authority review
Medicines Authority opinion
Notified Body review
Planned Devices Regulation
Analytical study
Clinical performance study
CE mark (Companion Diagnostic)



Application process for Competent Authority assessment of companion diagnostic IVD performance evaluation studies


Stage 1. Application and coordination
6 days + 6 days
1a Trial sponsor notifies application
1b Commission assigns SIN via electronic system
1c Agree coordinating Member State and inform sponsor
1d Trial sponsor submits changes
Within 1 week of the change


Stage 2. Verification
10 days from receipt with clock stops
10 days (extendable to 20+5 days)
5 days from receipt of comments (extendable by 5 days) with clock stops
2a Coordinating member state verifies application
2b In scope and complete?
2c Return to sponsor
2d In scope and complete?
2e Rejected
2f Member State appeals process
Stage 3. Assessment
45 days (extendable by 20 days)
3a Member State opinion

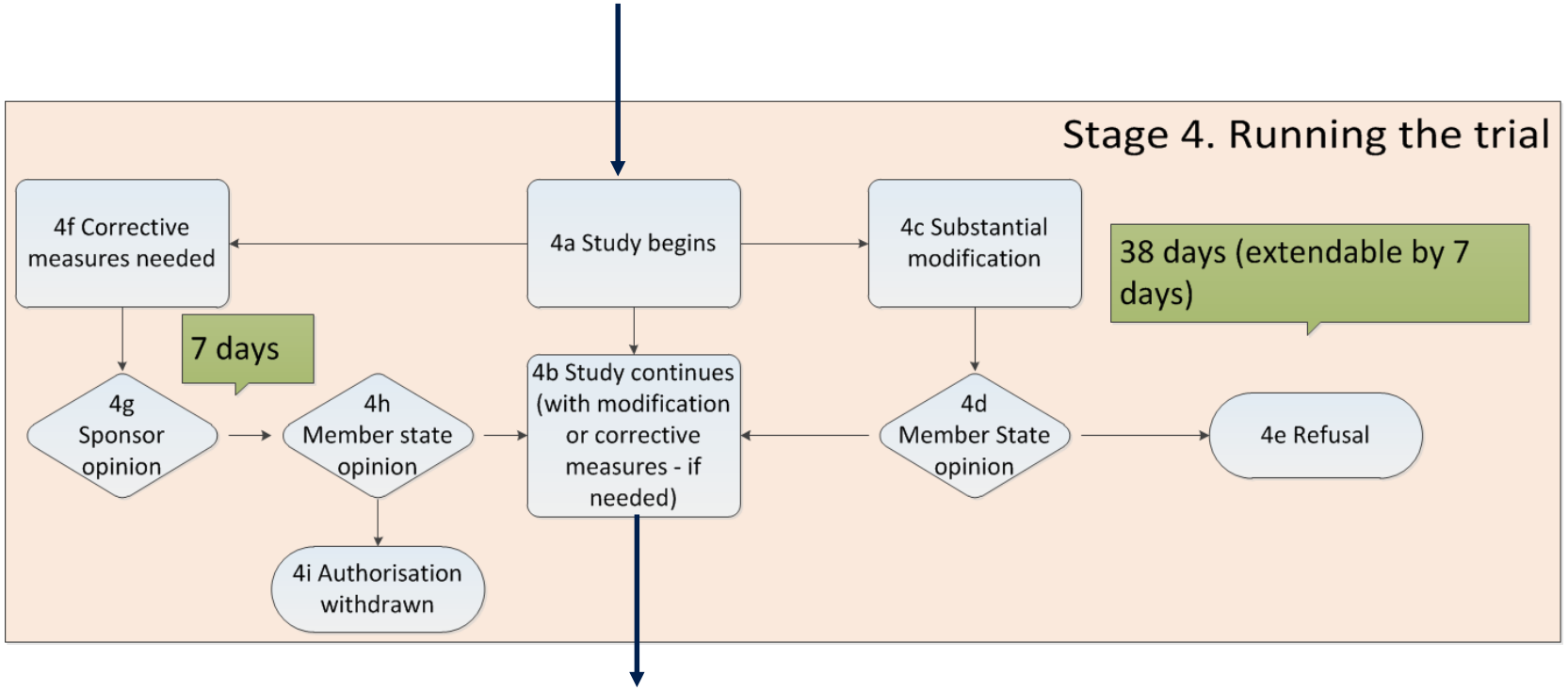
Performance indicators for IVDs

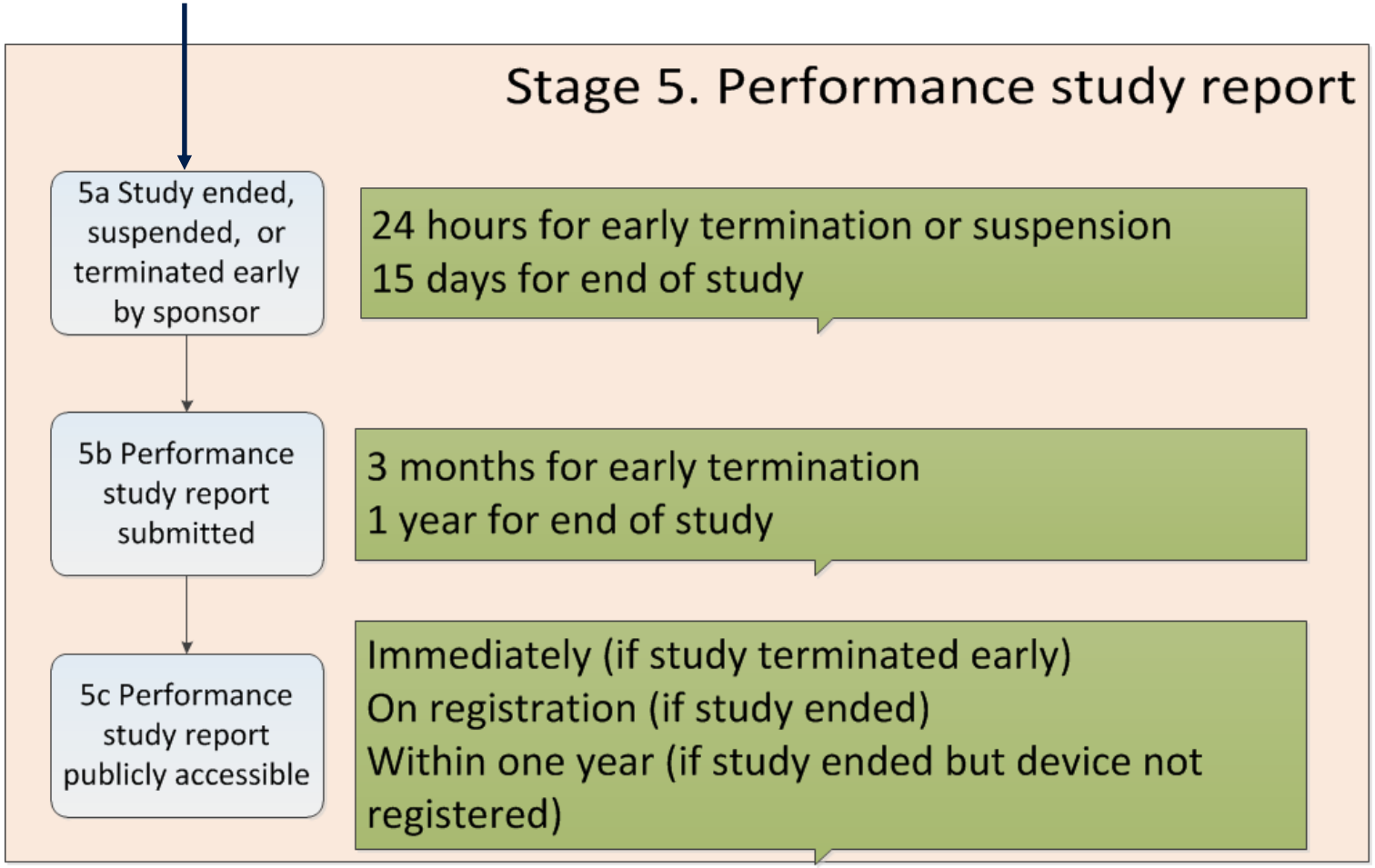
Scientific Validity	Analytical Performance	Clinical Performance
• the association of an analyte to a clinical condition or a physiological state	• the ability of a device to correctly detect or measure a particular analyte	• the ability of a device to yield results that are correlated with a particular clinical condition or a physiological or pathological process or state in accordance with the target population and intended user

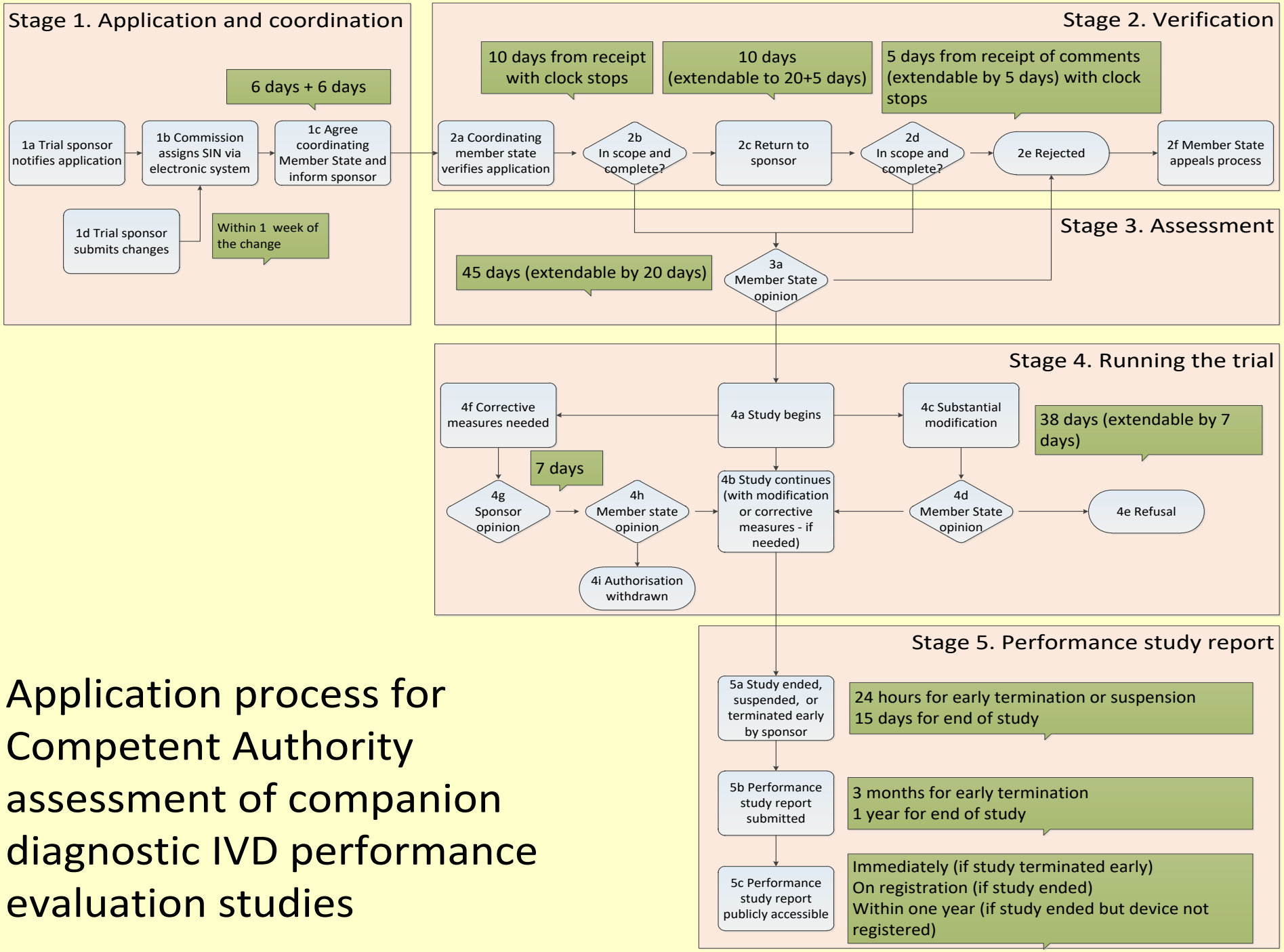
Performance indicators for IVDs

(clinical condition with a companion diagnostic ~ likely to respond to the medicinal product)

Scientific Validity	Analytical Performance	Clinical Performance
• the association of an analyte to a clinical condition or a physiological state	• the ability of a device to correctly detect or measure a particular analyte	• the ability of a device to yield results that are correlated with a particular clinical condition or a physiological or pathological process or state in accordance with the target population and intended user
• What is the evidence for the association between the *biomarker* and the likelihood of response to the corresponding *medicinal product*?	• How good is the IVD at detecting *biomarker*?	• How good is the *IVD* at predicting who is likely to respond to the corresponding *medicinal product*?


Stage 4. Running the trial
4f Corrective measures needed
4a Study begins
4c Substantial modification
38 days (extendable by 7 days)
7 days
4g Sponsor opinion
4h Member state opinion
4b Study continues (with modification or corrective measures - if needed)
4d Member State opinion
4e Refusal
4i Authorisation withdrawn


Stage 5. Performance study report
5a Study ended, suspended, or terminated early by sponsor
24 hours for early termination or suspension
15 days for end of study
5b Performance study report submitted
3 months for early termination
1 year for end of study
5c Performance study report publicly accessible
Immediately (if study terminated early)
On registration (if study ended)
Within one year (if study ended but device not registered)



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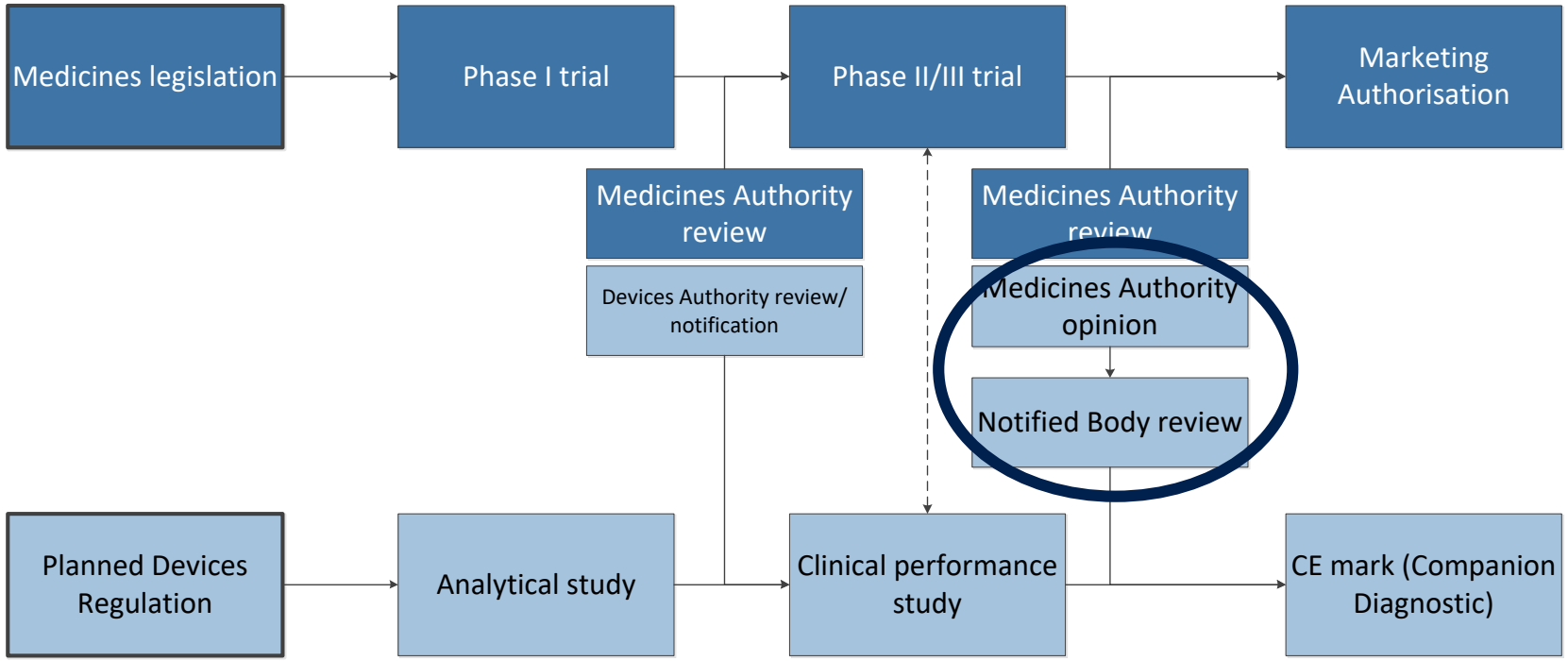
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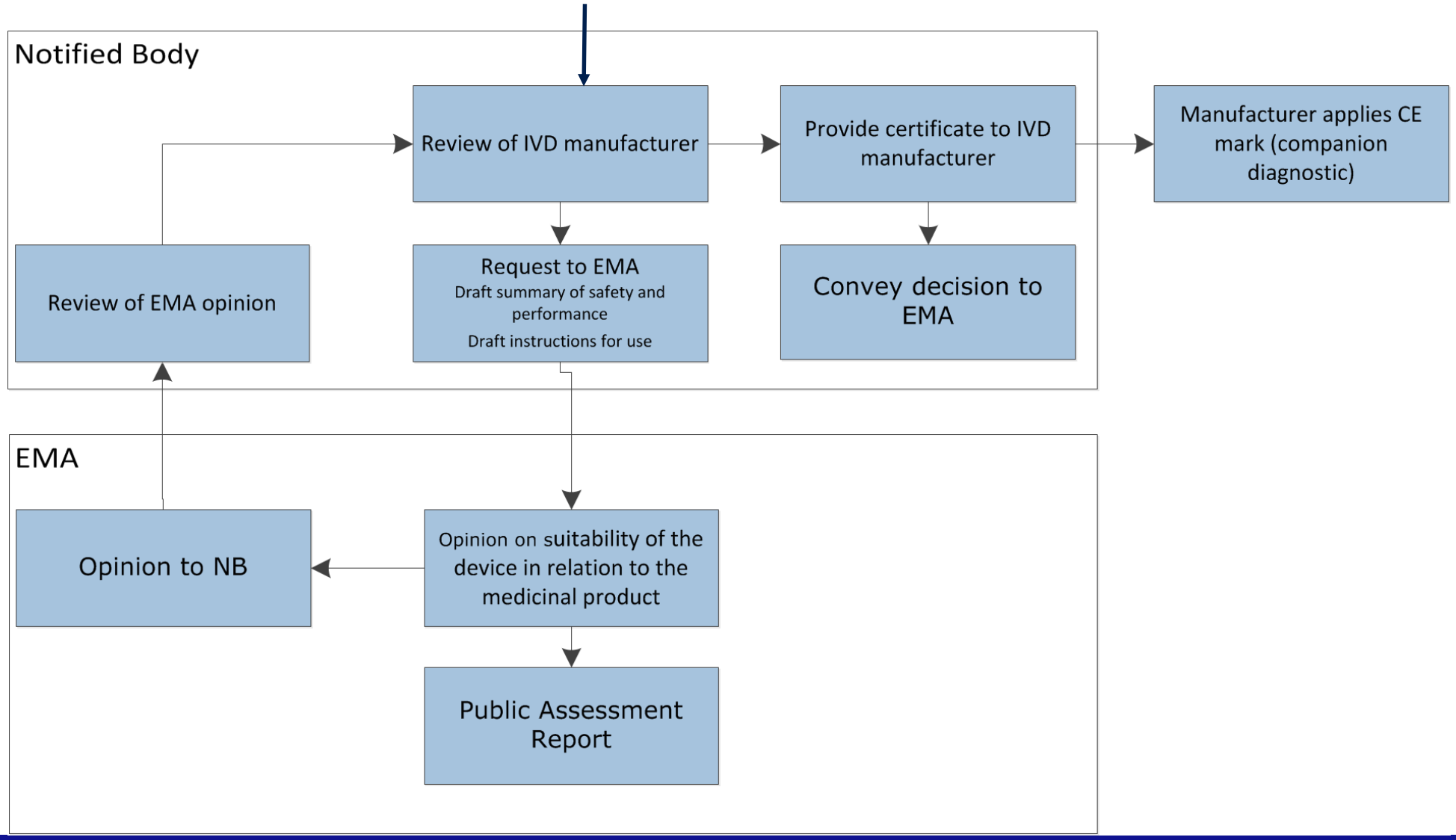
Role of Notified Bodies and EMA



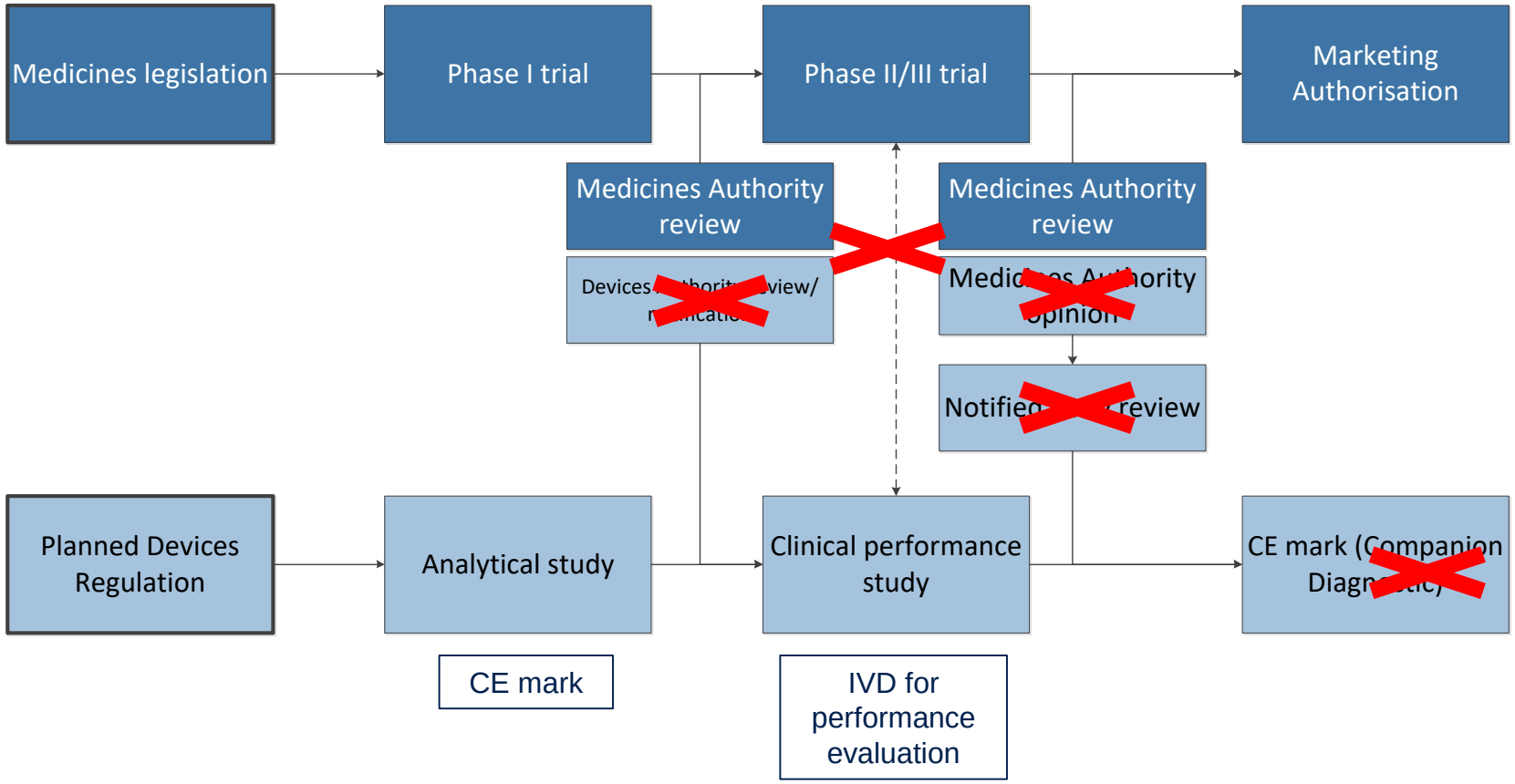
Regulation of diagnostic tests - exemptions

Health institution exemption

Distance sales

Exceptional use derogation

Current situation (MHRA view)



Current situation (MHRA view)

Unless an exemption applies, all IVDs being placed on the market or put into service in the EU are required to be CE marked.

This includes devices used in clinical trials to stratify patients for inclusion/exclusion in the trial or stratified to a cohort within a trial.

At the time of the clinical trial application, the CE mark need only be for the analytical performance of the IVD (eg detection of a biomarker) and will include reagents, equipment, calibrators, controls and software.

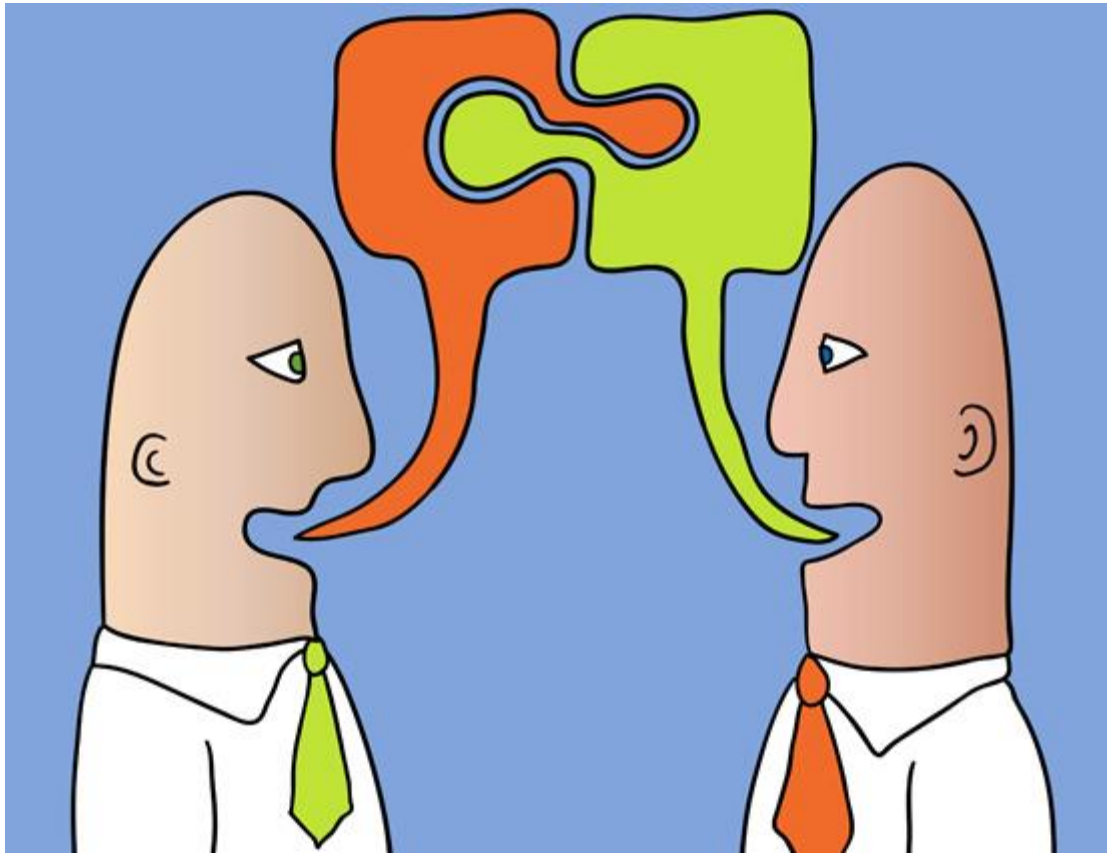
These are likely to be self certified IVDs.

Trials which determine the clinical performance of the assay (biomarker validity) will need to be registered as IVD performance evaluation studies.

Building partnerships

What's in the regulations?

What do the regulations mean?



What does the process look like?

How will it fit with our existing process?

Advice/enquiries

Medical device/IVD - devices.regulatory@mhra.gov.uk

Medicines clinical trial - clintrialhelpline@mhra.gov.uk

Innovation office - Innovationoffice@mhra.gov.uk

Thank you

stephen.lee@mhra.gov.uk

020 3080 7309