MHRA and its role in clinical investigations

Presented by Mark Grumbridge – Senior clinical advisor

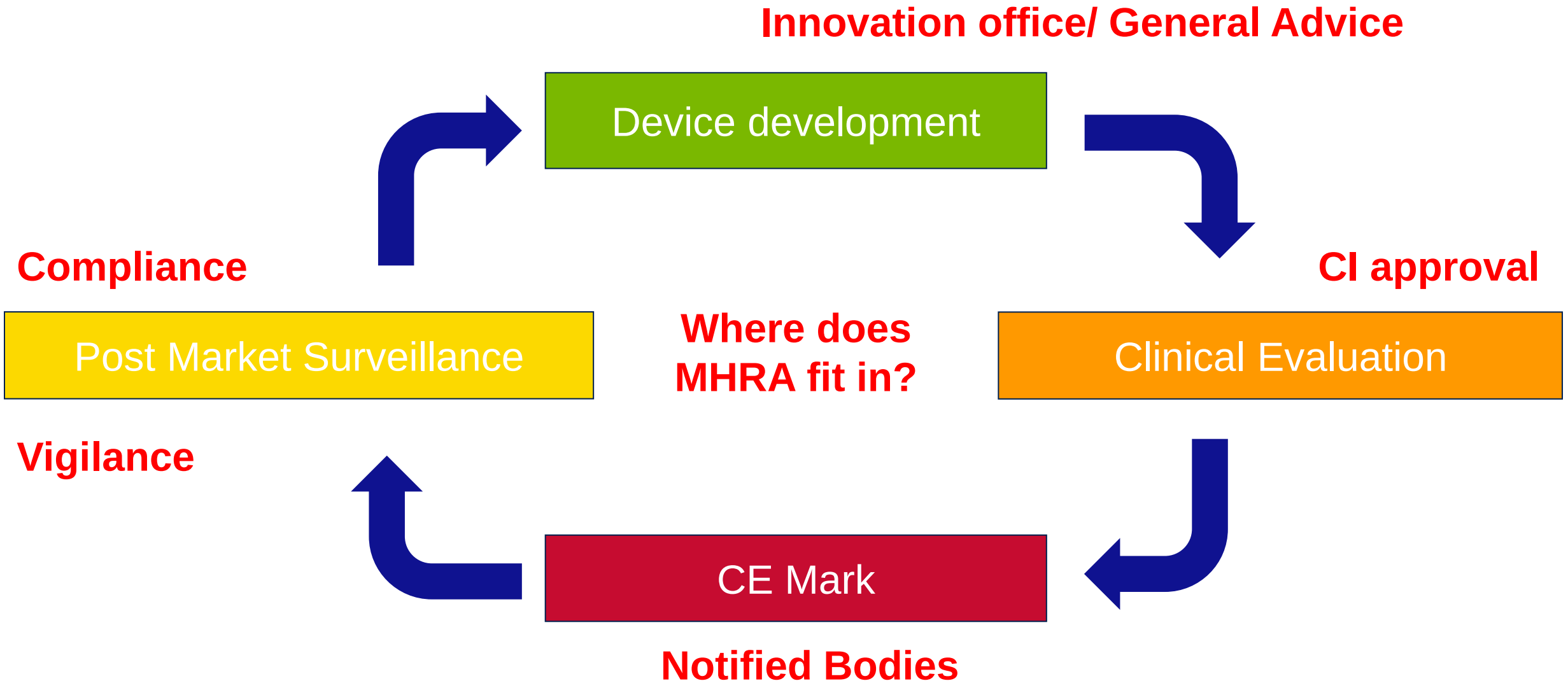
MHRA overview

The Medicines and Healthcare products Regulatory Agency regulates medicines, medical devices and blood components for transfusion in the UK.

The agency has 3 centres:

- Clinical Practice Research Datalink (**CPRD**), a data research service that aims to improve public health by using anonymised NHS clinical data
- The National Institute for Biological Standards and Control (**NIBSC**), a global leader in the standardisation and control of biological medicines
- The Medicines and Healthcare products Regulatory Agency (**MHRA**), the UK's regulator of medicines, medical devices and blood components for transfusion, responsible for ensuring their safety, quality and effectiveness

Medical Device Regulatory System



Devices Division

Devices Clinical Team

Devices Safety & Surveillance Group

Devices Regulatory Group

Devices Information & Operations Group

Internal / external resource

Internal clinical staff

Technical staff

External experts (around 100)

Sterilisation

Toxicology

Statisticians

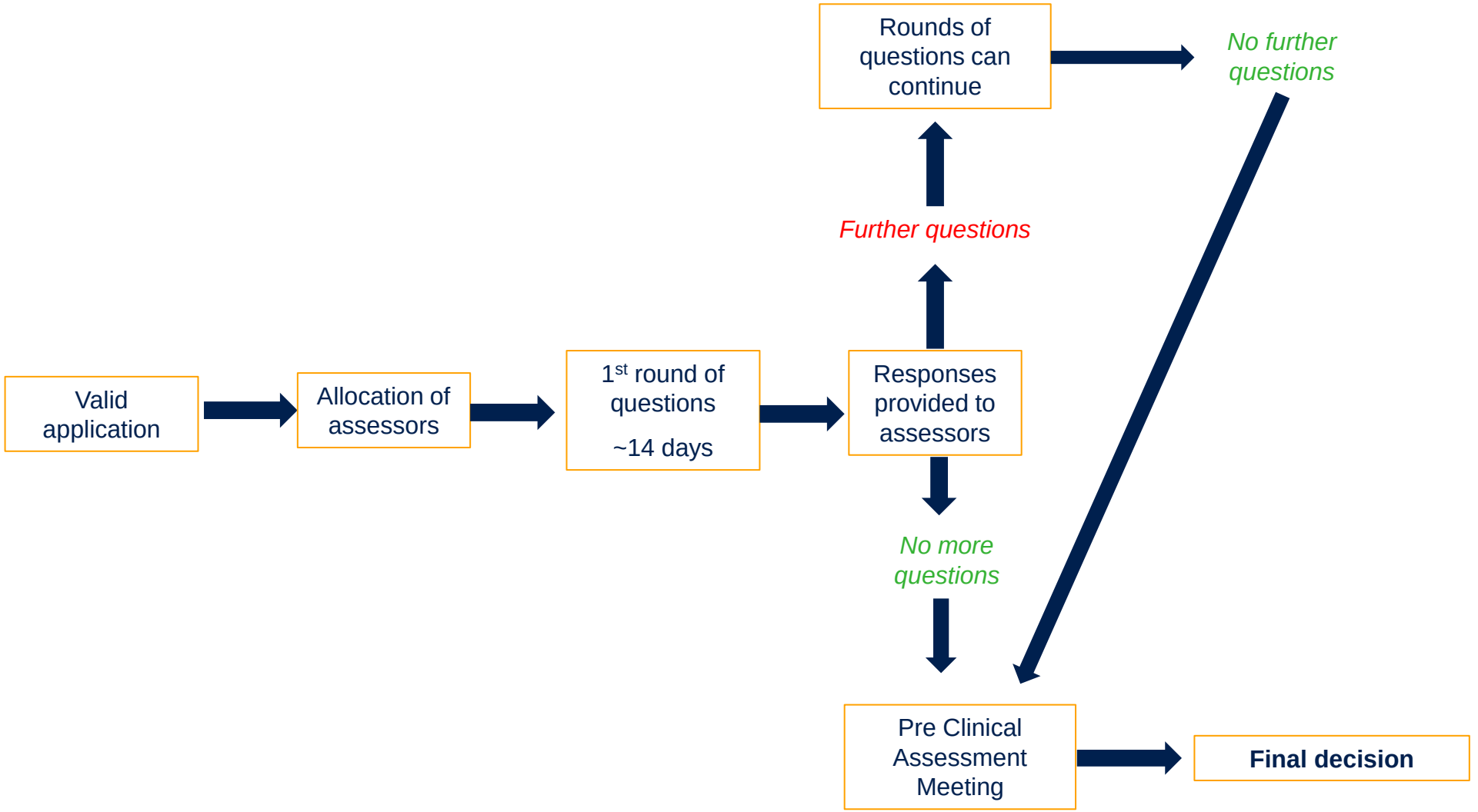
Clinical investigations – how to apply

Notify MHRA when:

- it is a non-CE marked device
- a CE-marked device being used outside of its intended use

First steps:

- E-portal hosted by Integrated Research Application System (IRAS)
- Validation - a checklist is available on the MHRA website.
  - Up to 5 working days
  - High level overview. Is it a device? Are the outcomes looking at safety and performance? Do we have all the relevant documentation? (checklist on our website)


Valid application
Allocation of assessors
1st round of questions
~14 days
Responses provided to assessors
Further questions
Rounds of questions can continue
No further questions
No more questions
Pre Clinical Assessment Meeting
Final decision

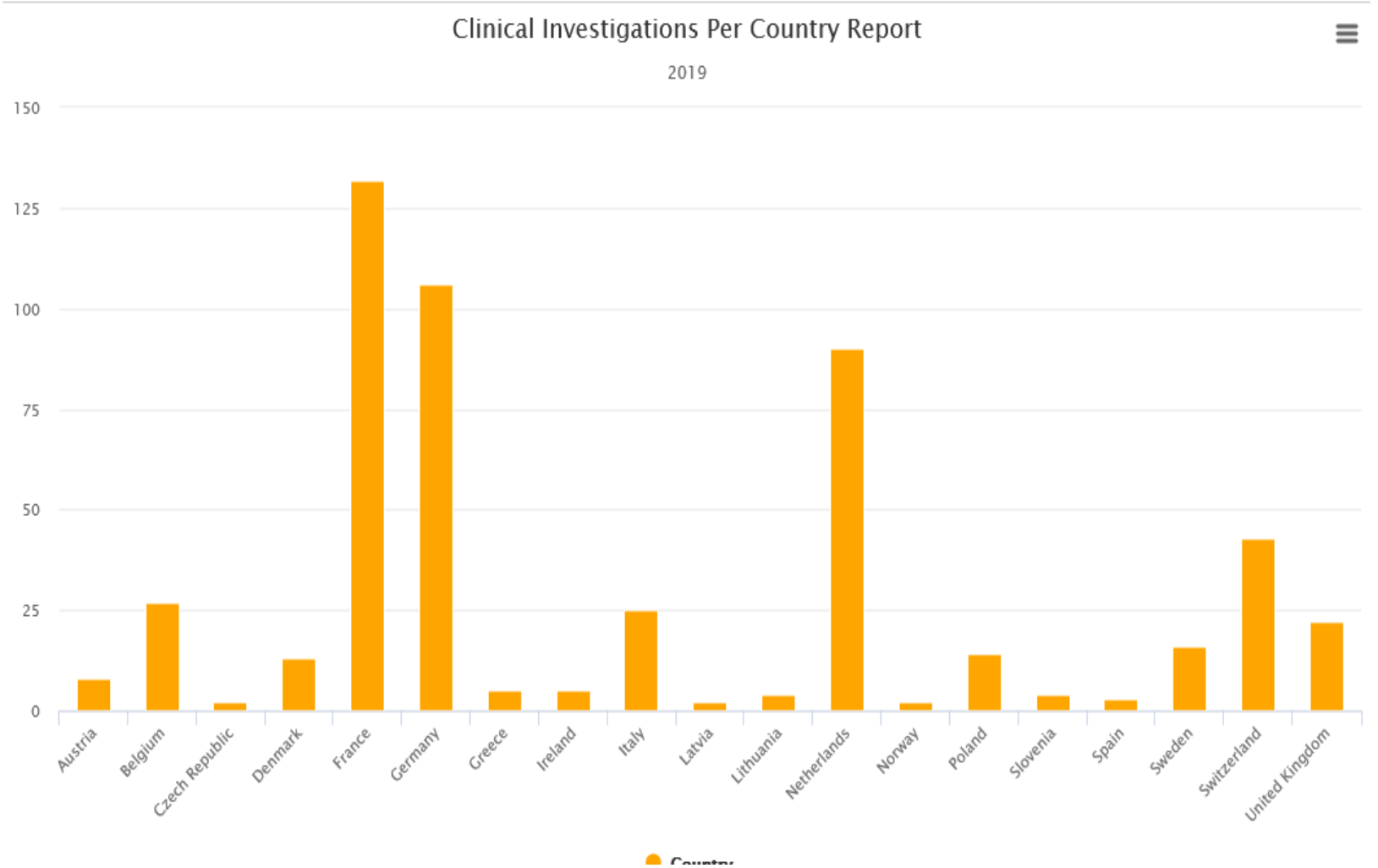
Application Data

2018 – 81

2019 – 60

2020 – 7 to date

EU trial applications (October 2019)



Clinical investigations – the assessment

What are we expecting?

Demonstration of Safety and Performance.

Annex X 2.1: The objectives of clinical investigation are:

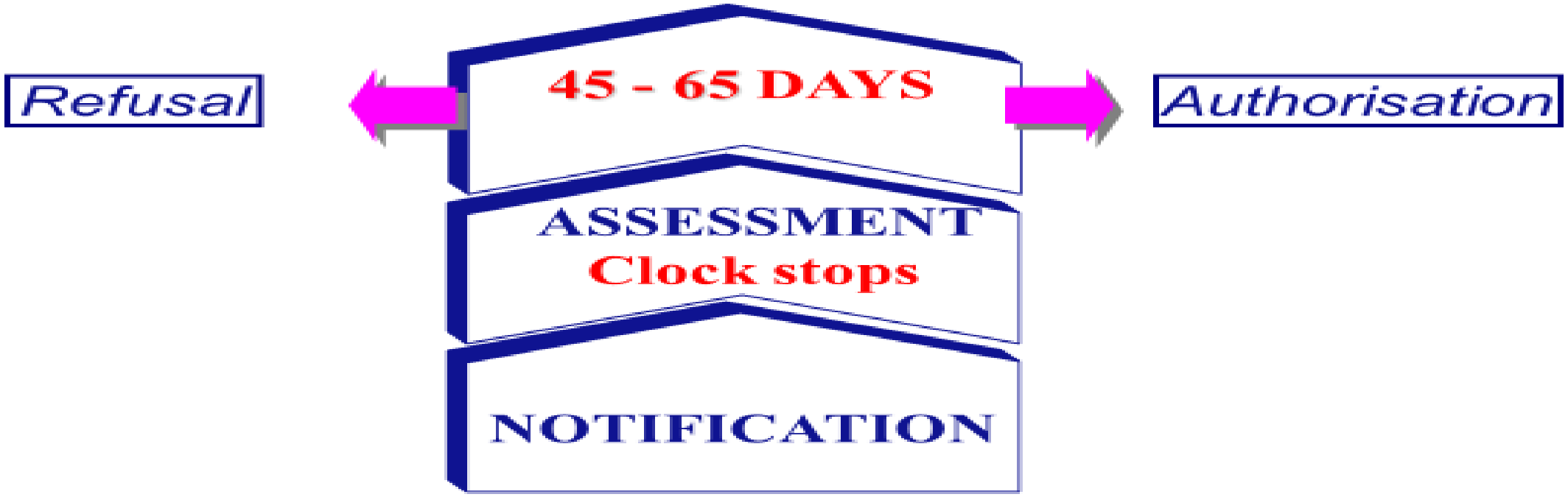
- **to verify that, under normal conditions of use, the performance of the devices conform to those referred to in Section 3 of Annex I, and**
- **to determine any undesirable side-effects, under normal conditions of use, and assess whether they constitute risks when weighed against the intended performance of the device**

Timelines - MDD

Timelines - MDR

HANDLING BY CA - MDR

MHRA



Possible outcomes

- No objection
- Conditional No objection
- Objection
  - Lack relevant clinical end points
  - Clinical parameters insufficient/ inappropriate
  - Inadequate pre-clinical testing/ assessment
  - Inadequate toxicological testing/ analysis
  - No sterilisation validation
  - Inadequate electrical testing
  - Risks outweigh benefits

No Objection - What next?

- Interim reports – case by case (approval subject to….)
- SAE reports – as and when (subject to internal review)
- Final report – assessment

What support can we offer?

- **Innovation office – earlier the better!**

- **Devices specific – face to face meeting/email enquiries**

Not a consultancy!

- signposting

- regulatory guidance

The Future in Devices…

Regulation (EU) 2017/745 – Medical Devices

Regulation (EU) 2017/746 - IVDs

MDR – May 2020

- Classification rules
  - certain devices will be reclassified under the MDR into a higher risk group
  - The MDR will also regulation certain groups of devices without a medical purpose_– Annex XVI sets out these groups

- Increased traceability
  - greater emphasis placed on the traceability of devices throughout the supply chain
  - increased control over safety alerts, potential recalls and surveillance activities

- Increased scrutiny
  - focus on the functioning of notified bodies, market surveillance, coordination of vigilance and communication and transparency
  - pre-market clinical scrutiny of selected high risk, novel devices – Expert Panels
  - enhanced market surveillance responsibilities – inspections

- Changes to obligations for economic operators
  - importers and distributers will be regulated
  - more rigorous vigilance reporting requirements – ongoing assessment

- Clinical evidence requirements
  - more stringent requirements for clinical evaluation and claiming equivalence
  - increase in the number of clinical investigations
  - continuous process throughout the lifecycle of the device
  - SSCP

MDR new - Site inspections

Annex XV (clinical investigations)

Chapter III (other obligations of the sponsor)

6. The Sponsor shall provide evidence that the investigation is being conducted in line with good clinical practice, for instance through internal or external inspection.

(MSs to inspect investigational sites)

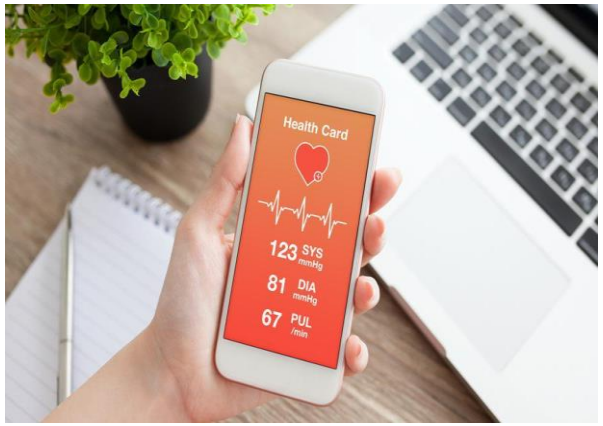
MDR new - Coordinated assessment process

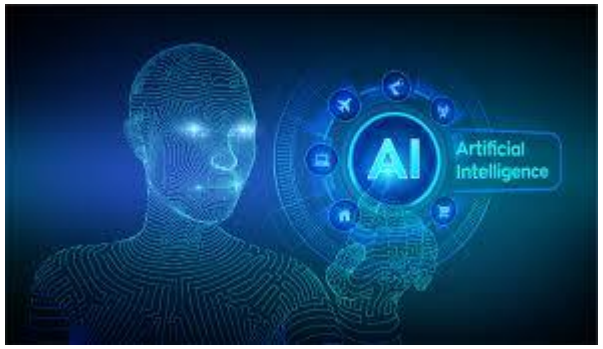
Sponsor may submit a single application for multi-centre studies

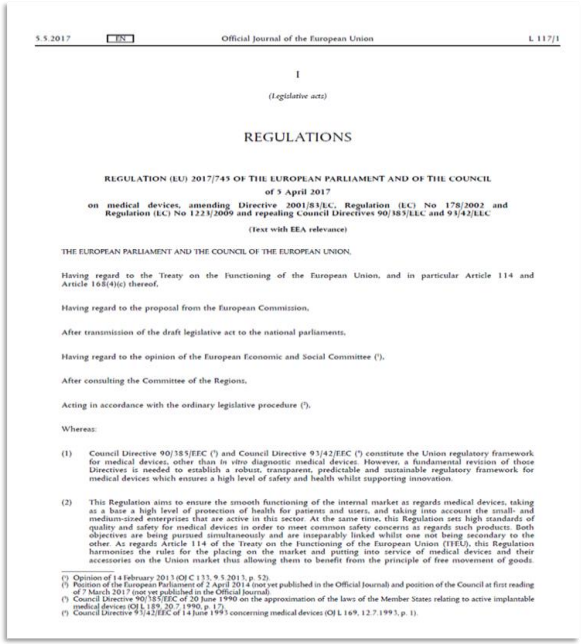
- **Sponsor shall propose coordinating MS**
- **MSs have 6 days to confirm coordinating MS**
- **Deadlines in article 51 start from day after coordinating MS has been confirmed**

The future…..

- New Regs
- A.I.
- Apps
- Operating outside the EU







5.5.2017 EN Official Journal of the European Union L 117/1

I

(Legislative acts)

REGULATIONS

REGULATION (EU) 2017/745 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL
of 5 April 2017
on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC

(Text with EEA relevance)

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty on the Functioning of the European Union, and in particular Article 114 and Article 168(4)(c) thereof,

Having regard to the proposal from the European Commission,

After transmission of the draft legislative act to the national parliaments,

Having regard to the opinion of the European Economic and Social Committee (1),

After consulting the Committee of the Regions,

Acting in accordance with the ordinary legislative procedure (2),

Whereas:

(1) Council Directive 90/385/EEC (3) and Council Directive 93/42/EEC (4) constitute the Union regulatory framework for medical devices, other than *in vitro* diagnostic medical devices. However, a fundamental revision of those Directives is needed to establish a robust, transparent, predictable and sustainable regulatory framework for medical devices which ensures a high level of safety and health whilst supporting innovation.

(2) This Regulation aims to ensure the smooth functioning of the internal market as regards medical devices, taking as a base a high level of protection of health for patients and users, and taking into account the small- and medium-sized enterprises that are active in this sector. At the same time, this Regulation sets high standards of quality and safety for medical devices in order to meet common safety concerns as regards such products. Both objectives are being pursued simultaneously and are inseparably linked whilst one not being secondary to the other. As regards Article 114 of the Treaty on the Functioning of the European Union (TFEU), this Regulation harmonises the rules for the placing on the market and putting into service of medical devices and their accessories on the Union market thus allowing them to benefit from the principle of free movement of goods.

(1) Opinion of 14 February 2013 (OJ C 133, 9.5.2013, p. 52).
(2) Position of the European Parliament of 2 April 2014 (not yet published in the Official Journal) and position of the Council at first reading of 7 March 2017 (not yet published in the Official Journal).
(3) Council Directive 90/385/EEC of 20 June 1990 on the approximation of the laws of the Member States relating to active implantable medical devices (OJ L 189, 20.7.1990, p. 17).
(4) Council Directive 93/42/EEC of 14 June 1993 concerning medical devices (OJ L 169, 12.7.1993, p. 1).

Resources

Guidance

Notify MHRA about a clinical investigation for a medical device

How to notify MHRA of your intention to carry out a clinical investigation for CE marking.

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Thank you