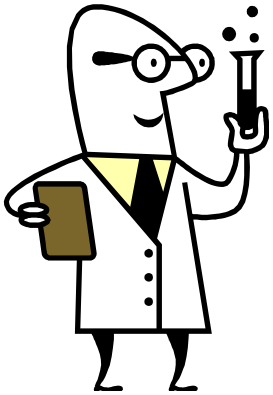
Medicines & Healthcare products Regulatory Agency

MHRA
Regulating Medicines and Medical Devices

Evidence requirements
CE marking and the IVD Regulations

Medicines and Healthcare Products Regulatory Agency

IVD Regulations



investigation
action

compliance

Notified Body

Competent
Authority

CE

European market

post market surveillance
vigilance

Harmonised Standards/CTS "presumption of conformity"

Current regulatory system

- Joint Action Plan
- Signal Detection

Proposals for change

- Classification
- Clinical evidence
- In house manufacturing
- Companion diagnostics

Joint Action Plan

- Qualifications of NB re-assessed
- Joint Audits of NB
- Unannounced visits of manufacturers
- Vigilance teleconference of Competent Authorities

Signal Detection

- Significant improvements in adverse incident reporting by UK healthcare
- New signal detection software
- Increased focus on signals

Risk based classification system

CLASS	RISK LEVEL	EXAMPLES
A	Low individual risk and Low public health risk	Clinical chemistry analyser Prepared selective culture media
B	Moderate individual risk and/or Low public health risk	Vitamin B12 test Pregnancy self testing Anti-nuclear antibody test Urine test strips
C	High individual risk and/or Moderate public health risk	Blood glucose self testing HLA typing PSA screening Rubella test
D	High individual risk and High public health risk	HIV blood donor screening HIV blood diagnostic

RISK

Clinical Evidence

"… compliance … should be based on clinical evidence. … As a general rule, clinical evidence should be sourced from clinical performance studies …"

Clinical Evidence

- Clinical evidence should be documented in a clinical evidence report
- Concepts of analytical performance, scientific validity and clinical performance introduced
- Post-market surveillance required to keep clinical evidence up to date

Clinical Evidence - Terminology

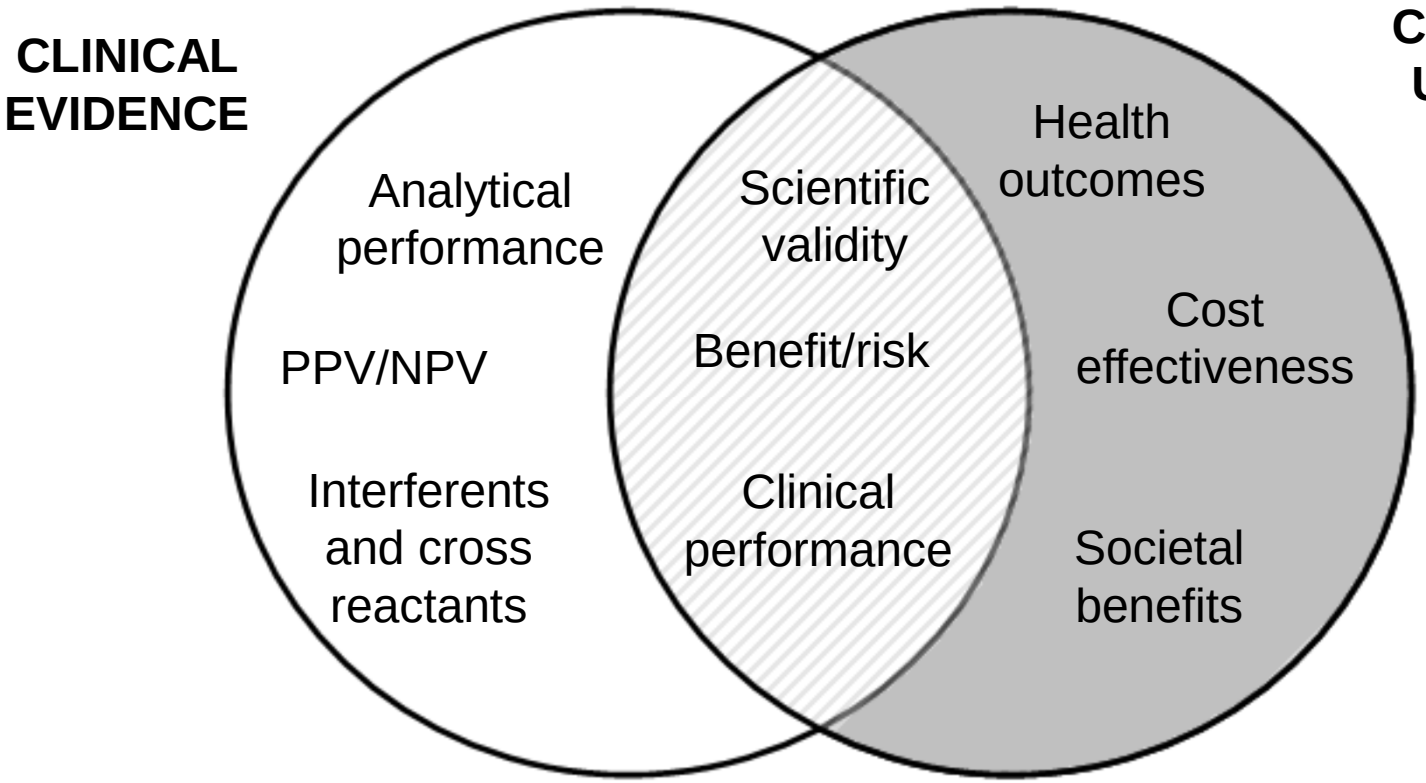
Clinical evidence - the clinical data and performance evaluation results pertaining to a device of sufficient amount and quality to allow a qualified assessment of whether the device achieves the intended clinical benefit(s) and safety, when used as intended by the manufacturer;

Clinical Evidence - Terminology

Analytical performance: the ability of a device to correctly detect or measure a particular analyte

Scientific validity: the association of an analyte to a clinical condition or a physiological state

Clinical performance: 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


CLINICAL EVIDENCE
CLINICAL UTILITY
Analytical performance
PPV/NPV
Interferents and cross reactants
Scientific validity
Benefit/risk
Clinical performance
Health outcomes
Cost effectiveness
Societal benefits

Performance studies

- General requirements on all studies (eg review by NB/ GCP)
- Class C and D IVDs – study outcomes are publicly available
- Competent authority approval for ‘interventional’ studies
  - affect patient management decisions (eg drug/diagnostic co-development) and
  - involve invasive procedures or other risks for patients.

The ‘in-house’ exemption

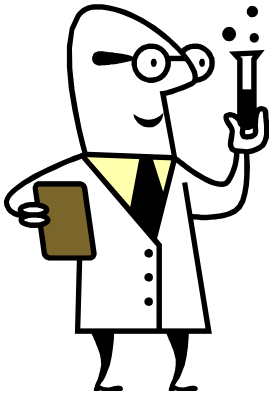
- Currently:
  - blanket exemption for all IVDs manufactured and used within same health institution
- Proposals:
  - quality management system
  - accreditation to ISO 15189
  - vigilance reporting

Companion Diagnostic
Latest version (subject to change)

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

- *identify patients who are most likely to benefit from the medicinal product, or;*
- *identify patients likely to be at increased risk for serious adverse reactions as a result of treatment with the medicinal product, or;*
- *monitor response to treatment by the medicinal product for the purpose of adjusting treatment to achieve improved safety or effectiveness;*

IVD Regulations



investigation
action

compliance

Notified Body
plus EMA

Competent
Authority

CE

European market

post market surveillance
vigilance

Harmonised Standards/CTS "presumption of conformity"

Next steps for new regulations

General Approach

- Partial General Approach agreed 19th June
- General Approach published 22nd September

Trilogues

- Council/Commission/Parliament
- 13th October to 3rd December
- (Dutch Presidency can take forward in early 2016 if necessary)

1st Reading

2nd Reading

Publication

Consolidated text prepared by the Luxembourg Presidency with a view to the finalisation of a General Approach, thus completing the partial General Approach reached at the meeting of the Council (EPSCO) on 19 June 2015.

recitals and articles of the proposed Regulation on **medical devices**
http://data.consilium.europa.eu/doc/document/ST-12040-2015-REV-1/en/pdf

annexes to the proposed Regulation on **medical devices**
http://data.consilium.europa.eu/doc/document/ST-12040-2015-ADD-1/en/pdf

recitals and articles of the proposed Regulation on **in vitro diagnostic medical devices** http://data.consilium.europa.eu/doc/document/ST-12042-2015-INIT/en/pdf

annexes to the proposed Regulation on **in vitro diagnostic medical devices**
http://data.consilium.europa.eu/doc/document/ST-12042-2015-ADD-1/en/pdf

Thank you for listening

Steve Lee

020 3080 7309

Stephen.Lee@mhra.gsi.gov.uk