UK NEQAS

UK NEQAS FOR CLINICAL CHEMISTRY

UNITED KINGDOM NATIONAL EXTERNAL QUALITY ASSESSMENT SCHEMES

Monitoring Assay Traceability through EQAS Surveillance

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EQA and traceability

- the role of EQA
- EQA and the IVD MDD
- Traceability and EQA
- Performance surveillance and vigilance
- EQA targets and calibration issues
- Laboratory medicine as a partnership

External quality assessment and proficiency testing

- **For the purposes of this presentation**

EQA ≡ PT

In Europe:

- *"PT" has licensing connotations*
- *EQA implies an educational approach*

Role of external quality assessment

EQA provides assessment of:

- **individual laboratory performance**
- **the overall performance** (state of the art)
- **the influence of analytical procedures**
  (method, reagent, instrument, calibration)
- **the specimens distributed**

EQA PROVIDES AN EDUCATIONAL STIMULUS TO IMPROVEMENT
(providing information to a quality management system)

The *in vitro* medical diagnostic devices Directive (IVD MDD) - 1

- **Purpose**
  - a 'placing on the market' Directive - industry-driven
  - intended to eliminate (artificial) trade barriers
  - manufacturers set their own specifications
- **Effects**
  - 'stratification' of IVDs
    - general, self-test, Annex II list B
    - Annex II list A (blood safety)
  - traceability requirements - mostly profession-driven
  - common technical specifications for Annex II list A

The *in vitro* medical diagnostic devices Directive (IVD MDD) - 2

- **Scope**
  - all reagents, instruments, software, accessories
  - all calibration and control materials
  - EQA specimens and CRMs excluded

- **Timescale**
  - IVD MDD published December 1998
  - Transition period 2000 - 2003; completion:
    - December 2003 - all products (existing and new) must then comply
    - December 2005 - supply of products manufactured before Dec 2003

Support for the IVD MDD

- **European Standards**
  - mandated from CEN by European Commission
  - prepared through CEN TC140
    - *(some in parallel with ISO TC212)*
  - reference procedures and laboratories
    - EN 12286
    - prEN 15195
  - traceability
    - prEN 17511
    - prEN 18153 (enzymes)
  - EQA
    - prEN 14136

prEN 14136 - requirements on EQA

- **For data to be used in procedure assessment:**
  - for any procedure
  - **for an IVD** (or a combination of IVDs)

- **Two elements:**
  - basic recommendations of ISO/IEC Guide 43-1
  - additional requirements

A Standard, but role equivalent to ISO/IEC Guide 43-3

Additional requirements of prEN14136

- **Independence of judgement**
- **Quality management**
- **Unequivocal identification of IVDs used**
- **Data analysis**
- **Surveillance procedures**

NB: compliance with prEN14136 is <u>not</u> mandatory

- *applies only if data are to be used for procedure (IVD) assessment*

Additional requirements - 1

- **Independence of judgement**
  - from manufacturing or distribution interests
    - *avoid "ensure own pass"/"engineer failure of others"*
  - no mechanisms specified

- **Quality management**
  - accreditation advocated
  - EQAS design to ISO/IEC Guide 43-1 / ILAC G13
  - ISO 9000 quality management system

Additional requirements - 2

- **IVD identification**
  - must identify product(s) used
  - ensure adherence to manufacturer's protocol
  - exclude from analysis if variant protocol used
  - *an EU database would have been helpful*

establishing exactly what participants do is a problem for all EQASs !

Variant protocols

- **If believe manufacturer's protocol is wrong, it is unethical to follow it**
  - done on basis of (sufficient) scientific evidence
  - can advance manufacturers' understanding

- **In future, however, use of variant protocols**
  - excluded from assessment with other users
  - requires full documentation

NB1: how can EQAS reliably identify & exclude these?

NB2: laboratories are responsible for results reported - "only following protocol" not an acceptable defence

How to assess IVD performance?

- **Against manufacturer's claim?**
  - manufacturers' preference
  - basis for assessment under IVD MDD
  - only basis for vigilance
- **Against accepted performance criteria?**
  - laboratories are assessed against these
  - the tools they use must be judged similarly

NB: laboratory medicine must support and enhance patient care

Is EQA data a reliable assessment tool?

- **EQA reflects 'real life':**
  - routine use
  - many lots (instruments)
  - many laboratories (operators)
- **Confounding factors:**
  - excessive pressure to pass
  - use of data for licensing
    - requirement to pass EQA to maintain viability
    - temptations to 'cheat'
  - *nature and behaviour of specimens*

Educational role of EQA

- **Maintaining professional standards**
  - EQA is only one aspect of performance
  - must be supported by effective QA and IQC

- **EQA is an educational stimulus to improvement**
  - by laboratories
  - by manufacturers
  - *by EQA schemes*

Laboratory performance surveillance in UK

- **Performance or participation 'failure' stimulates:**
  - intelligent scrutiny of data & history by scheme
  - ? informal contact from scheme
  - formal contact from scheme
  - referral to National QA Advisory Panel (NQAAP)
  - formal contact from NQAAP
    - must be advised to accreditation body (CPA)

  - *referral to Joint Working Group on Quality Assurance **
  - *notification of hospital's Medical Director **

** these stages never reached in 20 years*

Apparent IVD-related problems in the UK

- **Guidelines drawn up by EQA, BIVDA, MDA, NQAAP, and endorsed by JWG**
  - *with/without communication to user laboratories*
  - talk to the manufacturer
    - ? "matrix effects", ie OK with clinical specimens
    - ? product changes - advance notification helps!
    - many issues are soluble at this level
  - inform NQAAP - routinely/urgently
  - inform Medical Devices Agency (Competent Authority for the UK) - ? as adverse incident report
  - document resolution
  - refer formally to MDA if not resolved

IVD-related actions - prEN14136

- **Investigate apparent problems further**
  - look at variability as well as median performance
  - try to exclude user effects (eg incorrect protocols)
  - compare with manufacturer's claims
    - *but is this good enough?*
- **Talk to the manufacturer first**
- **May refer to Competent Authority**
  - *but is it likely that vigilance issues will be identified first through EQA?*

Target values in EQA

- **Reference method laboratory value**
  - follow EN 12286, prEN 15195 & prEN 17511
  - assign uncertainty
  - expensive and impractical?
- **Known composition**
- **Consensus**
  - cheap and convenient
  - widely used, and will continue to be
  - *NB: must not accept automatically - validate wherever possible*

Reference method laboratory targets

- **Are the materials good enough?**
  - unreliable targets are a problem
  - excellent values on 'poor' material also bad news!
    - starting material matrix, quality
    - additives, preservatives
    - processing (eg lyophilisation)

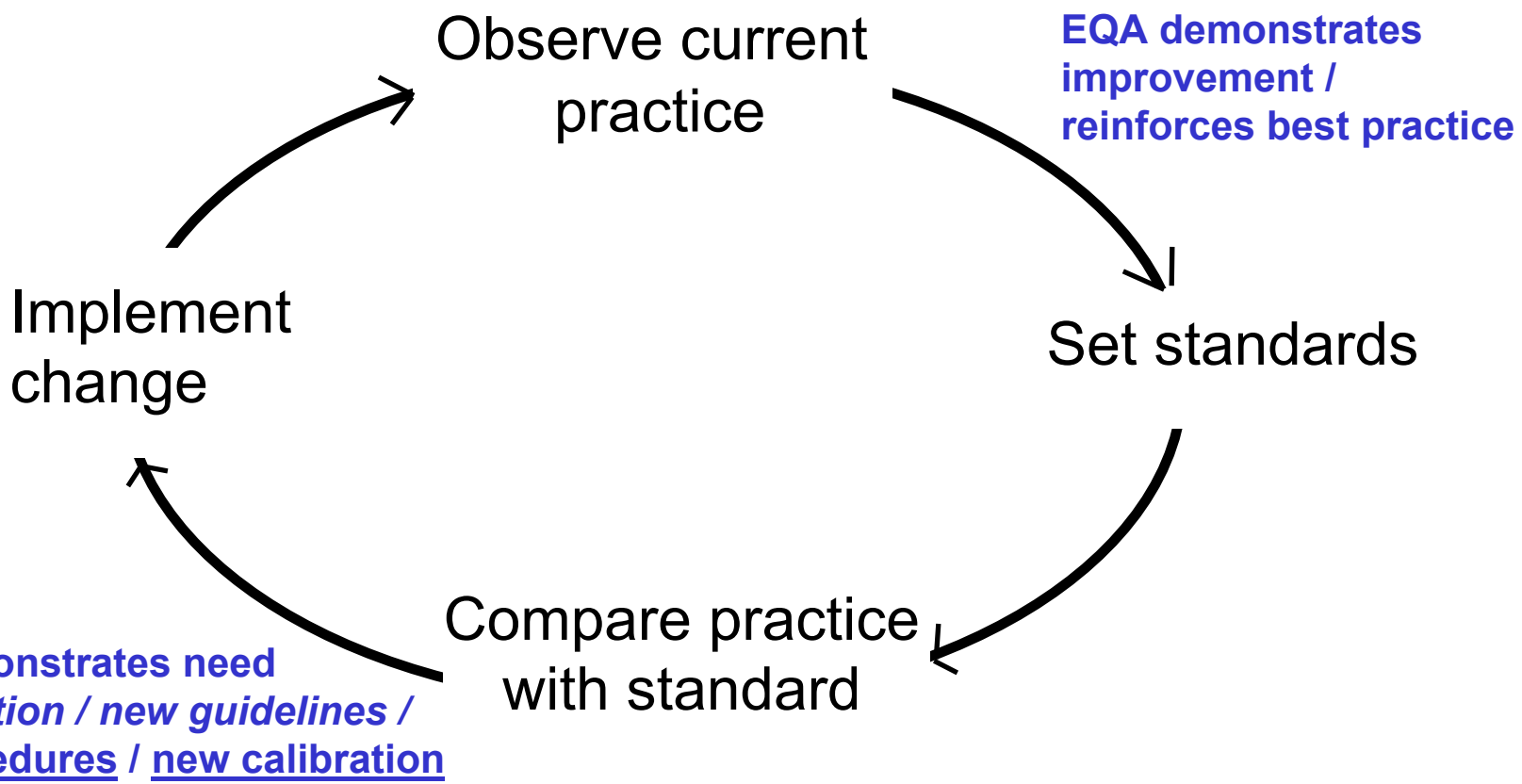
- **Can only apply reliably where there is confidence in the material's commutability & fidelity**

UK NEQAS examples

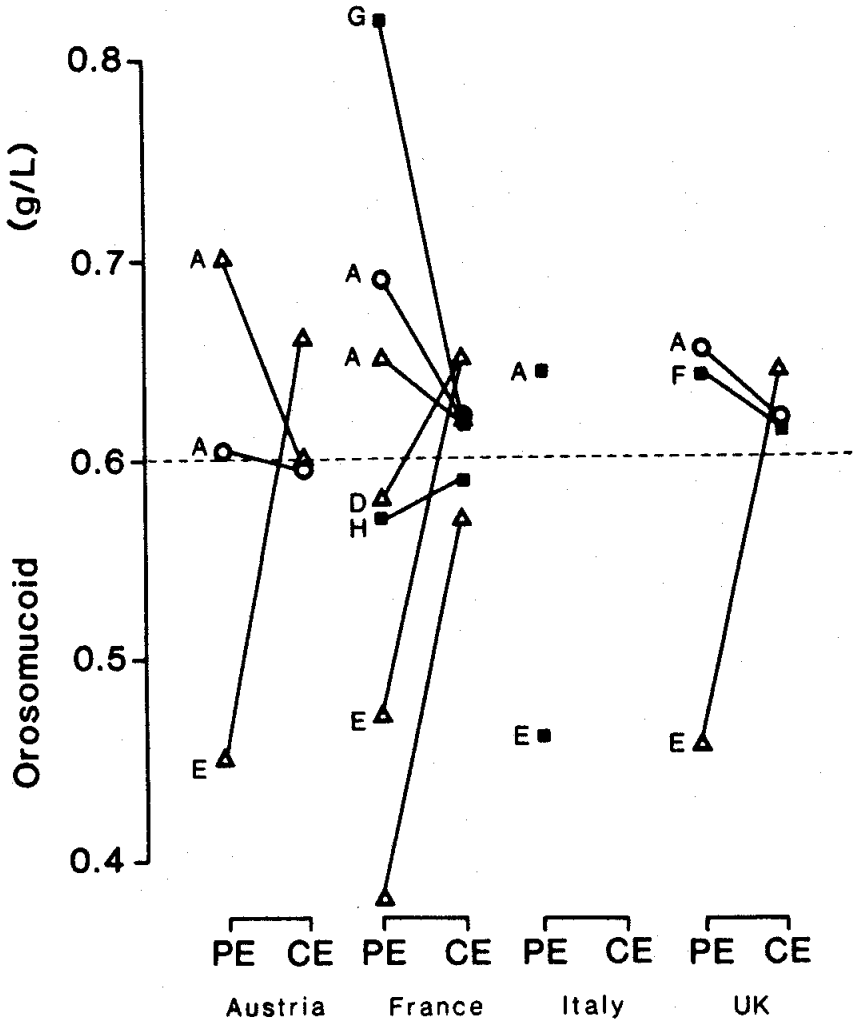
- **Glycated haemoglobin**
  - fresh whole blood from authentic diabetic volunteers
  - reference laboratory network values
  - *? basis for traceability - 'DCCT-aligned' or IFCC standardised*
- **Lipid assays**
  - fresh liquid serum without addition
  - reference laboratory network values
  - *? pool-related matrix effects still seen*
- **EU (global) IMEP-17 study**
  - frozen liquid sera without preservative (DEKS)
  - reference method laboratory targets
  - *final data awaited*

EQA as Audit -

A Quality Improvement Cycle



European survey - Orosomucoid



Symbols = method principles

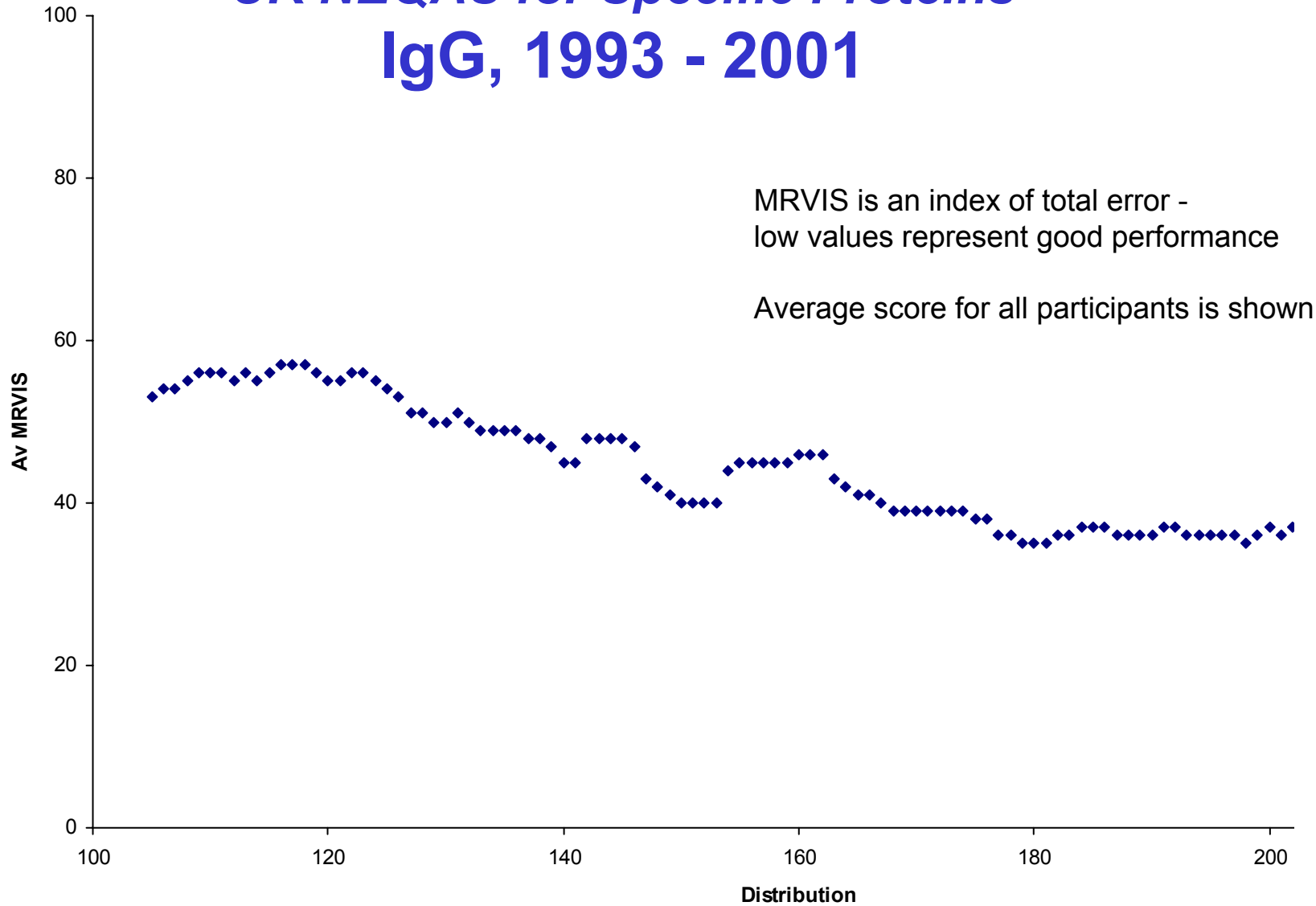
Letters = calibrants

PE = mean of results for specimen

CE = mean of results, recalculated using second specimen as calibrant

UK NEQAS for Specific Proteins

IgG, 1993 - 2001

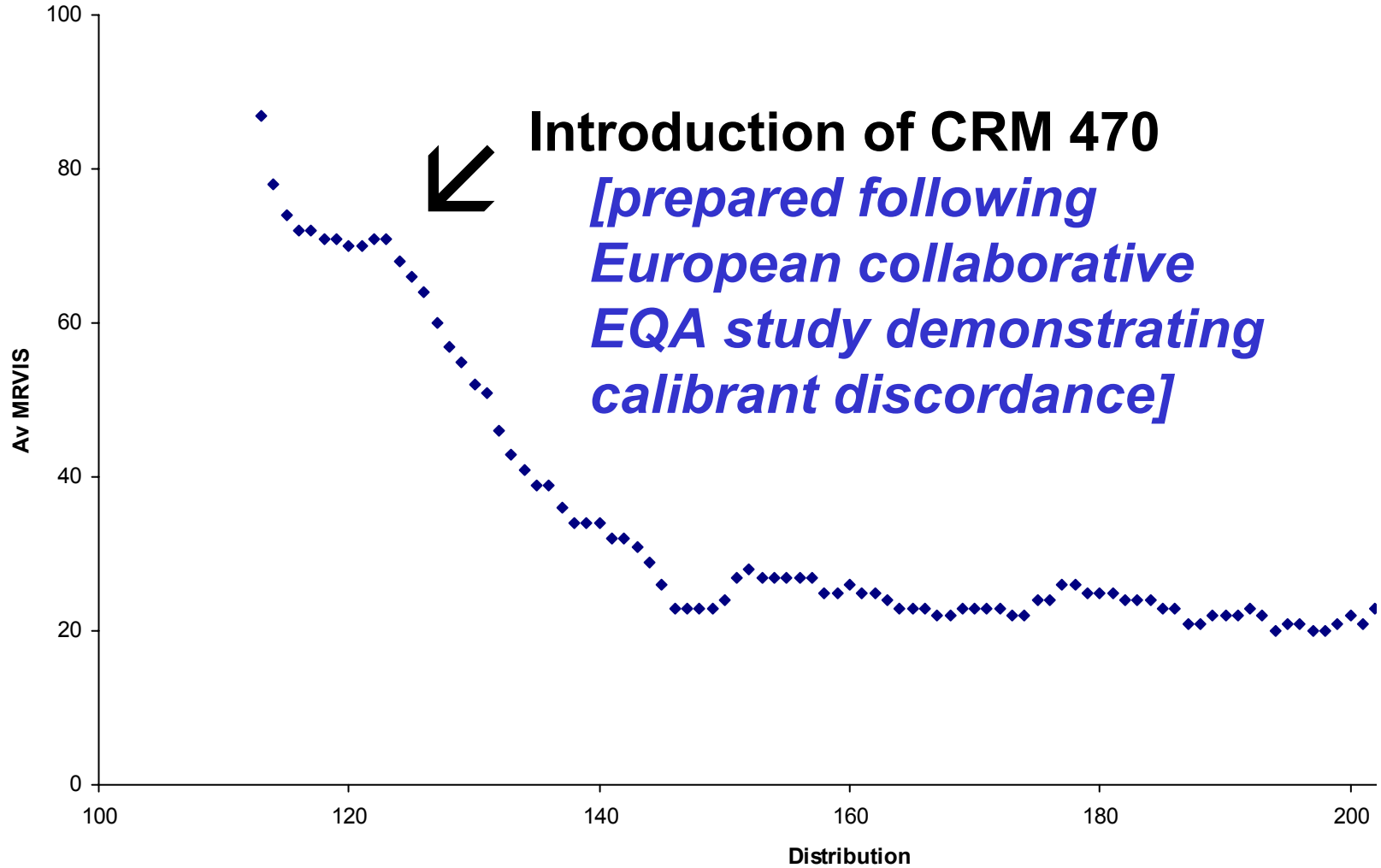


MRVIS is an index of total error -
low values represent good performance

Average score for all participants is shown

UK NEQAS for Specific Proteins

Orosomucoid, 1994 - 2001



EQA view on calibration revision

- **Global harmonisation is the aim**
  - EQA continues to encourages harmonisation
  - to attain this, calibration changes are inevitable
  - *movements should be towards the truth !*
- **Problems for EQA**
  - geographical differences (eg CEA RMs)
  - shifts in bias & diversity of bias during changes
  - please tell EQA schemes first . . .

Conclusions

- **Effective laboratory medicine is everyone's aim**
- **We must ensure an effective partnership:**
  - clinical laboratories
  - industry
  - EQA schemes
- **IVD MDD introduces more regulation, but:**
  - to be constructive, such systems rely on co-operation
  - slavish adherence to protocols will not be effective
    - post-marketing surveillance is not vigilance

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prEN ISO/DIS 15189 *Medical laboratories - Particular requirements for quality and competence.*

EN 12286 *In vitro diagnostic medical devices - Measurement of quantities in samples of biological origin - presentation of reference measurement procedures.*

prEN ISO/DIS 15195 *Clinical laboratory medicine - Requirements for reference measurement laboratories.*

prEN ISO/DIS 17511 *In vitro diagnostic medical devices - Measurement of quantities in samples of biological origin - Metrological traceability of values assigned to calibrators and control materials.*

prEN ISO/DIS 18153 *In vitro diagnostic medical devices - Measurement of quantities in samples of biological origin - Metrological traceability of assigned values for catalytic concentration of enzymes in calibrators and control materials.*

b. EQA schemes

prEN 14136 *Use of external quality assessment schemes in the assessment of the performance of in vitro diagnostic examination procedures.*

ISO/IEC Guide 43-1 *Proficiency testing by interlaboratory comparisons - Part 1: Development and operation of proficiency testing schemes.*

ISO/IEC Guide 43-2 *Proficiency testing by interlaboratory comparisons - Part 2: Selection and use of proficiency testing schemes by laboratory accreditation bodies.*

EQA scheme accreditation handbook. Sheffield, UK: Clinical Pathology Accreditation (UK) Ltd. [obtainable via www.cpa-uk.co.uk]

ILAC-G13:2000 *Guidelines for the requirements for the competence of providers of proficiency testing schemes.* [obtainable via www.ilac.org]

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