ISO/FDIS 17511 - Requirements for Traceability of Values Assigned to IVD Calibrators and Controls: A Viewpoint from US Industry

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Calibration Traceability

ISO/DIS 17511 - Major Areas of Concern to Industry

- International recognition status - reference methods and materials?
  - Is there international recognition of particular methods and materials by recognized scientific organizations?
  - Are different standards recognized in different regions of the world?
- Are available reference procedures and materials documented in compliance with ISO/FDIS 15193 & 15194?

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ISO/DIS 17511 - Major Areas of Concern to Industry

- Are available reference materials suitable for intended purpose?
  - Analyte clearly defined (e.g. troponin-I, HbA1c)?
  - Matrix (e.g. whole blood vs. serum)?
  - Suitable levels relative to patient sample range?
  - Low uncertainty of assigned values?
- Reference labs - availability and status
  - Compliance with ISO/CD 15195?
    - Is accreditation necessary?
  - Independence: Internal company labs vs. outsourcing

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ISO/DIS 17511 - Key Issues & Potential Problem Areas

Issue: Range/variety of measurands...

Of ~ 1000 measured analytes, less than 100 are well-defined chemical entities

- Many analyte mixtures (e.g. total protein)
- Analyte heterogeneity is common
  - –e.g. hormones, enzymes
  - –Post-translationally modified proteins
- Protein-bound and/or free analyte
- Variability of immunologic procedures
  - –selectivity of different antibodies for different epitopes
  - –antibody sourcing/batch changes

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ISO/DIS 17511 - Key Issues & Potential Problem Areas

Issue: Reference Systems status

- Gaps in availability of reference materials & methods
  - Several regional and international organizations (e.g. NIST, IFCC, IRMM, WHO, DS) have initiated programs to fill void, but...
  - No coordination among programs
- Few labs capable of performing reference measurements at reasonable cost in many geographic regions

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ISO/DIS 17511 - Key Issues & Potential Problem Areas

Issue: Reference Systems status (cont.)

- No recognized authority yet established to accredit reference methods, materials or labs on an international level, with periodic audits
  - What's needed?
  - Who will/should take the lead?

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ISO/DIS 17511 - Key Issues & Potential Problem Areas

Issue: Reference Systems status (cont.)

- Potential for mis-application of EQAS results by Competent Authorities or reimbursement agencies
  - EQAS providers may treat survey materials as Reference Materials ("Trueness" Controls) w/o full validation
    - ISO FDIS 15194 (Description of Reference Materials…) is NOT a normative reference for prEN 14136 (Use of EQAS in assessment of performance…)
  - Is commutability of EQAS survey material known?
    - prEN 14136 does not address this issue
  - Different approaches to setting targets and acceptable ranges among programs

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ISO/DIS 17511 - Key Issues & Potential Problem Areas

Issue: Uncertainty of Assigned Values - Information must be available (on request)

- Complexity & unknowns in calculating combined total uncertainty
  - Directly measurable/observed (type A) uncertainties
  - *A priori* uncertainties (type B)
  - Uncertainty calculation when using multipoint calibration
- Value of uncertainty information to customers/end-users in routine applications has been challenged
  - Fuentes-Arderiu, X. *Clin Chem* 2000;46:1437-1438, Uncertainty of Measurement in Clinical Laboratory Sciences

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ISO/DIS 17511 - Key Issues & Potential Problem Areas

US Industry recommendations

- Ensure end-user (customer) input on proposed changes to standardization (laboratories and attending physicians)
  - Priorities for standardization improvement projects linked to medical need & expectation of improved outcomes
- Establish and maintain formal list of Recognized Type A & Type B analytes
- Establish and maintain formal list of Recognized Reference Materials and Methods
- Develop guideline on determination/evaluation of uncertainty of assigned values in IVD calibrators

Calibration Traceability

ISO/DIS 17511 - Key Issues & Potential Problem Areas

US Industry recommendations (cont)

- Develop strategy and timeline for establishing additional independent regional Reference Measurement Laboratories for value assignment of primary and secondary standards in support of industry.
- Define minimum transition time for IVD manufacturers to complete changes/updates to IVD MD calibration if an international mandate requires change
- Establish channels for global funding of programs for traceability, to develop new reference materials and reference methods
    - Broad Government sponsorship is critical

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THANK YOU!