Procedures and barriers for the introduction of a new or improved method: the example of inhibitor testing

Dr. Albert Huisman, UMC Utrecht, Utrecht, Netherlands

- Clinical Chemist at UMC Utrecht
- Department of Clinical Chemistry and Haematology
  - 3.4 million test results/year
  - 300 employees
  - >1300 QC documents (of which the inhibitor SOP is just 1)

  - > 60 assays in coagulation (of which the inhibitor is just 1)
  - > 40 assays in (benign) hematology

The example of inhibitor testing:

Is it really important?

- From a *volume* point of view: The UMC Utrecht example (Dept. of clinical chemistry and haematology):
  - Approximately 600 inhibitor assays/year
    - Of which 10% is positive (i.e. > 0.3 BE)
    - < 0.5% of coagulation production
    - Coagulation accounts for approximately 2.5% of total lab production, so inhibitor assay: < 0.02% of total lab production (and << 0.01% when total UMC Utrecht lab production is considered).

Procedures and Barriers……

- When to introduce a new (or improved) test?
  - Guideline
  - Literature
- Laboratory Accreditation
  - ISO 9001
  - ISO 15189

Why introduce something new in the lab?

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Why introduce something new in the lab?

- When to introduce a new test?
  - Analyzer too old or outdated
    - (“breaks down when turning it on”)
  - New and/or improved method available
    - Better clinical performance
    - Better analytical performance
    - Cheaper
    - Guideline
    - Literature
    - ……. etcetera

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    - **Guideline**
    - Literature
    - ……. etcetera

Guideline

- A guideline is a statement by which to determine a course of action
- A guideline aims to streamline particular processes according to a set routine or sound practice.
- By definition, following a guideline is never mandatory.
- Guidelines are not binding and are not enforced.

Guidelines

- Professional Guidelines
  - ISTH (2010- 2014): 65 (SSC guidelines published in JTH)
  - CLSI: 10 guidelines on coagulation
  - ICSH
  - National
    - BCSH (UK): 29 guidelines on coagulation
    - DGHO (Germany)
    - ASH, CAP (USA)
    - NVKC, NVVH (Netherlands)

"I'm not here for committing a crime — I'm here for failing to comply with a guideline."

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  - CLSI: 10 guidelines on coagulation
  - ICSH
  - National
    - BCSH (UK): 29 guidelines on coagulation
      - » 1 guideline on inhibitors (Nijmegen assay) (2013)
    - DGHO (Germany)
    - ASH, CAP (USA)
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    - Guideline
    - **Literature**
    - ……. etcetera

Literature

- There are currently 68 journals on “hematology”
- In 2013 the top 10 journal had in total 329448 citations
  - Blood: 10,000 pages/year
  - JTH: 2200 pages/year
  - BJH: 2500 pages/year
  - Heamatologica 2000 pages/year
  - Haemophilia 1000 pages/year
    - All excluding: e-papers, supplements, proceedings etcetera
  - Every day approximately 400 pages in the field of hematology alone! (365 days/year)

Procedures and Barriers……

- When to introduce a new test?
  - Guideline
  - Literature
- Laboratory Accreditation
  - ISO 9001
  - **ISO 15189**

When you want to introduce or modify a new assay:

- ISO 15189 (5.5.1.2 **Verification**)
  - Buying a test or analyser "off the shelf" (without modifications: "**intended use**"):
    - Independent Verification before introduction into routine use:
      - The laboratory shall select examination procedures which have been validated for their intended use.
      - The specified requirements (performance specifications) for each examination procedure shall relate to the intended use of that examination.
      - Preferred procedures are those specified in the instructions for use of *in vitro* medical devices or those that have been published in stablished/authoritative textbooks, peer-reviewed texts or journals, or in international consensus standards or guidelines, or national or regional regulations.
      - The laboratory shall document the procedure used for the verification and record the results obtained. Staff with the appropriate authority shall review the verification results and record the review.

When you want to introduce or modify a new assay:

- ISO 15189 (5.5.1.3 **Validation**)
  - The laboratory shall validate examination procedures derived from the following sources:
    - non-standard methods;
    - laboratory designed or developed methods;
    - standard methods used outside their intended scope;
    - validated methods subsequently modified.

When you want to introduce or modify a new assay:

- ISO 15189 (5.5.1.3 **Validation**)
  - The validation shall be as extensive as is necessary and confirm, through the provision of objective evidence (in the form of performance characteristics), that the specific requirements for the intended use of the examination have been fulfilled.
  - Performance characteristics of an examination procedure should include consideration of:
    - Measurement trueness,
    - Measurement accuracy,
    - Measurement precision including measurement repeatability and measurement intermediate precision;
    - Measurement uncertainty,
    - Analytical specificity, including interfering substances,
    - Analytical sensitivity,
    - Detection limit and quantitation limit,
    - Measuring interval,
    - Diagnostic specificity and
    - Diagnostic sensitivity.

When you want to introduce or modify a new assay:

- ISO 15189 (5.5.1.3 **Validation**)
  - The laboratory shall document the procedure used for the validation and record the results obtained. Staff with the authority shall review the validation results and record the review.
  - When changes are made to a validated examination procedure, the influence of such changes shall be documented and, when appropriate, a new validation shall be carried out.

Validation of a new or modified assay:

It’s just a lot of work……

Time and other priorities

Time and other excuses

Time

- Time-consuming
  - What is essential and what is not, in terms of laboratory work and core business.
  - Core business for the clinical laboratory is the provision of (meaningful/relevant) results in an environment that involves a rapid turnover of sometimes complex assays.
  - In all laboratory settings professionals are forced to prioritize the increasing demands for patient care and associated workloads.
  - Lack of resources to implementation

Procedures and Barriers: the reason why it takes so long (Excuses)

- An inhibitor assay, is a “low number” assay (and is just one of many things)
- Time consuming and other priorities
- Guidelines
  - There are many guidlines
  - They (usually) are not mandatory
  - There is 1 (?) guideline (BCSH) on inhibitors
- Literature: enormous
- Validation according to ISO 15189: a lot of work

Procedures and Barriers:
but this is no excuse!

Improved analytical quality means improved patient care

Thank you for your attention

Dr Albert Huisman
University Medical Center Utrecht
Department of Clinical Chemistry and Haematology G.03.550
Heidelberglaan 100
3584 CX Utrecht
Netherlands