New York State Laboratory Specific Assay Validation Review and Approval

As applied to

Genetic Testing

Program authority

- 10 NYCRR 58-1.10 states that *all technical procedures employed in a laboratory shall be of proven reliability and generally accepted by leading authorities in the specialties of laboratory medicine and/or approved by the Department*.

- A laboratory:
  - shall perform only those assays that have been validated or verified at the site where the assay will be performed;
  - must hold the appropriate permit category for the test;
  - and must meet all other requirements related to personnel and proficiency testing

Assays requiring validation review

- A laboratory must acquire Department approval **prior** to offering the following types of assays:
- Commercially distributed assays labeled for Research Use Only (RUO) and those assays using Analyte Specific Reagents (ASRs).
- FDA approved assays or IUO assays that have in any way been modified from their intended use or IDE
- In-house developed methods
- A **change in intended use** is a change in the specimen type; the type of analysis (e.g., qualitative vs. quantitative); the purpose of the assay (e.g., screening, diagnosis, prognosis, monitoring, and confirmation); or the target population(s) as specified by the FDA or outlined in the package insert.

Materials Submitted for Review

- The assay name,
- Manufacturer of reagents or materials, if any other than the laboratory itself,
- If using manufactured components, commercial designation(RUO, ASR, etc.)
- Method or scientific principle
- NYS permit category inclusive of the assay (subject to program review)
- Specimen type(s)
- Target population(s)
- Purpose (diagnostic, prognostic, screening, etc)
- Qualitative or quantitative assay
- Performance evaluation method
  - Comparability to established method or by reference lab splits
  - Correlation of results to clinical status of test subject

Materials submitted for Review cont'd

- Assay description and complete standard operating procedure method including any algorithms, flowcharts and safety requirements
- Practitioner /patient information including test limitations
- Indications for ordering and interpreting the test
- Specimen collection instructions
- Principle of the assay and indication of clinical validity (known association with clinical condition of the analytical target, generally as reported in the literature) (For molecular tests, description of the gene structure)
- Equipment list
- Reagents and their sources (copies of all relevant manufacturers' package inserts)
- Controls

Materials submitted for Review cont'd

- Means of result calculation or interpretation
- Interferences and limitations
- Copy of test requistion
- For germline genetic tests, policy and documents relevant to compliance with informed consent requirements
- Sample reports, normal and abnormal, including all necessary or required disclaimers
- Pertinent references

Materials submitted for Review cont'd

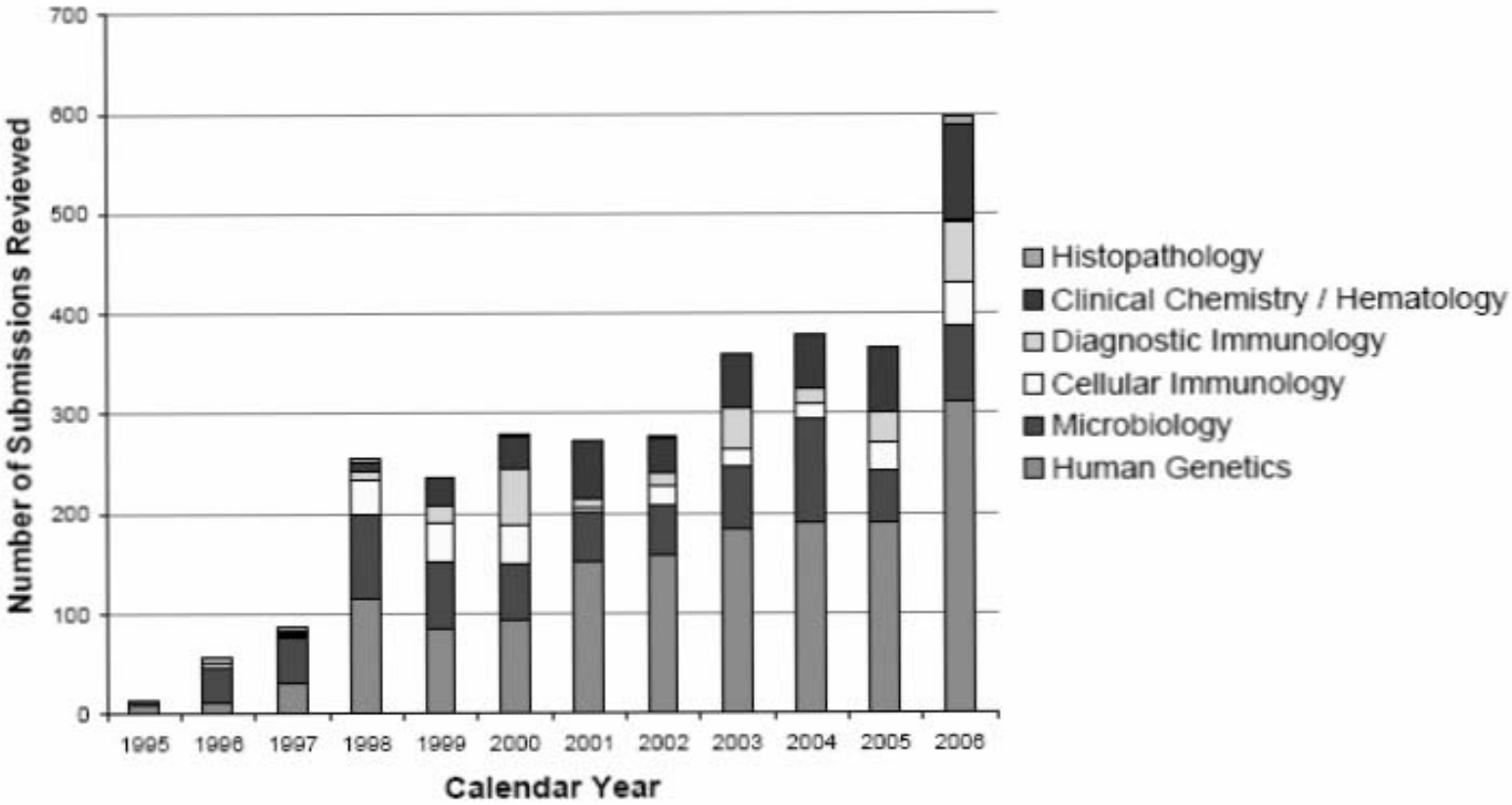
- Analytical validation
- Analyte and specimen matrix stability
- Reagent source, quality (particularly for RUO's)
- Assay performance
    - Accuracy
    - Precision/reproducibility
    - Reportable range
    - Sensitivity
    - Specificity

Materials submitted for Review cont'd

- Where performance evaluation is based on clincial outcome or test subject status
  - Protocols to establish clinical status
  - Protocols to blind specimen evaluation from prior clincical status
  - Resolution of discrepant results
  - Predictive value calculation
- Reporting
  - Interpretation
  - Reference ranges (for germline genetics, heterozygote and homozygote results)
  - Does assay predict disease state
- Assay Data for representative runs
- Quality Assurance plan and internal PT design

Clinical Laboratory Reference System

Test Approval Workload



Genetic Testing Workload 2006

Genetic testing-DNA based	86
Genetic Testing-biochemistry	5
Cytogenetics (FISH)	44
Paternity/Identity	3
Forensic Identity	81
Oncology-molecular markers	92

Impact of NYS Validation Review Program

- Cytogenetics Laboratories impacted 70
  - Includes 5 labs performing preimplantation genetic diagnosis
  - Genetic Testing Laboratories
- Biochemistry 32
- Molecular 71
  - includes 4 labs performing preimplantation genetic diagnosis

Impact of NYS Validation Review Program

- As all major reference laboratories solicit and receive specimens from New York and are therefore subject to New York clinical laboratory permit requirements, including approval of in house developed assays, **it is estimated that as much as 75% of all cytogenetic and genetic testing performed in the US is subject to NYS oversight**
  - Tort law (medical mal practice) cases have not looked favorably on laboratories subject to NYS standards applying less stringent standards to testing of specimens from other jurisdictions.

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