An Application of the Kipling Method to DNA Validation in the 21st Century

From Validation to SOP

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Outline

- Development of Technical SOPs
- Development of Interpretation SOPs
- Implementation of New SOPs

From Validation → Generation of New SOP

- Procedural or Technical SOPs –
  - what to do procedurally (how much to use, what reagents to use, buttons to push, what temperature, etc.)
- Interpretation SOPs –
  - What to do with the data generated
    - How analyze
    - How to make comparisons
    - How to generate statistical estimates
    - How report accurately
  - This has become much more complicated!

From Validation → Generation of New SOP

MOST CRITICAL ASPECT to focus on:

- What are the limitations of the system?
- Where are there failures?
- What can be done to improve or correct?
- What is the actual capacity & capability of the system being validated?

Technical SOPs

- Generally this is the easiest part since the procedural steps are often provided by the developer or supplier
  - Often can "cut and paste" into the technical or procedural SOP
  - But must evaluate the validation data to make adjustments
- Did the kits, instruments, etc. perform as expected from developmental validation studies using the technical procedures provided by the developer or supplier?

Technical SOPs

- Critical to evaluate all parameters tested during the validation
  - What are the ranges of the assay where "good" data are generated?
  - What are the "edges" of the system?
  - Is more testing needed to define "the edges?"
  - What are the limitations of the assay?
- May have to modify the provided procedures
- Important to define the testing parameters ranges that MUST be followed

Interpretation SOPs

- This is an area needing MUCH attention at this time
- Important to recognize that interpretation guidelines and SOPs MUST come from the data generated in the validation studies
  - Some guidance from published data and recommendations (e.g., ISFG, SWGDAM)

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Interpretation SOPs

- Do the validation study samples tested reflect all of the types of samples accepted and tested in the laboratory?
- Do the interpretation SOPs cover all types of samples accepted and tested in the laboratory?
- Can't make interpretation procedures regarding low template samples or complex mixtures without having validation data to evaluate
  - and needed for training!

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Interpretation SOPs

- Important to determine:
  - What are the limitations of the assay?
    - Under what conditions…
      - Are correct full results obtained?
      - Are the data reproducible in your laboratory and by another lab?
      - Can the results lead to possible misinterpretations due to partial profiles or additional data?
  - Where and what cautions are needed
  - When do the results become uninterpretable or inconclusive?

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Validation of the Interpretation SOPs

It is important to demonstrate that the interpretation SOPs:

- Generate correct and accurate conclusions
- Are detailed enough to provide consistency within the laboratory
  - Do all analysts report the same alleles and genotypes from the same data?
    - How are decisions made regarding artifacts? Thresholds? What flexibility exists?
  - Do all analysts get the same conclusions from the same data?

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Validation of Interpretation SOPs

- If inconsistency within the laboratory:
  - SOPs not detailed or clear enough
  - SOPs do not cover all needed parameters or scenarios adequately
  - Have possibly identified types of samples that should not be interpreted in your laboratory

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Validation of the Interpretation SOPs

Should be evaluated using **known** samples and profiles so expected results are available for analysis and comparison

- With known contributors (know genotypes for all contributors)
  - Have all of the data? missing data?
  - Have "extra" data? (artifacts being called; drop in)
- With known ratios of contributors
- Which are different from the samples used in the validation studies to generate the interpretation SOPs

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Sources of Known Samples and Profiles for Evaluation

- Samples generated in the lab
- Proficiency test samples
- NIST SRMs, NIST mixtures (MIX 05, MIX 13)
- Samples from other laboratory's validations
- Boston University profiles (http://www.bu.edu/dnamixtures)
- NOT CASEWORK SAMPLES
  - With possible exception of 2 person mixtures in non-sperm/epithelial fraction of sexual assault samples where non-sperm donor profile is known and sperm fraction profile is single source

Implementation of New SOPs

- New QA/QC measures
  - Incorporate into proficiency test cycle
  - Critical reagents or instruments
  - Periodic monitoring/assessment
- Training of Analysts
  - May be short or long depending on what is being introduced
  - Competency test
- Assessment for QAS and accreditation at next external audit/inspection

Implementation of New SOPs

- Additional training/notification of availability
  - Law enforcement
  - Attorneys – prosecution and defense
  - Judges
- Discovery
  - New SOPs (some laboratories post on internet)
  - Validation studies supporting the new SOPs
    - Summaries, tables/graphs of results, actual data
  - List of publications supporting the new assay
  - Training files

Implementation of New SOPs

- Consider if changes are needed to case acceptance policies
  - Are these new procedures suited to all types of samples currently accepted?
  - Need to decrease acceptance of any types?
  - Can you expand the types of samples accepted?
- Consider impact on previous cases
  - Can additional studies now be done?
  - Do the new studies invalidate anything done previously?

Implementation of New System

- Plan and prepare for possible admissibility hearing
  - Publications
  - SOPs
  - Validation studies
- May need guidance from experienced attorneys and scientists
  - Very different from routine trial testimony

Thank You!

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