Organization: Siemens Healthcare Diagnostics

JCTLM Member status: Stakeholder

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Period covered: 2015 – 2017

1. **Major achievement(s) in support of standardization in laboratory medicine**

   Two commercial product improvement projects were completed for minimizing uncertainty of assay results. First, uncertainty was minimized for HbA1c through implementation of a more robust value assignment procedure that leverages the NGSP reference method and IFCC Standards. Siemens maintains certification for Hemoglobin A1C on multiple platform families: the Dimension and Vista Instrument Family, the ADVIA Instrument Family, the Atellica CH Analyzer, and the DCA Vantage. Second, High Density Lipoprotein Cholesterol reagent lot to lot variability was minimized after the implementation of reagent lot-specific scalers referenced to the Abell-Kendall Reference Method.

   New product launches include the Vitamin D Assay with established traceability to the ID-LC/MS/MS reference method service provided by Ghent University and the Testosterone Assay with established traceability to the ID-LC/MS/MS reference method service provided by the CDC. Siemens has been CDC certified for VitD for the last four years.

   In 2016, Siemens Healthcare released the ADVIA Chemistry Enzyme Calibrators to support the enzymatic assays on the ADVIA Chemistry Systems. Previously, the IFCC traceable enzymatic assays were calibrating through use of a fixed factor coefficient that was traceable to the IFCC Primary reference method, however the fixed factor coefficient would not meet customer traceability requirements. With the release of the enzyme calibrators, Siemens was able to minimize system to system variability, as well as provide a calibrator material required for customers to meet RiliBÄK and EU requirements on traceability.

   Siemens Analytical Services developed UPLC-MS/MS methods for Vitamin D and Tacrolimus. Both methods are validated and were used to standardize those assays on the Centaur systems.

   Traceability and uncertainty information was provided for all assays as part of the recent Atellica™ Solution chemistry and immunochemistry analyzers release.

   In 2015, Siemens launched a new strategy for control system design for new products; this strategy covers all product lines and harmonizes processes across them. The strategy includes statistically determined test protocols and value assignment ranges based on variance components for all control system components. In addition the use of medical decision pools are required for all new assays to minimize lot to lot bias. Medical decision pools are human serum-based materials targeted at medical decision levels that have been demonstrated to behave similar to patient samples. Assay standardization and traceability procedures have been adopted that align to ISO 17025. In the case where international/national standards are not available or not accepted by the scientific community, internal reference standards and/or methods are generated based on defined robust criteria.

2. **Planned activity(ies) in support of standardization in laboratory medicine**

   Collaboration with the JCTLM as a Stakeholder Member.

   Member of Strategic Partners Group in the International Consortium for Harmonization of Clinical Laboratory Results (ICHCLR).

Siemens Analytical Services is working on the development and validation of UPLC-MS/MS method for Everolimus

Participation in multiple IFCC Scientific Division committees and working groups for standardization of specific measurands (e..g, TSH, FT4, albumin in urine, PAPP-A, TNI, PTH, etc.) as well as overall standardization practices (e.g., C-TLM, WG-C)

Participation in the ISO TC212 Working Group 2 concerned with traceability, uncertainty calculations, and harmonization.

Standardization update to Cystatin C Method for ADVIA Chemistry to align with IFCC Standardization.

Based on the success of our approach to control systems for new products, we have engaged in a project to convert the control systems of a significant number our legacy products that would benefit most from the upgrade.

3. **Promoting traceability in laboratory medicine**
Siemens provides customers with clear and unambiguous traceability statements and uncertainty values for all Immunoassay and Clinical Chemistry tests.

Siemens attended the annual SEQC meeting, presenting information on maintaining standardization from the perspective of an in-vitro diagnostics company.

Siemens attended the Endocrine Society's 97th Annual Meeting and Expo and presented THR-235: The Value of a Standardized and Certified Vitamin D Total Assay for Clinical Confidence

- http://press.endocrine.org/doi/abs/10.1210/endo-meetings.2015.BCHVD.13.THR-235

Evaluation of the new Siemens ADVIA Centaur Testosterone II Assay was published in Pathology

- http://www.pathologyjournal.rcpa.edu.au/article/S0031-3025(16)40920-7/pdf

4. **Reference laboratory networks /collaborations focusing on developing /implementing reference measurement systems**

Collaboration on harmonization of FT4 and TSH IFCC Committee of Standardization.

- Standardization of Free Thyroxine Measurements Allows the Adoption of a More Uniform Reference Interval FT4 Clin. Chem. 63:10, 1642-1652, 2017
- Harmonization of Serum Thyroid-Stimulating Hormone Measurements Paves the Way for the Adoption of a More Uniform Reference Interval Clin. Chem 63:7, 1248-1260, 2017

5. **Open questions and suggestions to be addressed by JCTLM**
Would like to see JCTLM consider

- Guidance to manufacturers for how to approach conversion to use of new versions or lots of international standards when they become available. Cases such as switching from recombinant to native, for example.
- Guidance to manufacturers who experience drift and want to re-standardize.
- Guidance to manufacturers for standardization maintenance programs.
- How can IVD best support JCTLM in efforts to lobby FDA and other such regulatory bodies to accept re-standardization efforts?