Development of SI-traceable certified reference materials for clinical applications by KRISS

Ji-Seon Jeong, Ha-Jeong Kwon, and Ji-Youn Lee

Center for Bioanalysis, Division of Chemical and Medical Metrology, Korea Research Institute of Standards and Science (KRISS)

Metrological traceability in Laboratory medicine (LM)

As a national metrology institute in Korea, KRISS has provided the foundation for the national standards and international equivalencies through the development of RM and participation into international key comparisons based on the CIPM-MRA.

CRM by KRISS for LM and its applications

Numerous CRMs for clinical applications have developed and disseminated to establish metrological traceability based on clinical matrices such as serum, plasma, hemolysate. Target compounds were aligned to target disease and applications in related fields. CRMs have been applied to accuracy-based proficiency testing, and to product quality assessment in IVD devices development.

The "Korean Health Index" for blood glucose and cholesterol were established by National Standard Reference Data based on KRISS CRMs.

Current available CRM/RM list for clinical applications produced by KRISS

<table>
<thead>
<tr>
<th>CRM No.</th>
<th>Name</th>
<th>JCTLM DB</th>
</tr>
</thead>
<tbody>
<tr>
<td>111-01-007</td>
<td>Human Serum for Glucose (3 Levels)</td>
<td>-</td>
</tr>
<tr>
<td>111-01-010</td>
<td>Human Serum for Lipids (2 Levels)</td>
<td>Under review</td>
</tr>
<tr>
<td>111-01-019</td>
<td>Human Plasma for Amino Acid Analysis (2 Levels)</td>
<td>Under review</td>
</tr>
<tr>
<td>111-01-005</td>
<td>Human Serum for Creatinine (2 Levels)</td>
<td>Under review</td>
</tr>
<tr>
<td>111-01-012</td>
<td>Glycated hemoglobin (2 Levels)*</td>
<td>(new batch coming in 2021)</td>
</tr>
</tbody>
</table>

Comparison with CBC analyzer and AHD method - MS/MS in human plasma.

Comparison with traditional primary method of protein (ID diluted and purified).

Various amino acids and acylcarnitines were established and to product quality of standards.

CRM for Total Hemoglobin (KRISS CRM 111-01-021)

Another hemolysate CRM for total hemoglobin quantification were produced with 3 different concentrations using purified hemolysate. Concentrated erythrocytes were diluted and purified. Instead of traditional primary method of protein (ID-MS) or reference method (HICN), AHD* method was adopted as certification method, and the certified value will be SI-traceable via purity assessed hemin chloride.

Dried Blood Spot CRM for Metabolites (KRISS CRM 111-01-022)

A new type of matrix, dried blood spot will be released for newborn screening.

CRM for Monosaccharides (KRISS CRM 111-01-019)

Five amino acids as markers for inherited metabolic diseases (Phenylketonuria (PKU), and Maple Syrup Urine Disease (MSUD)) were certified with two different concentrations using isotope-dilution HPLC-MS/MS in human plasma. Five amino acids; phenylalanine, tyrosine, valine, isoleucine, and leucine were certified, and results of 19 amino acids by conventional AAA method were produced as additional information.

Human Plasma For Amino Acid Analysis (KRISS CRM 111-01-019)

Five amino acids as markers for inherited metabolic diseases (Phenylketonuria (PKU), and Maple Syrup Urine Disease (MSUD)) were certified with two different concentrations using isotope-dilution HPLC-MS/MS in human plasma. Five amino acids; phenylalanine, tyrosine, valine, isoleucine, and leucine were certified, and results of 19 amino acids by conventional AAA method were produced as additional information.

Human Serum For Glucose Analysis

Four monosaccharides; glucose, galactose, mannose, and fructose, will be certified with two different concentrations for diagnosis diabetes mellitus, and galactosemia.

Certification method was fully validated with a wide range of concentrations; 1 – 3000 mg/dL.

Purity assessment for pure material should be progressed for SI-traceability.

Method validation with CRM for glucose in serum by two methods (A)Typical TIC using HUIC separation and OTOF MS in APCI negative mode (B)Optimized HPAEC-PAD method

Comparison with DEE analysis and AHD method using high CRM precision.

Human Serum For Monosaccharide Analysis

Four monosaccharides: glucose, galactose, mannose, and fructose, will be certified with two different concentrations for diagnosis diabetes mellitus, and galactosemia.

For certification HPAEC-PAD* method was adopted for clear separation and sensitivity.

Human Plasma For Amino Acid Analysis

Comparison with traditional primary method of protein (ID diluted and purified).

Various amino acids and acylcarnitines were established and to product quality of standards.

CRM for Total Hemoglobin (KRISS CRM 111-01-021)

Another hemolysate CRM for total hemoglobin quantification were produced with 3 different concentrations using purified hemolysate. Concentrated erythrocytes were diluted and purified. Instead of traditional primary method of protein (ID-MS) or reference method (HICN), AHD* method was adopted as certification method, and the certified value will be SI-traceable via purity assessed hemin chloride.

Dried Blood Spot CRM for Metabolites (KRISS CRM 111-01-022)

A new type of matrix, dried blood spot will be released for newborn screening.

Various amino acids and acylcarnitines, and monosaccharides will be certified stepwise from start with amino acid in 2020.

For SI-traceability, whole spot (50 μL) is used and the result by punch sampling will be given as additional information.

CRM For Total Hemoglobin (KRISS CRM 111-01-021)

Another hemolysate CRM for total hemoglobin quantification were produced with 3 different concentrations using purified hemolysate. Concentrated erythrocytes were diluted and purified. Instead of traditional primary method of protein (ID-MS) or reference method (HICN), AHD* method was adopted as certification method, and the certified value will be SI-traceable via purity assessed hemin chloride.

Dried Blood Spot CRM for Metabolites (KRISS CRM 111-01-022)

A new type of matrix, dried blood spot will be released for newborn screening.

Various amino acids and acylcarnitines, and monosaccharides will be certified stepwise from start with amino acid in 2020.

For SI-traceability, whole spot (50 μL) is used and the result by punch sampling will be given as additional information.

Dried Blood Spot CRM for Metabolites (KRISS CRM 111-01-022)

A new type of matrix, dried blood spot will be released for newborn screening.

Various amino acids and acylcarnitines, and monosaccharides will be certified stepwise from start with amino acid in 2020.

For SI-traceability, whole spot (50 μL) is used and the result by punch sampling will be given as additional information.

Dried Blood Spot CRM for Metabolites (KRISS CRM 111-01-022)

A new type of matrix, dried blood spot will be released for newborn screening.

Various amino acids and acylcarnitines, and monosaccharides will be certified stepwise from start with amino acid in 2020.

For SI-traceability, whole spot (50 μL) is used and the result by punch sampling will be given as additional information.