The biennial activity report (2020-2021) from the Joint Research Centre (JRC)

All JCTLM Members are invited to attend the Members' and Stakeholders’ Meeting, which is held once every two years, and submit a report of their activities in support of traceability in laboratory medicine over the preceding period.

For that purpose this template document provides guidance to JCTLM Members for drafting their biennial activity report. Organizations are invited to provide the information below for submission to the Executive Committee.

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<th>Organization Name: Joint Research Centre, JRC, European Commission</th>
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<td>JCTLM Member status: National and Regional Member</td>
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<td>Period covered: 2020 – 2021</td>
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1. Major achievement(s) in support of standardization in laboratory medicine

   a. Proteins in cerebrospinal fluid (CSF)

   To support measurement standardisation of biomarkers for the early detection of Alzheimer's disease, the JRC released a panel of three pooled CSF materials with different levels of amyloid-β 1-42 (Aβ1-42): ERM-DA480/IFCC, ERM-DA481/IFCC and ERM-DA482/IFCC. This project was done in close collaboration with the working group of the International Federation of Clinical Chemistry on CSF proteins (IFCC WG-CSF). An article on the release of the CRMs was published:


   After the release of the CRMs several commercial immunoassays were re-calibrated and a round-robin study was organized to see the effect of re-calibration on the measurements of patient samples. The results of this study showed that the agreement between the methods after recalibration is acceptable. The results of this study were presented by the IFCC WG-CSF at the Alzheimer Association International Conference (AAIC) 2021.

   b. Autoimmune disorders

   The JRC has developed a candidate RM for immunoglobulin G antibodies against β2-glycoprotein I (anti-β2GPI IgG) in human serum. The commutability of this RM has been assessed with several commercial enzyme-linked immunosorbent assays (ELISA) purchased from in vitro diagnostic manufacturers. The RM has been found to be commutable for most of the assays tested and the results have been published in:

This material is intended to become the international standard (with arbitrary values in IU/ml) approved by the WHO. For this project, the JRC collaborates with NIBSC. The preliminary application to start the project has been approved by the WHO in October 2020 and the full application and documentation will be submitted in 2022.

c. COVID-19

The JRC has produced and released two RM for antibodies against SARS-CoV-2 in human serum (EURM-017, EURM-018) in December 2020. These RM are initially intended to be used as quality control materials immunoassays measuring IgG or total antibodies and virus neutralisation assays. Additional studies to investigate the possibility to certify the concentration of IgG against the different viral antigens present in the commercial immunoassays are currently ongoing.

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

In the upcoming years, the JRC will continue the development of CRMs for biomarkers in various clinical fields:

a. Proteins in CSF

The existing CRMs ERM-DA480/IFCC, ERM-DA481/IFCC and ERM-DA482/IFCC may also be certified for their concentration of amyloid-β 1-40 (Aβ 1-40). In case those CRM are not suitable for the certification of Aβ 1-40 a new CRM will be developed.

The JRC will also support the development of an RMP for Tau in CSF which is done within the IFCC WG on CSF proteins. When the RMP is available the JRC intends to produce a CRM for tau in CSF.

The possibility to develop a CRM for Neurofilament light chain (NF-L) is also under investigation. NF-L is a component of the neuronal cytoskeleton and it is increasingly recognized as promising biomarker in the clinical evaluation of neurological patients.

b. Autoimmune disorders

The production of a CRM for IgG and IgA antibodies targeting tissue transglutaminase (anti-tTG IgG and IgA) in human serum is ongoing. An initial commutability study was performed to select the most suitable starting material. The candidate RM was produced in a large batch that will be checked for homogeneity and stability in 2022. The material will be certified for the concentration of anti-tTG IgG and IgA using a calibrator solutions consisting of highly purified anti-tTG IgG and IgA.

The production of a CRM for IgG autoantibodies targeting glomerular basement membrane (anti-GBM) has started. An initial commutability study was performed and the most suitable starting material has been selected.

c. Apolipoproteins

The JRC supports the development of a reference measurement system (RMS) for a panel of clinically relevant serum apolipoproteins (apo) A-I, B, C-I, C-II, C-III, E and apo (a) which is done within the IFCC working group on Apolipoproteins by Mass Spectrometry. The RMS will be based on peptide-calibrated, LC-MS/MS reference measurement procedure (RMP) and commutable serum-based RM. The candidate RMP has been developed and a correlation and initial commutability study has been performed. The candidate RMP correlates well with the immunoassay-based measurement procedures with results in nmol/L. Only RMs based on unspiked human serum pools have the potential to be good candidates for a future CRM.

d. HbA2

The JRC has started with the development of two CRMs for haemoglobin A2 (low and high level) in collaboration with the members of the IFCC working group on standardisation of haemoglobin A2 (WG-
HbA2). For each CRM a large batch has been processed and these batches will be tested for homogeneity and stability in 2022. The materials will be certified using a MS-based RMP calibrated with recombinant hemoglobins.

3. Promoting traceability in laboratory medicine

In addition to the publications mentioned above, staff members of the JRC also contribute to the following published manuscripts:


Staff members of the JRC also gave presentations at various congresses or workshops including:


“Commutability: Challenges in the Harmonisation/Standardisation of Assays for Autoimmune Disorders” presented by E. Monogioudi at EMN TraceLabMed & TC-MC Open Workshop on Measurement Challenges – laboratory medicine (08.11.2021)

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

a. Collaborations with IFCC

A staff member of the JRC is an observer in the Executive Committee of the Scientific Division of the IFCC. Several staff members of the JRC are members or consultants in the following IFCC working groups:

- CSF-Proteins (WG-CSF)
- Apolipoproteins by Mass Spectrometry (WG-APO MS)
- Fecal Immunochemical Testing (WG-FIT)

In addition, the JRC supports the IFCC Scientific Division Committee on Harmonization of Autoimmune Tests (C-HAT), the working group on Standardisation of Haemoglobin A2 (WG-HbA2) and the working group on Pancreatic Enzymes (WG-PE) by the production of CRMs as mention before.

b. Collaboration Euramet’s European metrology networks (EMN)

The JRC intends to join the EMN for Traceability in Laboratory Medicine.

5. Open questions and suggestions to be addressed by JCTLM

(Suggestions on issues related to standardization and metrological traceability that should be considered by the JCTLM)