

# Update on Reference Materials for Apolipoproteins

## Background

The Clinical Standardization Programs at the Centers for Disease Control and Prevention (CDC) is the custodian laboratory for WHO Biological Reference Materials for Apolipoprotein A-1 (Code: SP1-01), Apolipoprotein B (Code: SP3-08), and Lipoprotein (a) (Code: IFCC SRM 2B). As part of this function, it holds and distributes these materials.

## Current WHO Reference Materials

The current WHO/IFCC International Reference Material for Lipoprotein (a) [Lp(a)] (SRM-2B) was generated in 2003. Several measurement procedures for Lp(a) are traceable to this material, which was previously value assigned through an ELISA-based KIV<sub>2</sub> independent method (Tate JR, et al. *Clin Chem Lab Med.*, 1999).

**Note:** The CDC contact information provided on the WHO website is incorrect. Requests for these materials should be addressed, together with a brief summary about the intended use, to:

Centers for Disease Control and Prevention  
Clinical Standardization Programs  
4770 Buford Hwy NE MS S110-2  
Atlanta, GA 30341  
USA  
Phone: 001-770-488-3360  
Email: [standardization@cdc.gov](mailto:standardization@cdc.gov)

In addition to providing IFCC SRM-2B, CDC-Clinical Standardization Programs (CSP) will request measurement of additional serum materials by the recipient and report of measurement results to CDC-CSP. The information will be used to document that the IFCC SRM-2B material was used as intended.

***The IFCC SRM-2B material is almost depleted. Also, the ELISA-based KIV<sub>2</sub> independent method is no longer available. It is anticipated that SP1-01 and SP3-08 are depleted soon as well.***

## New JRC-IFCC/LNE Reference Materials

The IFCC Working Group for Apolipoproteins by Mass Spectrometry (IFCC WG APO-MS), led by Dr. Christa Cobbaert, is developing an LC-MS/MS-based reference measurement procedure for apolipoproteins, as well as primary and secondary reference materials for apolipoproteins including Lp(a) (<https://www.ifcc.org/ifcc-scientific-division/sd-working-groups/wg-apo-ms/>). The LC-MS/MS-based reference measurement procedure will be used to assign reference values to serum-based reference materials which will be characterized for commutability.

***A reference measurement procedure and primary and secondary reference materials for Lp(a) are planned to be available in respectively 2022 and 2023.***

The new serum-based reference materials will be made available by the European Commission's Joint Research Centre (EC-JRC) (<https://crm.jrc.ec.europa.eu/>). The new primary reference materials for calibration of the LC-MS/MS reference measurement procedure in IFCC-endorsed calibration labs will be available at Laboratoire National de Métrologie et d'Essais (LNE) ([metrology@lne.fr](mailto:metrology@lne.fr)).

## Interim Solutions

- CDC is assisting manufacturers ensuring continuation of traceability of existing methodologies to the current reference system as long as material is available as outlined by WHO (<https://www.who.int/activities/providing-international-biological-reference-preparations>) and described further above.
- CDC is helping manufacturers and laboratories preparing for the transition to the new IFCC reference system by making available individual donor and pooled serum materials with Lp(a) values assigned by the IFCC's LC-MS/MS method (molar units, not KIV<sub>2</sub>-dependent). Although this method is not approved as a reference method yet, data obtained with these materials can provide information about the agreement of a laboratory method with the LC-MS/MS method.
- LNE will make available trueness verifiers and EQA materials with values traceable to the IFCC-developed reference system (<https://www.lne.fr/en/metrology-measurement/certified-reference-materials-clinically-relevant-biomarkers>).
- CDC-CSP will setup a formal standardization program using measurements traceable to the IFCC WG APO-MS. In preparation of this activity, CDC-CSP will be conducting an **Inter-Laboratory Comparison Study for Lp(a)** with routine clinical laboratories as participants.

For participation in the study or information on materials, please send an e-mail to [Standardization@cdc.gov](mailto:Standardization@cdc.gov)

## Information on availability of other lipoprotein materials

### Materials available from CDC's Clinical Standardization Programs:

#### Individual Donor Serum

Individual donor sera prepared according to the newest version of CLSI C37 (Danilenko U, et al. *Clin Chem Lab Med.* 2020) with Lp(a) values (nmol/L) assigned by the IFCC WG APO-MS LC-MS/MS method, and with KIV<sub>2</sub> size information.

#### Pooled Sera

Pools of donor sera prepped according to the newest version of CLSI C37 (Danilenko U, et al. *Clin Chem Lab Med.* 2020) with Lp(a) values (nmol/L) assigned by the IFCC WG APO-MS LC-MS/MS method, and with KIV<sub>2</sub> size information.

For participation in the study or information on materials, please send an e-mail to [Standardization@cdc.gov](mailto:Standardization@cdc.gov)

### Materials available from LNE:

#### Study Sera

Serum materials with values assigned with LC/MS/MS, Immunonephelometry reference method for ApoB, ES-DMA, NMR, VAP, TGE, GGE and, in the future, values assigned by the IFCC WG APO-MS LC-MS/MS method (for further information see: Delatour V et al. *Clin Chem.* 2018;64(10):1485-1495). For these materials, values for ApoA-I, A-II, A-IV, B, C-I, C-II, C-III, E, the size and particle number concentration of different lipoprotein classes and sub-classes, the lipoprotein number concentration profile and the cholesterol distribution profile are available.

#### Pooled Sera

LNE RM LIPO 201a, 202a and 203a are pools of human frozen serum prepared according to CLSI C37.

#### Individual Donor Sera :

LNE RM LIPO CS 001 to 025 is a set of 25 single donations prepared according to CLSI C37.

For information about these materials contact:

Laboratoire National de Métrologie et d'Essais

1 rue Gaston Boissier 75724 Paris Cedex 15

France

Phone : +33 (0) 140 434 075 and email [info@lne.fr](mailto:info@lne.fr)