JOINT RESEARCH CENTRE
Directorate F – Health, Consumers and Reference Materials

CERTIFICATE OF ANALYSIS

ERM®-DA481/IFCC

HUMAN CEREBROSPINAL FLUID		
Mass concentration		
	Certified value [2] [µg/L]	Uncertainty [3] [µg/L]
Amyloid β_{1-42} peptide[1]	0.72	0.11

[1] As obtained by solid phase extraction and subsequent quantification by liquid chromatography with mass spectrometry detection, according to the reference methods (Leinenbach *et al.* Clin. Chem. 60 (2014) 987-94; Korecka *et al.* J. Alzheimers Dis. 41 (2014) 441-451).

[2] Certified values are values that fulfil the highest standards of accuracy and represent the unweighted mean value of the means of 5 accepted sets of data, each set being obtained in a different laboratory. The certified value and its uncertainty are traceable to the International System of Units (SI).

[3] The uncertainty of the certified value is the expanded uncertainty with a coverage factor k = 2 corresponding to a level of confidence of about 95 % estimated in accordance with ISO/IEC Guide 98-3, Guide to the Expression of Uncertainty in Measurement (GUM:1995), ISO, 2008.

This certificate is valid for one year after purchase.

Sales date:

The minimum amount of sample to be used is 15 µL.

Geel, November 2017

Signed:

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DESCRIPTION OF THE MATERIAL

ERM-DA481/IFCC is part of a series of three cerebrospinal fluid (CSF) certified reference materials (CRMs) containing different levels of the amyloid β_{1-42} peptide ($A\beta_{1-42}$). The three CRMs (ERM-DA480/IFCC, ERM-DA481/IFCC and ERM-DA482/IFCC) were produced and certified under the responsibility of the European Commission's Joint Research Centre. The starting material used to prepare ERM-DA481/IFCC was human CSF collected from normal pressure hydrocephalus patients by continuous lumbar drainage. After collection, the CSF was aliquoted and frozen at -80 °C. For the preparation of the certified reference material a selected number of CSF donations were thawed, pooled, mixed, filled in microvials and stored at (-70 ± 10) °C.

ANALYTICAL METHODS USED FOR CERTIFICATION

The material was characterised using one of the two reference measurement procedures (Leinenbach *et al.* Clin. Chem. 60 (2014) 987-94; Korecka *et al.* J. Alzheimers Dis. 41 (2014) 441-451). Homogeneity was assessed using a fully automated immunoassay (Roche Elecsys β-amyloid (1-42)) and an ELISA (EUROIMMUN beta-amyloid (1-42)). The stability of the material was assessed with an ELISA (EUROIMMUN beta-amyloid (1-42)).

PARTICIPANTS

- ADx NeuroSciences, Gent, BE
- European Commission, Joint Research Centre (JRC), Geel, BE
- Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, US
- PPD Laboratories, Richmond, VA, US
- Roche Diagnostics GmbH, Penzberg, DE
- The Sahlgrenska Academy, University of Gothenburg, Mölndal, SE
- Waters Corporation, Milford, MA, US

SAFETY INFORMATION

The usual laboratory safety measures apply. Do not discharge the waste into the drain. Each individual CSF donation was tested for anti-HIV1/HIV2 antibodies and found to be negative. Since the donors were under continuous medical surveillance, there is no particular risk that this donor population should have had any bacterial or viral infections of the central nervous system at the time of CSF collection. However, the product must be handled with adequate care as any material of human origin. It is intended for *in vitro* use only..

INSTRUCTIONS FOR USE AND INTENDED USE

The vials shall be thawed at room temperature. Avoid vortexing or inverting the vial in order to prevent contact between the solution and additional surface of the vial.

The materials are intended for the calibration of methods, quality control and/or the assessment of method performance. As with any reference material, they can be used for establishing control charts or in validation studies. ERM-DA481/IFCC was shown to be commutable for the combination of the following routine measurement procedures:

- EUROIMMUN beta-amyloid (1-42) (EUROIMMUN AG, Lübeck, DE)
- IBL Amyloid-beta (1-42) CSF ELISA (IBL International GmbH, Hamburg, DE)
- INNOTEST® β-AMYLOID(1-42) (Fujirebio Europe, N.V., Gent, BE)
- Lumipulse® (Fujirebio Europe N.V., Gent, BE)
- V-PLEX® Aβ Peptide Panel 1 (6E10) (Meso Scale Discovery, LLC., Rockville, MD, US)
- Roche Elecsys β-amyloid (1-42) (Roche Diagnostics GmbH, Penzberg, DE)

If ERM-DA481/IFCC is used for the calibration of other $A\beta_{1-42}$ routine measurement procedures it should be verified by the user that the material or its dilutions used are commutable.

The minimum sample intake for which within-vial homogeneity was proven is 15 µL. For smaller sample intakes the user needs to verify the within-vial homogeneity.

STORAGE

The materials should be stored at -70 ± 10 °C.

However, the European Commission cannot be held responsible for changes that happen during storage of the material at the customer's premises, especially of opened samples.

LEGAL NOTICE

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NOTE

A detailed certification report is available at https://crm.jrc.ec.europa.eu/.

A paper copy is obtainable from the Joint Research Centre, Directorate F – Health, Consumers and Reference Materials on request.

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