CERTIFICATE OF ANALYSIS

Human multi-enzymes reference material

JCCLS CRM – 001d

	Certified values[3)] U/L	Uncertainties[4) 5)] U/L
AST[1)]	160	± 4
ALT[1)]	158	± 4
CK[1)]	425	± 10
ALP[1)]	424	± 13
LD[1)]	406	± 8
γ －GT[1)]	153	± 5
AMY[1)]	344	± 9
IFCC – ALP[2)]	153	± 6
IFCC – LD[2)]	430	± 11

1) The catalytic concentrations were determined by the JSCC primary reference measurement procedures.
2) The catalytic concentrations were determined by the IFCC reference method.
3) The certification procedure was based on ISO GUIDE 35. The certified values were unweighted mean values independently obtained by 25 labs.
4) Each estimated expanded uncertainty U was calculated as U=*k*u, where k was the coverage factor corresponding to the 95% level of confidence and u was the combined standard uncertainty, as defined in the Guide to Expression of Uncertainty in Measurement ISO/IEC Guide 98-3, 2008. Each uncertainty includes homogeneity and experimental error components.
5) The inter-laboratory and vial-to-vial differences, as factors causing variation of experimental data, were evaluated by three-way analysis of variance.

INTENDED USE

This material is equivalent to the secondary calibration material in metrological traceability defined in ISO 17511(2003).

The material is intended to provide, when reconstituted, a calibration solution with each known catalytic concentration. This material can also be used for evaluation of routine methods.

DESCRIPTION OF MATERIAL

This human multi-enzyme reference material (human multi-ERM) was lyophilized from a solution containing 8 kinds of human and recombinant type enzymes, bovine serum albumin Fraction V, purity ≧98 % (30 g/L), saccharose, Reagents grade, (80 g/L), and antibiotic with a trace concentration. Each vial contains recombinant alanine aminotransferase originated from human liver (isoenzyme:S),

recombinant aspartate aminotransferase from human liver, recombinant creatine kinase from human muscle (MM), lactate dehydrogenase from human red blood cells (Ⅰ,Ⅱ,Ⅲ), recombinant gamma-glutamyltransferase from human liver (Ⅱ), recombinant alkaline phosphatase from human liver (liver), mixture of recombinant amylase from human pancreas and that from human saliva, and recombinant lipase from human pancreas. A bovine serum albumin for adjustment of viscosity, and saccharose for stabilizing the enzymes were added. Thus the five enzymatic activities in this material are stable.

VIAL CONTENTS AND PACKAGE

This material contains the lyophilized residue of a homogeneous solution of enzymes, bovine serum albumin, and saccharose.

1 set : 1 bottle (3 ml:reconstituted) x 2 bottles. The bottle is a glass one which is tightly sealed.

The package accommodating a bottle is designed for avoiding shock, which is wrapped with cushion in order to avoid damage.

TRANSPORTATION AND STORAGE

This material should be transported and stored frozen (lower than －20 ℃).

RECONSTITUTION PROCEDURE AND USAGE

1. The entire contents of each vial should be completely dissolved in an accurately measured amount of water according to the procedure below:

(1) Allow the vial to equilibrate at room temperature.

(2) Tap the vertically positioned vial gently to ensure that the lyophilized material is at the bottom of the vial.

(3) Carefully remove the stopper.

(4) Reconstitute by slow addition to the sides of the vial of (3.00 ± 0.015) mL distilled water (15-25 °C) with calibrated volumetric equipment. Note the temperature.

(5) Replace the stopper.

(6) Let to stand for 10 minutes at room temperature.

(7) Mix gently by reversing 20-30 times in order to dissolve the content perfectly.

2. Keep the reconstituted material at 2 to 8 ℃.

3. Each enzyme activity must be measured within 24 hours from the reconstitution time and the vial should not be stored for re-use.

The minimum amount of sample to be used is 50 μl.

4. After reconstitution according to the above instruction, the material is regarded as a homogeneous solution.

EXPIRATION DATE

This material should be kept at lower than –20 °C. The certified value is valid until the end of July 2023.

* This material will be monitored periodically over the period until the expiration date. If there are substantive changes with regard to its stability, it will be notified to the purchaser, and distribution will be stopped.

ATTENTION

1. Before using this material, thoroughly read the present inserted document.
2. Do not refreeze the material for re-use once it has been dissolved.

WARNINGS “ *in vitro* USE ONLY ”

1. This material has been tested to be free of HBs antigen, HIV antibody (HIV-1 and HIV-2), HTLV-1 antibody and HCV antibody. Regarding other infectious viruses, as no test method that can ensure non-infectivity has yet been established, this material must be handled like any other routine test specimens with the assumption it poses a risk for infection.

2. If this material comes in contact with eyes or mouth, thoroughly wash the affected area using water, and consult a medical doctor.

3. Used containers are disposed of as medical or industrial waste in accordance with the waste material regulations.

MANUFACTURER

This material was manufactured by Asahi Kasei Pharma Corporation.

DATE OF CERTIFICATION AND CERTIFICATION BODY

August 31 , 2018 Yasushi Takagi Shigemi Hosogai

The Japanese Committee for Clinical Laboratory Standards

http://tc.xii.jp/jccls/

PROVIDER

ReCCS (Reference Material Institute for Clinical Chemistry Standards)

1-3-3 , Azaminominami, Aoba-ku, Yokohama , Kanagawa 225-0012 , Japan

TEL 81-45-507-6145

FAX 81-45-530-9036

URL http://www.reccs.or.jp

FOR INQUIRY

ReCCS (Reference Material Institute for Clinical Chemistry Standards)
1-3-3, Azaminominami, Aoba-ku, Yokohama, Kanagawa, 225-0012 Japan
TEL 81-45-507-6145
FAX 81-45-530-9036

REFERENCES

1) G.Schumann,et al, IFCC primary reference procedures for the measurement of catalytic activity concentrations of enzymes at 37℃ : Part 8. Reference procedure for the measurement of catalytic concentration of α-amylase. Clin Chem Lab Med 2006 ; 44 (9) : 1146-1155

2) TP. Linsinger et al. Estimating the uncertainty of stability for matrix CRMs. Fresenius J Anal Chem 2001; 370 : 183-188

3) G.Schumann,et al. IFCC primary reference procedures for the measurement of catalytic activity concentrations of enzymes at 37℃: Part 9. Reference procedure for the measurement of catalytic concentration of alkaline phosphatase. Clin Chem Lab Med 2011;49 (9) : 1439-1466

4) G.Schumann, et al. IFCC primary reference procedures for the measurement of catalytic activity concentrations of enzymes at 37℃: Part3. Reference Procedure for the Measurement of Catalytic Concentration of Lactate Dehydrogenase. Clin Chem Lab Med 2002 ; 40(6) :643-648

JCCLS CRM-001d
Reference Value for Lipase

The activity of Lipase (Lipase: LIP) was determined by DGGR[1)] substrate method at 37 ℃	Reference value U/L	Uncertainties[2)] U/L
LIP	127	± 4
1) DGGR : 1,2-o-Dilauryl-rac-glycero-3-glutaric acid-6 (6-methylresorufin) ester 2) The coverage factor *k*, determined from the Student's *t* distributor, is *k*=2.0.		

(Reference)

1) Medicine and Pharmacy 1999 ; 41 : 489-496

2) Mauro Panteghini, et al, Measurement of pancreatic lipase activity in serum by a kinetic colorimetric assay using a new chromogenic substrate. Ann Clin Biochem 2001 ; 38 : 365-370

3) Japanese Journal of Clinical Laboratory Standards 2004 ; 19 : 1-52

4) Japanese Journal of Clinical Laboratory Standards 2002 ; 27 : 115-119

JCCLS CRM -001d
Reference Value for P-AMY

The activity of P-AMY was determined by JCCLS Standard Operation Procedure using anti-S-AMY antibody (see reference)	Reference value U/L	Uncertainties[1)] U/L
P-AMY	154	± 5
1) The coverage factor *k*, determined from the Student's *t* distributor, is *k*=2.0.		

*The AMY contains P form and S form as isoenzyme. The AMY which is added to this material expresses more than 5% different activities relative to human AMY according to the substrate due to its origin and ratio between P form and S form. In this case, it is possible to correct the difference, but it must follow the manufacturer's instruction.

(Reference)

1） Rinsyo Kensa Kiki Shiyaku 1996 ; 19 : 27-36

2) Tsukuba Rinsyo Kagaku Seminar : 2000-15 ; 72-115

3) G.Schumann,et al. IFCC primary reference procedures for the measurement of catalytic activity concentrations of enzymes at 37℃: Part 8. Reference procedure for the measurement of catalytic concentration of α-amylase.. Clin Chem Lab Med 2006 ; 44 (9) : 1146-1155

4) Japanese Journal of Clinical Laboratory Standards 2004; 19 : 1-52

5) Japanese Journal of Clinical Laboratory Automation 2002 ; 27 : 16-21