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SEKISUI

In Vitro Diagnostics

Approval No.13A2X00197218042

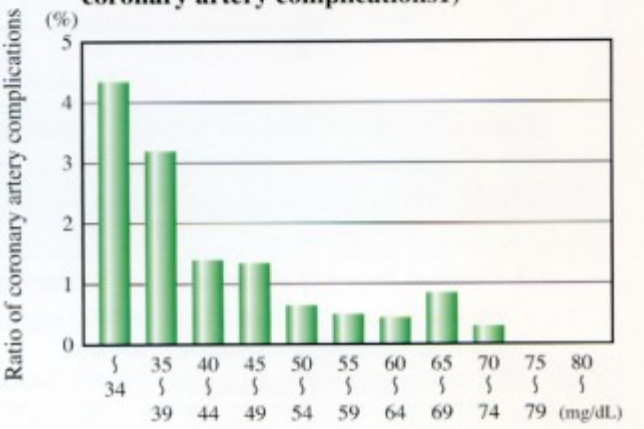
Current laboratory test requirements for basic HDL-cholesterol measurement

1. Significance of and methods for HDL-cholesterol measurement

1) Measurement significance

It has been established that coronary artery diseases are more frequent if the HDL-C value is low by epidemiological surveys, not only in the US and Europe, but also in Japan. It has been reported that the risk to develop coronary artery diseases increases if the HDL-C value is below 40 mg/dL (Figure 1).
Japan Atherosclerosis Society(JAS) Guidelines for Prevention of Atherosclerotic Cardiovascular Diseases define low blood HDL-C as <40 mg/dL.[1)]

Figure 1. HDL-cholesterol value and ratio of coronary artery complications1)



2) Measurement method and standardization used in epidemiological surveys

HDL-C has been measured by precipitation methods using precipitation reagents consisting of heparin and manganese, or dextran sulfate and magnesium, etc. in these domestic and overseas epidemiological surveys, resulting in established evidence of the clinical significance of HDL-C. Subsequently the Centers for Disease Control and Prevention (CDC) established the dextran sulfate-magnesium precipitation method as the Designated Comparison Method (DCM) of HDL-C for measurement standardization in the field of laboratory tests.[2)] This method provides the HDL-C value by adding the precipitation reagent consisting of dextran sulfate and magnesium to serum, followed by centrifugation, and measurement of cholesterol in the supernatant. Based on that, the Japan Society of Clinical Chemistry also adopts the dextran sulfate-magnesium precipitation method as a recommended method.[3)]

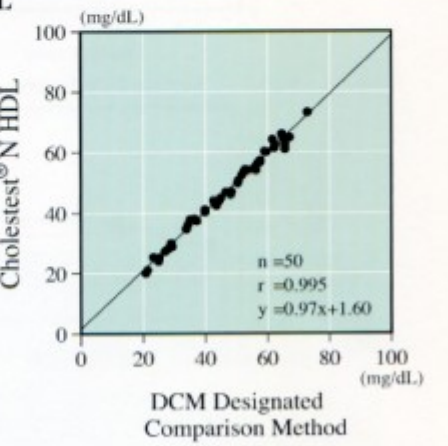
Figure 2. Various measurement methods and fractionation agents

CDC method: Heparin-manganese precipitation	Fractionation agents mainly used in epidemiologic surveys
CDC CRMLIN method (DCM method): Dextran sulfate-magnesium precipitation	
JSCC recommendation: Dextran sulfate-magnesium precipitation	
Others: 13% polyethylene glycol precipitation	

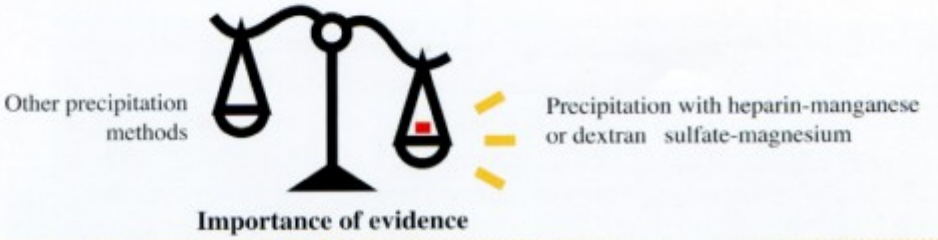
3) Standards of Cholestest® N HDL

The HDL-cholesterol direct method reagent "Cholestest® N HDL" manufactured and distributed by Sekisui Medical Co., Ltd. is designed so that it agrees with the international standard DCM method (dextran sulfatemagnesium precipitation method) (Figure 3).

Figure 3. Correlation between DCM and Cholestest® N HDL



Note: Currently available measurement methods for laboratory tests include several direct measurement methods by different principles.



Importance of evidence

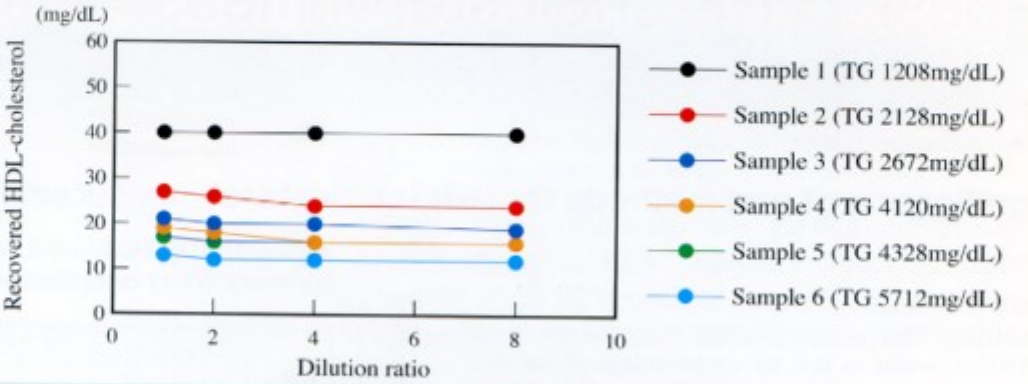
2. Advantages of Cholestest® N HDL

1) High TG samples

High TG samples are often seen because the test targets patients with dyslipidemia. In hypertriglyceridemia, there often is low HDL-cholesterol, thus it is necessary to know accurate HDL-cholesterol values.

1-1. Dilution recovery study in high TG samples (internal data)

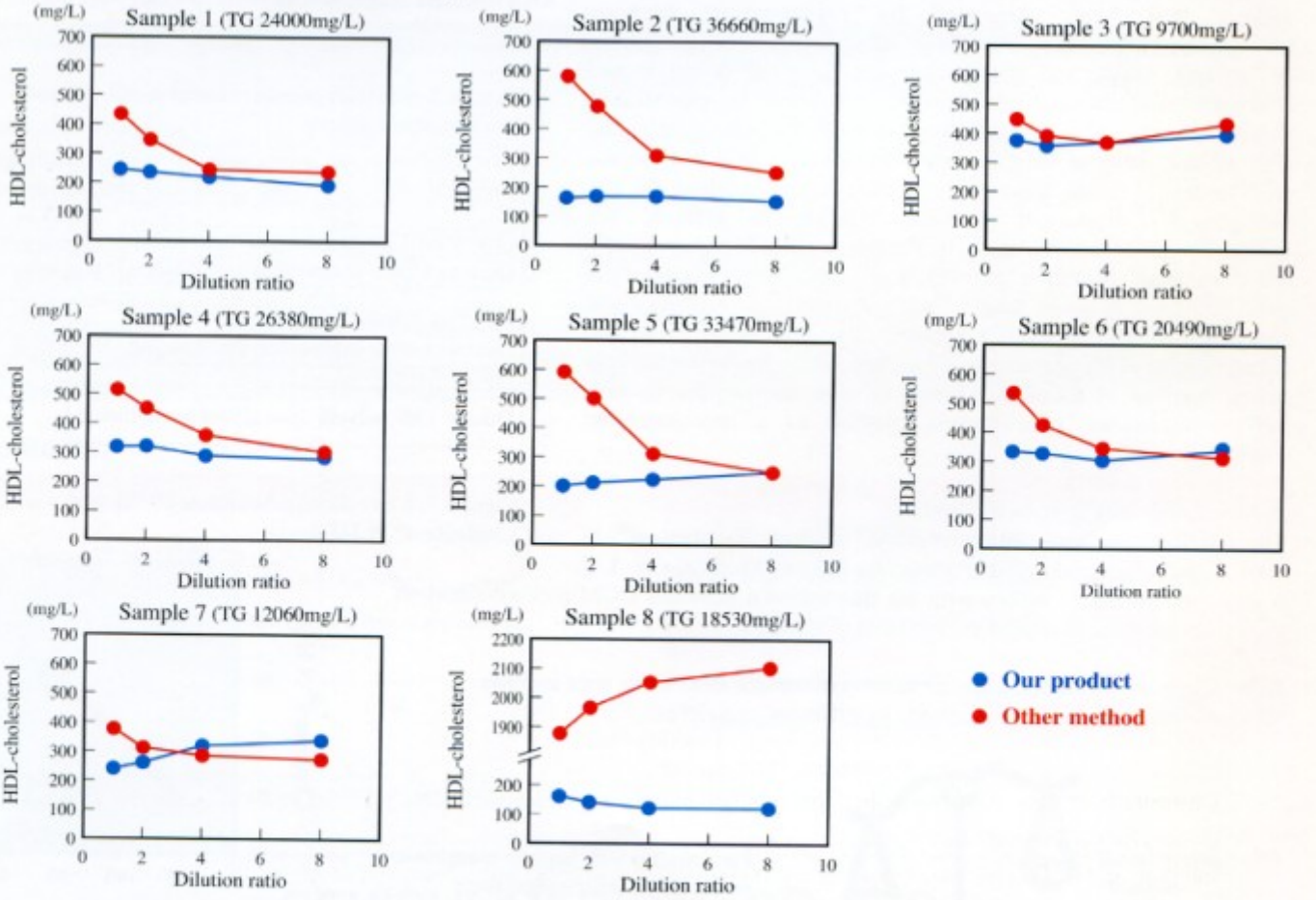
Figure 4. Samples with TG over 1000 mg/dL were diluted 2-, 4- and 8-fold, and measured with the product to calculate recovery.



Comment: The product did not show significant errors in recovery in a dilution recovery study using marked high TG samples (Figure 4, internal data). This indicates that the product can conduct accurate HDL-C measurement, even in high TG samples, without dilution and re-measurement.

1-2. Dilution recovery study in high TG samples (published data)[4)]

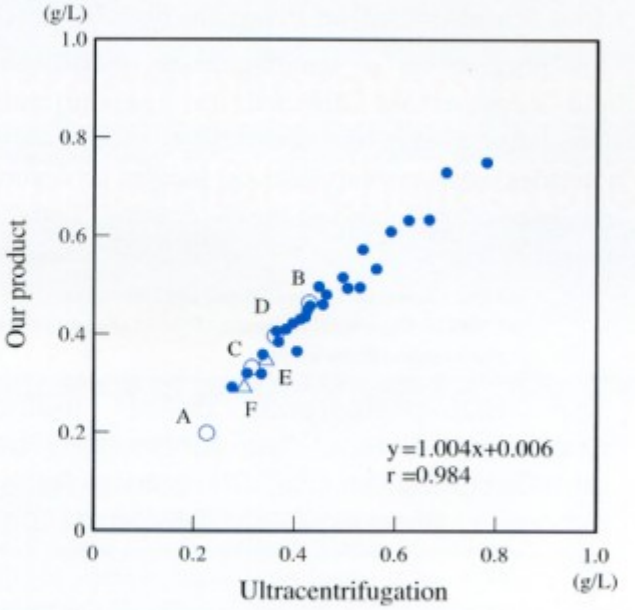
Figure 5. Samples with TG over 8000 mg/dL were diluted 2-, 4- and 8-fold, and measured with the product and another method to calculate recovery.



Comment: It has been reported that the product did not show significant errors in recovery in a dilution recovery study using high TG samples with TG over 800 mg/dL 4) (Figure 5).

2. Correlation between ultracentrifugation and the product (including high TG samples) (published data)[5]

Figure 6.



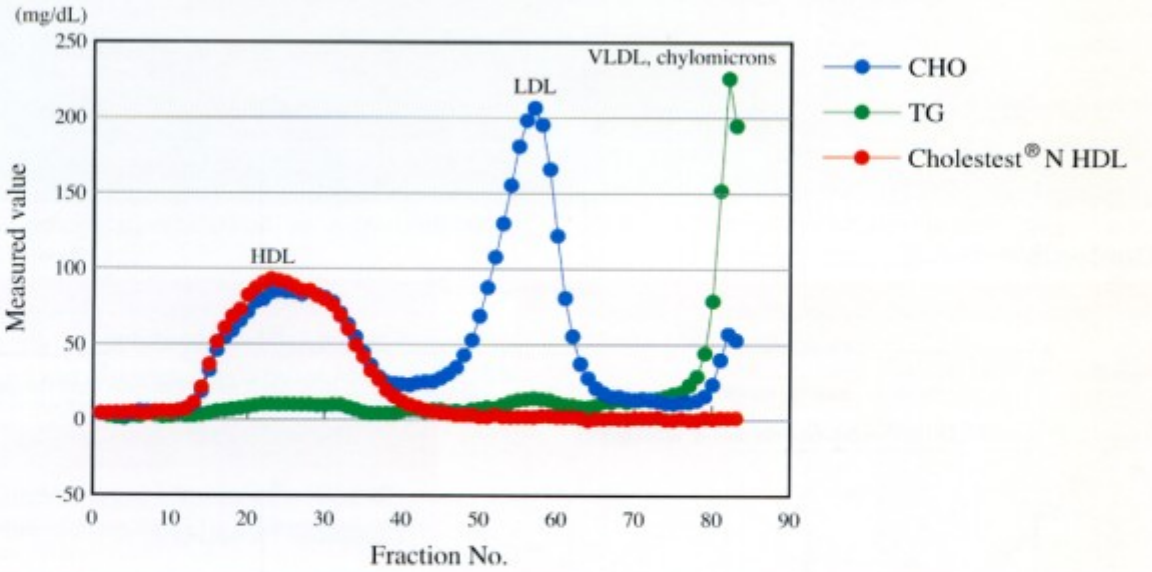
Comment: Correlation with ultracentrifugation was examined in serum samples from hypertriglyceridemia patients (TG 259-1497 mg/dL), and it has been reported that the product did not show discrepancy[5] (Figure 6).

2) Cross-reaction with other lipoproteins

As the test targets patients with dyslipidemia, samples with marked increase in lipoproteins other than HDL (such as VLDL) are often seen. In hypertriglyceridemia, there often is low HDL-cholesterol, thus it is necessary to know accurate HDL-cholesterol values.

1. Reactivity of the product to density-gradient ultracentrifugation of human serum (internal data)

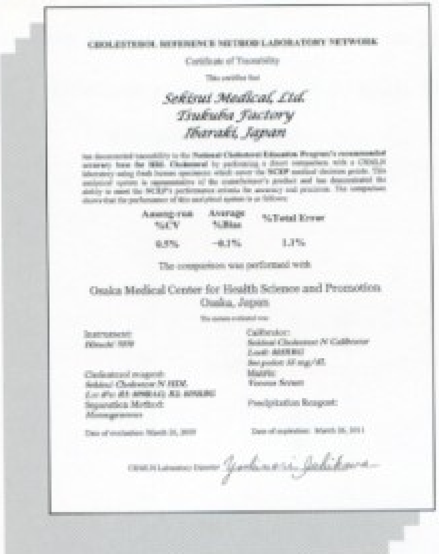
Figure 7.



Comment: It was confirmed that the product reacts only with the HDL fraction and not with the LDL, VLDL, or chylomicrion fractions by examination using density-gradient ultracentrifugation of human serum (Figure 7, internal data). In addition, it has been reported that the product hardly showed cross-reactivity to lipoproteins other than HDL, such as VLDL, by examination using FPLC fractions of human serum.[5]

These indicate that the product can accurately measure HDL-cholesterol even in high TG samples with a marked increase in VLDL and chylomicrons.

3. Measurement accuracy



CHOLESTEROL REFERENCE METHOD LABORATORY NETWORK

Certificate of Traceability

Sekisui Medical, Ltd.
Tsukuba Factory
Ibaraki, Japan

Among-run %CV	Average %Bias	%Total Error
0.5%	−0.1%	1.1%

The comparison was performed with

Osaka Medical Center for Health Science and Promotion
Osaka, Japan

Lipid Standardization Program by CDC/CRMLN

This program is a standardization (certification) system for lipid measurement directed to reagent manufacturers and laboratories all over the world.
It verifies measurement accuracy focused on accuracy and precision, and issues certification to prove accuracy control when the criteria are met.

- CDC: Centers for Disease Control and Prevention
- CRMLN: Cholesterol Reference Method Laboratory Network by seven countries (nine centers) in the world

The HDL-cholesterol direct method reagent "Cholestest® N HDL" has continuously been acquiring certification by the CDC Cholesterol Reference Method Laboratory Network (CDC/CRMLN) in our factory.

<References>
1) Japan Atherosclerosis Society(JAS) Guidelines for Prevention of Atherosclerotic Cardiovascular Diseases, 2007 edition.
2) Kimberly MM, et al. Clin Chem 1999; 45 (10): 1803-12.
3) Yuzo Kasiwamori, et al. Japanese Journal of Clinical Chemistry 2009; 38: 308-31.
4) Ueda Y, et al. J Clin Lab Anal 2003; 17: 201-08.
5) Keiichi Ono, et al. Japanese Journal of Clinical Chemistry 2002; 31: 44-50.

<History of HDL-C measurement reagents>

	Release month/year	Trade name	Method
First generation (fractionation)	April 1979	HDL-C set	dextran sulfate-magnesium method
	November 1983	HDL-C 2 "Dai-ichi"	dextran sulfate magnesium/ phosphotungstate magnesium method
	November 1988	HDL fractionation solution	dextran sulfate magnesium/ polyethylene glycol method
Second generation (direct method)	November 1995	HDL-C auto "Daiichi"	method utilizing specificity of surfactant (preparation reagent)
	September 1996	Cholestest HDL	method utilizing specificity of surfactant (liquid reagent)
	July 2000	Cholestest N HDL	method utilizing reaction accelerator and specificity of surfactant (liquid reagent)

<Contents>

Name		Package
Cholestest® N HDL	Enzyme solution 1	60 mL x 2
	Enzyme solution 2	20 mL x 2

Storage: 2-10°C Shelf life: 24 months from the date of manufacture

Name	Package
Cholestest® N Calibulator	2.0mL x 3

Storage: 2-10°C Shelf life: 12 months from the date of manufacture

Name	Package
Cholestest® Control 1	1mL x 12
Cholestest® Control 2	1mL x 12

Storage: 2-10°C Shelf life: 24 months from the date of manufacture

Read this package insert carefully before using the kit.

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