Для лабораторий, использующих
Набор для количественного определения липазы
на анализаторе **cobas c** 311,
на модулях **cobas c** 501, **c** 502,
на модуле **cobas c** 702,
COBAS INTEGRA 400 plus
и cobas **c** 111
г. Москва

Дата: 19.06.2024
Исх.: 0226/1906/2024
Ref.: QN-RDS-CoreLab-2024-035

Уведомление по качеству
Касательно анализа для количественного определения липазы (LIPC): обновленная информация об интерференции гемолиза, снижение 1000 HI с 300 до 100 соответственно

Название продукта	**GMMI / Кат. №**	**Идентификатор продукта (Номер лота или серийный номер)**	**Номер РУ, Дата РУ**	**Производитель**
Набор реагентов для количественного определения липазы методом ферментного спектрофотометрического анализа в сыворотке и плазме крови на анализаторах и модулях биохимических COBAS INTEGRA и Roche/Hitachi cobas c (LIPC / Lipase colorimetric), варианты исполнения Набор реагентов для количественного определения липазы методом ферментного спектрофотометрического анализа в сыворотке и плазме крови на анализаторах и модулях биохимических COBAS INTEGRA и Roche/Hitachi cobas c (LIPC / Lipase colorimetric), варианты исполнения (LIPC/Lipase colorimetric COBAS INTEGRA / cobas c system)	03029590322		РЗН 2019/9214 от 25.08.2023	Sandhofer Strasse116, 68305 Mannheim, Germany DE
Набор реагентов для количественного определения липазы методом ферментного спектрофотометрического анализа в сыворотке и плазме крови на анализаторах и модулях биохимических COBAS INTEGRA и Roche/Hitachi cobas c (LIPC / Lipase colorimetric), варианты исполнения	07041918190		РЗН 2019/9214 от 25.08.2023	Sandhofer Strasse116, 68305 Mannheim, Germany DE

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Название продукта	**GMMI / Кат. №**	**Идентификатор продукта (Номер лота или серийный номер)**	**Номер РУ, Дата РУ**	**Производитель**
Набор реагентов для количественного определения липазы методом ферментного спектрофотометрического анализа в сыворотке и плазме крови на анализаторах и модулях биохимических COBAS INTEGRA и Roche/Hitachi cobas c (LIPC / Lipase colorimetric), варианты исполнения: III. Реагенты в кассете (LIPC/Lipase colorimetric cobas c systems), 580 тестов (LIPC / Lipase colorimetric cobas c systems)				
Набор реагентов для количественного определения липазы методом ферментного спектрофотометрического анализа в сыворотке и плазме крови на анализаторах и модулях биохимических COBAS INTEGRA и Roche/Hitachi cobas c (LIPC / Lipase colorimetric), варианты исполнения Набор реагентов для количественного определения липазы методом ферментного спектрофотометрического анализа в сыворотке и плазме крови на анализаторах и модулях биохимических COBAS INTEGRA и Roche/Hitachi cobas c (LIPC / Lipase colorimetric), варианты исполнения: I. Реагенты во флаконах (LIPC/Lipase colorimetric assay cobas c 111), 2x50 тестов, в составе: 1. Реагент R1 во флаконе, 2 шт. 2. Реагент SR во флаконе, 2 шт. 3. Инструкция по применению (LIPC/Lipase colorimetric assay cobas c 111)	05401704190		РЗН 2019/9214 от 25.08.2023	Sandhofer Strasse116, 68305 Mannheim, Germany DE
Инструмент/Система	Анализатор **cobas c** 311 Модуль **cobas c** 501 Модуль **cobas c** 502 Модуль **cobas c** 702 Анализатор COBAS INTEGRA 400 plus Анализатор **cobas c** 111			

Уважаемый пользователь,

Сообщаем вам о том, что для колориметрического анализа липазы (LIPC) на всех анализаторах интерференция гемолиза, заявленная в Инструкции по использованию реагента в разделе «Ограничения/Интерференция» и в настройках анализатора, должна быть снижена с Индекса гемолиза (HI) 1000 на **cobas c** 501/**c** 311/**c** 502/**c** 702/**c** 503/**c** 303 и с 300 до 100 на COBAS INTEGRA 400 плюс / **cobas c** 111, соответственно. Эти изменения основаны на недавних результатах, полученных в ходе мастер-проекта **cobas c** 503, о котором сообщалось в маркетинговом Уведомлении MN-RDS-CoreLab-2022-183.

Описание ситуации

Обзор соответствующих Протоколов методики и анализаторов:

Протокол методики	Анализатор	Номер Протокола методики / ID теста
LIP	**cobas c** 501 / **c** 311	789
S-LIP	**cobas c** 501 / **c** 311	786
LIP	**cobas c** 502 / **c** 702	8789
S-LIP	**cobas c** 502 / **c** 702	8786
LIP	COBAS INTEGRA 400 plus	0-052
LIP	**cobas c** 111	789

В настоящее время в Инструкциях по использованию реагента утверждается, что до Индекса гемолиза 1000 существенной интерференции не наблюдается на инструментах **cobas c**501/**c**311/**c**502/**c**702, и до 300 на COBAS INTEGRA 400 plus / **cobas c** 111. Тем не менее интерференция наблюдалась при Индексе гемолиза > 100.

Максимальное наблюдаемое отклонение при уровне липазы ~50 Ед/л составляет +18 Ед/л (+36%) при уровне индекса гемолиза макс. 1000.
Максимальное наблюдаемое отклонение при уровне липазы ~200 Ед/л составляет +25 Ед/л (+13%) при уровне индекса гемолиза макс. 1000.

Вследствие этого, интерференция, заявленная в Инструкции по использованию реагента, снижается с указанием на то, что до концентрации гемоглобина 100 вместо 1000 и 300, соответственно, существенная интерференция не наблюдается.

Причина возникновения

Поскольку мы генерируем дополнительные данные о **cobas c** 503, мы должны соблюдать новейшие нормативные требования (например, IVDR). Некоторые рабочие процедуры изменились из-за обновления основных международных рекомендаций (например, CLSI). Новые внешние требования могут отразиться на настройках Протокола методики и привести к различиям в результатах, полученных на **cobas c** 503 по сравнению со старыми данными **cobas c** 501.

Однако точная причина возникновения интерференции со стороны иктеричности во время проведения анализа LIPC неизвестна.

Оценка риска

1.) Снижение заявленной интерференции гемолиза (затрагивает все страны)

Частота возникновения

Ни одна рекламация не была передана в Группу расследования случаев (CIR).

Вероятность обнаружения

Проблема может быть обнаружена только в том случае, если ошибочно завышенный уровень не соответствует ожидаемым значениям.

Серьезность последствий

Остаточный риск причинения вреда в сочетании с вероятностью возникновения проблемы и общим риском определяется как приемлемый. Оценка степени опасности для здоровья (HHE) не требуется. Для получения дополнительной информации обратитесь к Уведомлению SN-RDS-CoreLab-2024-093.

Важная информация

Пользователи, проводящие колориметрический анализ липазы (LIPC) на приборах Roche, должны быть проинформированы о том, что заявленная интерференция гемолиза была снижена, как описано выше.

Дополнительные обновления, реализованные в Инструкциях по использованию реагента, носят редакционный характер и не влияют на результаты или производительность анализа.

На инструментах **cobas c** 111 и COBAS INTEGRA 400 plus сывороточный индекс не является параметром, входящим в настройки прибора. В целом, контрольное поле сывороточного индекса во всех других системах **cobas c** относится к группе настроек, которые может изменять сам пользователь. Тем не менее, это единственное «редактируемое пользователем» поле, которое будет перезаписано обновленным электронным штрихкодом во всех системах **cobas c** (в **cobas c** 702/502 с частичной и полной перезаписью).

К настоящему Уведомлению по качеству прилагаются обновленные Инструкции по использованию реагентов и важные примечания для всех затронутых систем.

Срок публикации для разных анализаторов:

Обратите внимание:
Обновленные Инструкции по использованию реагента для **cobas c** 501/311/502 и **cobas c** 702 уже были опубликованы в конце марта / начале апреля без ссылки на настоящее Уведомление по качеству, а также без обновленных электронных штрихкодов и важных примечаний.

Обновленная электронная документация для всех систем будет опубликована на портале электронного контента со ссылкой на настоящее Уведомление по качеству.

Анализатор	Версия Инструкции по использованию реагента	Страна	Срок публикации
cobas c 111	3.0	Во всем мире	Апрель 2024 г.
COBAS INTEGRA 400 plus	3.0		
cobas c 301/501 **cobas c** 502	4.0		
cobas c 702	4.0		

Распространение настоящего уведомления по качеству на местах

Настоящее Уведомление по качеству предназначено для всех заинтересованных лиц в Вашей организации или других организациях, которые получали данную продукцию.

Пожалуйста, перешлите данное уведомление другим организациям/лицам, которых она может касаться.

Приносим свои извинения за причиненные неудобства, которые могут быть связаны с данной ситуацией, и надеемся на Ваше понимание и поддержку.

Контакты

В случае возникновения вопросов обратитесь, пожалуйста, в службу поддержки Roche:
Бесплатная линия: 8 800 100-68-96
Время работы: понедельник – пятница с 08:00 до 18:00 по Московскому времени
e-mail: russia.rcsc@roche.com.

С уважением,

Менеджер по продукции
Тел: +7 (916) 922-64-09
Электронная почта: ivan.kargov@roche.com

Иван Каргов
Иван Каргов
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Date: 2024.06.25 15:25:39 +03'00'

Медицинский менеджер
Тел: + 7 (495) 229-69-99
Электронная почта: maria.kosyakova@roche.com

Мария Косякова
Maria Kosyakova
Digitally signed by Maria Kosyakova
Date: 2024.07.01 11:20:14 +03'00'

LIPC

Lipase colorimetric assay

REF **03029590** 322

cobas c 501

Reason for change

ACN 789 / LIP	Old	**New**
Version	0101	**0102**
L/H/I	2000/1000/60	2000/**100**/60

ACN 786 / S-LIP	Old	**New**
Version	0101	**0102**
L/H/I	2000/1000/60	2000/**100**/60

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com

LIPC

Lipase colorimetric assay

REF **03029590** 322

cobas c 311

Reason for change

ACN 789 / LIP	Old	**New**
Version	0101	**0102**
L/H/I	2000/1000/60	2000/**100**/60

ACN 786 / S-LIP	Old	**New**
Version	0101	**0102**
L/H/I	2000/1000/60	2000/**100**/60

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com

LIPC

Lipase colorimetric assay

REF **03029590** 322

cobas c 502

Reason for change

ACN 8789 / LIP	Old	**New**
Version	0101	**0102**
Serum Index Check Value L/H/I	2000/1000/60	2000/**100**/60

ACN 8786 / S-LIP	Old	**New**
Version	0101	**0102**
Serum Index Check Value L/H/I	2000/1000/60	2000/**100**/60

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com

LIPC

Lipase colorimetric

REF **07041918** 190

cobas c 701

Reason for change

ACN 8789 / LIP	Old	**New**
Version	0101	**0102**
Serum Index Check Value L/H/I	2000/1000/60	2000/**100**/60

ACN 8786 / S-LIP	Old	**New**
Version	0101	**0102**
Serum Index Check Value L/H/I	2000/1000/60	2000/**100**/60

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com

LIPC

Lipase colorimetric

REF **07041918** 190

cobas c 702

Reason for change

ACN 8789 / LIP	Old	**New**
Version	0101	**0102**
Serum Index Check Value L/H/I	2000/1000/60	2000/**100**/60

ACN 8786 / S-LIP	Old	**New**
Version	0101	**0102**
Serum Index Check Value L/H/I	2000/1000/60	2000/**100**/60

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com

LIPC

cobas®

Lipase colorimetric assay

Order information

REF	CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
03029590322	Lipase colorimetric assay (200 tests)	System-ID 07 5900 7	**cobas c** 311, **cobas c** 501/502

Materials required (but not provided):

10759350190	Calibrator f.a.s. (12 x 3 mL)	Code 401	
10759350360	Calibrator f.a.s. (12 x 3 mL, for USA)	Code 401	
12149435122	Precinorm U plus (10 x 3 mL)	Code 300	
12149435160	Precinorm U plus (10 x 3 mL, for USA)	Code 300	
12149443122	Precipath U plus (10 x 3 mL)	Code 301	
12149443160	Precipath U plus (10 x 3 mL, for USA)	Code 301	
05117003190	PreciControl ClinChem Multi 1 (20 x 5 mL)	Code 391	
05947626190	PreciControl ClinChem Multi 1 (4 x 5 mL)	Code 391	
05947626160	PreciControl ClinChem Multi 1 (4 x 5 mL, for USA)	Code 391	
05117216190	PreciControl ClinChem Multi 2 (20 x 5 mL)	Code 392	
05947774190	PreciControl ClinChem Multi 2 (4 x 5 mL)	Code 392	
05947774160	PreciControl ClinChem Multi 2 (4 x 5 mL, for USA)	Code 392	
04489357190	Diluent NaCl 9 % (50 mL)	System-ID 07 6869 3	

English

New application

System information

For **cobas c** 311/501 analyzers:

LIP: ACN 789

S-LIP: ACN 786 (STAT, reaction time: 5)

For **cobas c** 502 analyzer:

LIP: ACN 8789

S-LIP: ACN 8786 (STAT, reaction time: 5)

Intended use

Enzymatic in vitro test for the quantitative determination of lipase in human serum and plasma on Roche/Hitachi **cobas c** systems.

Summary[1,2,3,4,5,6,7]

Lipases are glycoproteins with a molecular weight of 47000 daltons. They are defined as triglyceride hydrolases which catalyze the cleavage of triglycerides to diglycerides with subsequent formation of monoglycerides and fatty acids. In addition to α-amylase, pancreatic lipases have for many years been undeniably the most important clinical chemistry parameters for the differential diagnosis of diseases of the pancreas. The lipase activity determination has gained increasing international recognition because of its high specificity and rapid response. After acute pancreatitis the lipase activity increases within 4-8 hours, reaches a peak after 24 hours and decreases after 8 to 14 days. However, there is no correlation between the lipase activity determined in serum and the extent of damage to the pancreas.

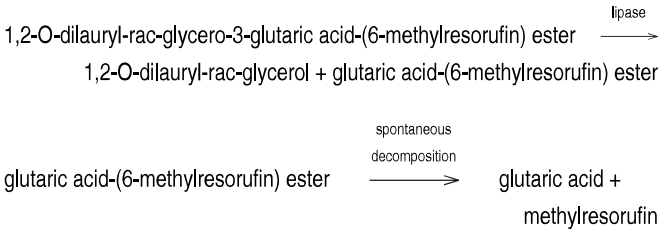
Numerous methods have been described for the determination of lipase which determine the decrease in substrate turbidimetrically or nephelometrically or determine degradation products.

This method is based on the cleavage of a specific chromogenic lipase substrate 1,2-O-dilauryl-rac-glycero-3-glutaric acid-(6-methylresorufin) ester emulsified with bile acids. The pancreatic enzyme activity is determined specifically by the combination of bile acid and colipase used in this assay. Virtually no lipase activity is detected in the absence of colipase. Colipase only activates pancreatic lipase, but not other lipolytic enzymes found in serum. The high amount of cholates ensures that the esterases present in the serum do not react with the chromogenic substrate due to the highly negative surface charge.

Test principle[8,9,10,11]

Enzymatic colorimetric assay with 1,2-O-dilauryl-rac-glycero-3-glutaric-acid-(6-methylresorufin) ester as substrate.

The chromogenic lipase substrate 1,2-O-dilauryl-rac-glycero-3-glutaric-acid-(6-methylresorufin) ester is cleaved by the catalytic action of alkaline lipase solution to form 1,2-O-dilauryl-rac-glycerol and an unstable intermediate, glutaric acid-(6-methylresorufin) ester. This decomposes spontaneously in alkaline solution to form glutaric acid and methylresorufin. Addition of detergent and colipase increases the specificity of the assay for pancreatic lipase.



The color intensity of the red dye formed is directly proportional to the lipase activity and can be determined photometrically.

Reagents - working solutions

R1 BICIN[a)] buffer: 50 mmol/L, pH 8.0; colipase (porcine pancreas): ≥ 0.9 mg/L; Na-deoxycholate: 1.6 mmol/L; calcium chloride: 10 mmol/L; detergent; preservative

R2 Tartrate buffer: 10 mmol/L, pH 4.16; 1,2-O-dilauryl-rac-glycero-3-glutaric acid-(6-methylresorufin) ester: 0.27 mmol/L; taurodeoxycholate: 8.8 mmol/L; detergent; preservative

a) BICIN = N,N-bis(2-hydroxyethyl)glycine

R1 is in position B and R2 is in position C.

Precautions and warnings

For in vitro diagnostic use for health care professionals. Exercise the normal precautions required for handling all laboratory reagents.

Infectious or microbial waste:
Warning: handle waste as potentially biohazardous material. Dispose of waste according to accepted laboratory instructions and procedures.

Environmental hazards:
Apply all relevant local disposal regulations to determine the safe disposal.

Safety data sheet available for professional user on request.

This kit contains components classified as follows in accordance with the Regulation (EC) No. 1272/2008:

Warning

LIPC

Lipase colorimetric assay

H317	May cause an allergic skin reaction.

Prevention:

P261	Avoid breathing mist or vapours.
P272	Contaminated work clothing should not be allowed out of the workplace.
P280	Wear protective gloves.

Response:

P333 + P313	If skin irritation or rash occurs: Get medical advice/attention.
P362 + P364	Take off contaminated clothing and wash it before reuse.

Disposal:

P501	Dispose of contents/container to an approved waste disposal plant.

Product safety labeling follows EU GHS guidance.
Contact phone: all countries: +49-621-7590, USA: 1-800-428-2336

Reagent handling
Ready for use

Storage and stability

LIPC

Shelf life at 2-8 °C:	See expiration date on **cobas c** pack label.
On-board in use and refrigerated on the analyzer:	4 weeks

Diluent NaCl 9 %

Shelf life at 2-8 °C:	See expiration date on **cobas c** pack label.
On-board in use and refrigerated on the analyzer:	12 weeks

Specimen collection and preparation
For specimen collection and preparation only use suitable tubes or collection containers.
Only the specimens listed below were tested and found acceptable.
Serum.
Plasma: Li-heparin plasma
The sample types listed were tested with a selection of sample collection tubes that were commercially available at the time of testing, i.e. not all available tubes of all manufacturers were tested. Sample collection systems from various manufacturers may contain differing materials which could affect the test results in some cases. When processing samples in primary tubes (sample collection systems), follow the instructions of the tube manufacturer.
Centrifuge samples containing precipitates before performing the assay.
See the limitations and interferences section for details about possible sample interferences.
Sample stability claims were established by experimental data by the manufacturer or based on reference literature and only for the temperatures/time frames as stated in the method sheet. It is the responsibility of the individual laboratory to use all available references and/or its own studies to determine specific stability criteria for its laboratory.

Stability in serum:[12]	7 days at 20-25 °C
	7 days at 4-8 °C
	1 year at -20 °C (±5 °C)
Stability in plasma:	1 week at 15-25 °C
	1 week at 2-8 °C
	2 months at -20 °C (±5 °C)

Materials provided
See "Reagents – working solutions" section for reagents.

Materials required (but not provided)
- See "Order information" section
- General laboratory equipment

Assay
For optimum performance of the assay follow the directions given in this document for the analyzer concerned. Refer to the appropriate operator's manual for analyzer-specific assay instructions.
The performance of applications not validated by Roche is not warranted and must be defined by the user.

Application for serum and plasma

cobas c 311 **test definition**

Assay type	Rate A		
Reaction time / Assay points	10 / 10-14 (STAT 5 / 10-14)		
Wavelength (sub/main)	700/570 nm		
Reaction direction	Increase		
Units	U/L (µkat/L)		
Reagent pipetting		Diluent (H_2O)	
R1	80 µL	20 µL	
R2	48 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	2 µL	–	–
Decreased	2 µL	15	135
Increased	2 µL	–	–

cobas c 501/502 **test definition**

Assay type	Rate A		
Reaction time / Assay points	10 / 16-20 (STAT 5 / 16-20)		
Wavelength (sub/main)	700/570 nm		
Reaction direction	Increase		
Units	U/L (µkat/L)		
Reagent pipetting		Diluent (H_2O)	
R1	80 µL	20 µL	
R2	48 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	2 µL	–	–
Decreased	2 µL	15	135
Increased	2 µL	–	–

Calibration

Calibrators	S1: H_2O
	S2: C.f.a.s.
Calibration mode	Linear

LIPC

Lipase colorimetric assay

Calibration frequency	2-point calibration - after reagent lot change - as required following quality control procedures

Calibration interval may be extended based on acceptable verification of calibration by the laboratory.

Traceability: This method has been standardized manually against Roche reagent using the substrate-specific absorptivity, ε.

Quality control

For quality control, use control materials as listed in the "Order information" section.

In addition, other suitable control material can be used.

The control intervals and limits should be adapted to each laboratory's individual requirements. Values obtained should fall within the defined limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

Follow the applicable government regulations and local guidelines for quality control.

Calculation

cobas c systems automatically calculate the analyte activity of each sample.

Conversion factor: U/L x 0.0167 = µkat/L

Limitations - interference

Criterion: Recovery within ±10 % of initial values at a lipase activity of 60 U/L (1.00 µkat/L).

Icterus:[13] No significant interference up to an I index of 60 for conjugated and unconjugated bilirubin (approximate conjugated and unconjugated bilirubin concentration: 1026 µmol/L or 60 mg/dL).

Hemolysis:[13] No significant interference up to an H index of 100 (approximate hemoglobin concentration: 62 µmol/L or 100 mg/dL).

Lipemia (Intralipid):[13] No significant interference up to an L index of 2000. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Drugs: No interference was found at therapeutic concentrations using common drug panels.[14,15]

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[16]

For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

ACTION REQUIRED

Special Wash Programming: The use of special wash steps is mandatory when certain test combinations are run together on **cobas c** systems. The latest version of the carry-over evasion list can be found with the NaOHD-SMS-SmpCln1+2-SCCS Method Sheets. For further instructions refer to the operator's manual. **cobas c** 502 analyzer: All special wash programming necessary for avoiding carry-over is available via the **cobas** link, manual input is required in certain cases.

Where required, special wash/carry-over evasion programming must be implemented prior to reporting results with this test.

Limits and ranges

Measuring range

3-300 U/L (0.05-5.01 µkat/L)

Determine samples having higher activities via the rerun function. Dilution of samples via the rerun function is a 1:10 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 10.

Lower limits of measurement

Limit of Blank, Limit of Detection and Limit of Quantitation

Limit of Blank	= 3 U/L (0.05 µkat/L)
Limit of Detection	= 3 U/L (0.05 µkat/L)
Limit of Quantitation	= 5 U/L (0.08 µkat/L)

The Limit of Blank, Limit of Detection and Limit of Quantitation were determined in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP17-A2 requirements.

The Limit of Blank is the 95th percentile value from n ≥ 60 measurements of analyte-free samples over several independent series. The Limit of Blank corresponds to the concentration below which analyte-free samples are found with a probability of 95 %.

The Limit of Detection is determined based on the Limit of Blank and the standard deviation of low concentration samples.

The Limit of Detection corresponds to the lowest analyte concentration which can be detected (value above the Limit of Blank with a probability of 95 %).

The Limit of Quantitation is the lowest analyte concentration that can be reproducibly measured with a precision coefficient of variation of 20 %. It has been determined using low concentration of lipase samples.

Expected values[17]

Adults: 13-60 U/L (0.22-1.00 µkat/L)

Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.

Specific performance data

Representative performance data on the analyzers are given below. Results obtained in individual laboratories may differ.

Precision

Repeatability and intermediate precision were determined using human samples and controls in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP5 requirements (2 aliquots per run, 2 runs per day, 21 days). The following results were obtained:

Repeatability	*Mean* *U/L (µkat/L)*	*SD* *U/L (µkat/L)*	*CV* *%*
PCCC Multi 1	46.2 (0.77)	0.57 (0.01)	1.2
PCCC Multi 2	98.9 (1.65)	1.20 (0.02)	1.2
Human serum 1	12.3 (0.21)	0.36 (0.01)	2.9
Human serum 2	48.0 (0.80)	0.49 (0.01)	1.0
Human serum 3	75.2 (1.26)	1.18 (0.02)	1.6
Human serum 4	140 (2.34)	1.66 (0.03)	1.2
Human serum 5	288 (4.81)	2.82 (0.05)	1.0

Intermediate precision	*Mean* *U/L (µkat/L)*	*SD* *U/L (µkat/L)*	*CV* *%*
PCCC Multi 1	46.2 (0.77)	0.70 (0.01)	1.5
PCCC Multi 2	100 (1.67)	1.34 (0.02)	1.3
Human serum 1	12.3 (0.21)	0.40 (0.01)	3.2
Human serum 2	48.0 (0.80)	0.65 (0.01)	1.4
Human serum 3	75.2 (1.26)	1.43 (0.02)	1.9
Human serum 4	138 (2.30)	2.28 (0.04)	1.7
Human serum 5	288 (4.81)	3.54 (0.06)	1.2

PCCC = PreciControl ClinChem

The data obtained on **cobas c** 501 analyzer(s) are representative for **cobas c** 311 analyzer(s).

Method comparison

Lipase values for human serum and plasma samples obtained on a **cobas c** 501 analyzer (y) were compared with those determined using the corresponding reagent on a Roche/Hitachi MODULAR P analyzer (x).

Sample size (n) = 100

Passing/Bablok[18]	Linear regression
y = 1.02x - 1.38 U/L	y = 1.01x - 1.06 U/L

LIPC

Lipase colorimetric assay

T = 0.983 r = 1.000

The sample activities were between 4.9 and 293 U/L (0.08 and 4.9 µkat/L).

The data obtained on **cobas c** 501 analyzer(s) are representative for **cobas c** 311 analyzer(s).

References

1 Greiling H, Gressner AM, eds. Lehrbuch der Klinischen Chemie und Pathobiochemie, 3rd ed. Stuttgart/New York: Schattauer Verlag 1995.

2 Keller H, ed. Klinisch-chemische Labordiagnostik für die Praxis, 2nd ed. Stuttgart/New York: Georg Thieme Verlag 1991:354-361.

3 Kazmierczak S, Catrou P, Van Lente F. Diagnostic accuracy of pancreatic enzymes evaluated by use of multivariate data analysis. Clin Chem 1993;39:1960-1965.

4 Steinberg WM, Goldstein SS, Davies ND, et al. Diagnostic assays in acute pancreatitis [Review]. Ann Intern Med 1985;102:576-580.

5 Panteghini M, Pagani F, Bonora R, et al. Diagnostic value of four assays for lipase determination in serum: A comparative reevalution. Clin Biochem 1991;24:497-503.

6 Tietz NW, Shuey DF. Lipase in serum - the elusive enzyme: An overview. Clin Chem 1993;39(5):746-756.

7 Tietz NW, ed. Clinical Guide to Laboratory Tests, 3rd ed. Philadelphia PA: WB Saunders Company 1995;865.

8 Neumann U, Junius M, Batz HG, et al. New substrates for the optical determination of lipase. EP 207252 1987.

9 Borgström B. The action of bile salts and other detergents on pancreatic lipase and the interaction with colipase. Biochimica et Biophysica Acta 1977;488:381-391.

10 Gargouri Y, Julien R, Bois A, et al. Studies on the detergent inhibition of pancreatic lipase activity. J of Lipid Research 1983;24:1336-1342.

11 Leybold A, Junge W. Importance of colipase for the measurement of serum lipase activity. Adv Clin Enzymol 1986;4:60-67.

12 Guder W, Fonseca-Wollheim W, Heil O, et al. Maximum permissible transport and storage times for analysis of blood (serum, plasma), urine and cerebrospinal fluid. DG Klinische Chemische Mitteilungen 1995;26:207-224.

13 Glick MR, Ryder KW, Jackson SA. Graphical Comparisons of Interferences in Clinical Chemistry Instrumentation. Clin Chem 1986;32:470-475.

14 Breuer J. Report on the Symposium "Drug effects in Clinical Chemistry Methods". Eur J Clin Chem Clin Biochem 1996;34:385-386.

15 Sonntag O, Scholer A. Drug interference in clinical chemistry: recommendation of drugs and their concentrations to be used in drug interference studies. Ann Clin Biochem 2001;38:376-385.

16 Bakker AJ, Mücke M. Gammopathy interference in clinical chemistry assays: mechanisms, detection and prevention. Clin Chem Lab Med 2007;45(9):1240-1243.

17 Junge W, Abicht K, Goldmann J, et al. Evaluation of the Colorimetric Liquid Assay for Pancreatic Lipase on Hitachi Analyzers in 7 Clinical Centers in Europe, Japan and USA. Clin Chem Lab Med 1999;37(Special Suppl):469.

18 Bablok W, Passing H, Bender R, et al. A general regression procedure for method transformation. Application of linear regression procedures for method comparison studies in clinical chemistry, Part III. J Clin Chem Clin Biochem 1988 Nov;26(11):783-790.

A point (period/stop) is always used in this Method Sheet as the decimal separator to mark the border between the integral and the fractional parts of a decimal numeral. Separators for thousands are not used.

Any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the Member State in which the user and/or the patient is established.

Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard (for USA: see navifyportal.roche.com for definition of symbols used):

CONTENT	Contents of kit
→	Volume for reconstitution
GTIN	Global Trade Item Number
Rx only	For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

FOR US CUSTOMERS ONLY: LIMITED WARRANTY

Roche Diagnostics warrants that this product will meet the specifications stated in the labeling when used in accordance with such labeling and will be free from defects in material and workmanship until the expiration date printed on the label. THIS LIMITED WARRANTY IS IN LIEU OF ANY OTHER WARRANTY, EXPRESS OR IMPLIED, INCLUDING ANY IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR PARTICULAR PURPOSE. IN NO EVENT SHALL ROCHE DIAGNOSTICS BE LIABLE FOR INCIDENTAL, INDIRECT, SPECIAL OR CONSEQUENTIAL DAMAGES.

CE 0123

For USA: Rx only

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com
+800 5505 6606

Distribution in USA by:
Roche Diagnostics, Indianapolis, IN
US Customer Technical Support 1-800-428-2336

LIPC

cobas®

Lipase colorimetric

Order information

REF	CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
07041918190	Lipase colorimetric (580 tests)	System-ID 05 5900 8	**cobas c** 701/702
Materials required (but not provided):			
10759350190	Calibrator f.a.s. (12 x 3 mL)	Code 401	
10759350360	Calibrator f.a.s. (12 x 3 mL, for USA)	Code 401	
12149435122	Precinorm U plus (10 x 3 mL)	Code 300	
12149435160	Precinorm U plus (10 x 3 mL, for USA)	Code 300	
12149443122	Precipath U plus (10 x 3 mL)	Code 301	
12149443160	Precipath U plus (10 x 3 mL, for USA)	Code 301	
05117003190	PreciControl ClinChem Multi 1 (20 x 5 mL)	Code 391	
05947626190	PreciControl ClinChem Multi 1 (4 x 5 mL)	Code 391	
05947626160	PreciControl ClinChem Multi 1 (4 x 5 mL, for USA)	Code 391	
05117216190	PreciControl ClinChem Multi 2 (20 x 5 mL)	Code 392	
05947774190	PreciControl ClinChem Multi 2 (4 x 5 mL)	Code 392	
05947774160	PreciControl ClinChem Multi 2 (4 x 5 mL, for USA)	Code 392	
05172152190	Diluent NaCl 9 % (119 mL)	System-ID 08 6869 3	

English

New application

System information

LIP: ACN 8789

S-LIP: ACN 8786 (STAT, reaction time: 5)

Intended use

Enzymatic in vitro test for the quantitative determination of lipase in human serum and plasma on Roche/Hitachi **cobas c** systems.

Summary[1,2,3,4,5,6,7]

Lipases are glycoproteins with a molecular weight of 47000 Da. They are defined as triglyceride hydrolases which catalyze the cleavage of triglycerides to diglycerides with subsequent formation of monoglycerides and fatty acids. In addition to α-amylase, pancreatic lipases have for many years been undeniably the most important clinical chemistry parameters for the differential diagnosis of diseases of the pancreas. The lipase activity determination has gained increasing international recognition because of its high specificity and rapid response. After acute pancreatitis the lipase activity increases within 4-8 hours, reaches a peak after 24 hours and decreases after 8-14 days. However, there is no correlation between the lipase activity determined in serum and the extent of damage to the pancreas.

Numerous methods have been described for the determination of lipase which determine the decrease in substrate turbidimetrically or nephelometrically or determine degradation products.

This method is based on the cleavage of a specific chromogenic lipase substrate 1,2-O-dilauryl-rac-glycero-3-glutaric acid-(6-methylresorufin) ester emulsified with bile acids. The pancreatic enzyme activity is determined specifically by the combination of bile acid and colipase used in this assay. Virtually no lipase activity is detected in the absence of colipase. Colipase only activates pancreatic lipase, but not other lipolytic enzymes found in serum. The high amount of cholates ensures that the esterases present in the serum do not react with the chromogenic substrate due to the highly negative surface charge.

Test principle[8,9,10,11]

Enzymatic colorimetric assay with 1,2-O-dilauryl-rac-glycero-3-glutaric-acid-(6-methylresorufin) ester as substrate.

The chromogenic lipase substrate 1,2-O-dilauryl-rac-glycero-3-glutaric-acid-(6-methylresorufin) ester is cleaved by the catalytic action of alkaline lipase solution to form 1,2-O-dilauryl-rac-glycerol and an unstable intermediate, glutaric acid-(6-methylresorufin) ester. This decomposes spontaneously in alkaline solution to form glutaric acid and methylresorufin. Addition of detergent and colipase increases the specificity of the assay for pancreatic lipase.

1,2-O-dilauryl-rac-glycero-3-glutaric acid-(6-methylresorufin) ester $\xrightarrow{\text{lipase}}$ 1,2-O-dilauryl-rac-glycerol + glutaric acid-(6-methylresorufin) ester

glutaric acid-(6-methylresorufin) ester $\xrightarrow[\text{decomposition}]{\text{spontaneous}}$ glutaric acid + methylresorufin

The color intensity of the red dye formed is directly proportional to the lipase activity and can be determined photometrically.

Reagents - working solutions

R1	BICIN[a)] buffer: 50 mmol/L, pH 8.0; colipase (porcine pancreas): ≥ 0.9 mg/L; Na-deoxycholate: 1.6 mmol/L; calcium chloride: 10 mmol/L; detergent; preservative
R3 (STAT R2)	Tartrate buffer: 10 mmol/L, pH 4.16; 1,2-O-dilauryl-rac-glycero-3-glutaric-acid-(6-methylresorufin) ester: 0.27 mmol/L; taurodeoxycholate: 8.8 mmol/L; detergent; preservative

a) BICIN = N,N-bis(2-hydroxyethyl)glycine

R1 is in position B and R3 (STAT R2) is in position C.

Precautions and warnings

For in vitro diagnostic use for health care professionals. Exercise the normal precautions required for handling all laboratory reagents.

Infectious or microbial waste:
Warning: handle waste as potentially biohazardous material. Dispose of waste according to accepted laboratory instructions and procedures.

Environmental hazards:
Apply all relevant local disposal regulations to determine the safe disposal.

Safety data sheet available for professional user on request.

This kit contains components classified as follows in accordance with the Regulation (EC) No. 1272/2008:

Warning

H317 May cause an allergic skin reaction.

Prevention:

LIPC

Lipase colorimetric

P261	Avoid breathing mist or vapours.
P272	Contaminated work clothing should not be allowed out of the workplace.
P280	Wear protective gloves.

Response:

P333 + P313	If skin irritation or rash occurs: Get medical advice/attention.
P362 + P364	Take off contaminated clothing and wash it before reuse.

Disposal:

P501	Dispose of contents/container to an approved waste disposal plant.

Product safety labeling follows EU GHS guidance.

Contact phone: all countries: +49-621-7590, USA: 1-800-428-2336

Reagent handling

Ready for use

Storage and stability

LIPC

Shelf life at 2-8 °C:	See expiration date on **cobas c** pack label.
On-board in use and refrigerated on the analyzer:	4 weeks
On-board on the Reagent Manager:	24 hours

Diluent NaCl 9 %

Shelf life at 2-8 °C:	See expiration date on **cobas c** pack label.
On-board in use and refrigerated on the analyzer:	4 weeks
On-board on the Reagent Manager:	24 hours

Specimen collection and preparation

For specimen collection and preparation only use suitable tubes or collection containers.

Only the specimens listed below were tested and found acceptable.
Serum.
Plasma: Li-heparin plasma

The sample types listed were tested with a selection of sample collection tubes that were commercially available at the time of testing, i.e. not all available tubes of all manufacturers were tested. Sample collection systems from various manufacturers may contain differing materials which could affect the test results in some cases. When processing samples in primary tubes (sample collection systems), follow the instructions of the tube manufacturer.

Centrifuge samples containing precipitates before performing the assay.

See the limitations and interferences section for details about possible sample interferences.

Sample stability claims were established by experimental data by the manufacturer or based on reference literature and only for the temperatures/time frames as stated in the method sheet. It is the responsibility of the individual laboratory to use all available references and/or its own studies to determine specific stability criteria for its laboratory.

Stability in serum:[12]	7 days at 20-25 °C
	7 days at 4-8 °C
	1 year at -20 °C (±5 °C)
Stability in plasma:	1 week at 15-25 °C
	1 week at 2-8 °C
	2 months at -20 °C (±5 °C)

Materials provided

See “Reagents – working solutions” section for reagents.

Materials required (but not provided)

- See “Order information” section
- General laboratory equipment

Assay

For optimum performance of the assay follow the directions given in this document for the analyzer concerned. Refer to the appropriate operator’s manual for analyzer-specific assay instructions.

The performance of applications not validated by Roche is not warranted and must be defined by the user.

Application for serum and plasma

cobas c 701/702 **test definition**

Assay type	Rate A	
Reaction time / Assay points	10 / 22-25 (STAT 5 / 10-13)	
Wavelength (sub/main)	700/570 nm	
Reaction direction	Increase	
Units	U/L (µkat/L)	
Reagent pipetting		Diluent (H_2O)
R1	80 µL	20 µL
R3 (STAT R2)	48 µL	–

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	2 µL	–	–
Decreased	2 µL	15	135
Increased	2 µL	–	–

Calibration

Calibrators	S1: H_2O
	S2: C.f.a.s.
Calibration mode	Linear
Calibration frequency	2-point calibration • after reagent lot change • as required following quality control procedures

Calibration interval may be extended based on acceptable verification of calibration by the laboratory.

Traceability: This method has been standardized manually against Roche reagent using the substrate-specific absorptivity, ε.

Quality control

For quality control, use control materials as listed in the "Order information" section.

In addition, other suitable control material can be used.

The control intervals and limits should be adapted to each laboratory’s individual requirements. Values obtained should fall within the defined limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

Follow the applicable government regulations and local guidelines for quality control.

Calculation

cobas c systems automatically calculate the analyte activity of each sample.

LIPC

Lipase colorimetric

Conversion factor: U/L x 0.0167 = µkat/L

Limitations - interference

Criterion: Recovery within ±10 % of initial values at a lipase activity of 60 U/L (1.00 µkat/L).

Icterus:[13] No significant interference up to an I index of 60 for conjugated and unconjugated bilirubin (approximate conjugated and unconjugated bilirubin concentration: 1026 µmol/L or 60 mg/dL).

Hemolysis:[13] No significant interference up to an H index of 100 (approximate hemoglobin concentration: 62 µmol/L or 100 mg/dL).

Lipemia (Intralipid):[13] No significant interference up to an L index of 2000. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Drugs: No interference was found at therapeutic concentrations using common drug panels.[14,15]

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[16]

For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

ACTION REQUIRED

Special Wash Programming: The use of special wash steps is mandatory when certain test combinations are run together on **cobas c** systems. All special wash programming necessary for avoiding carry-over is available via the **cobas** link, manual input is required in certain cases. The latest version of the carry-over evasion list can be found with the NaOHD/SMS/SmpCln1+2/SCCS Method Sheet and for further instructions refer to the operator's manual.

Where required, special wash/carry-over evasion programming must be implemented prior to reporting results with this test.

Limits and ranges

Measuring range

3-300 U/L (0.05-5.01 µkat/L)

Determine samples having higher activities via the rerun function. Dilution of samples via the rerun function is a 1:10 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 10.

Lower limits of measurement

Limit of Blank, Limit of Detection and Limit of Quantitation

Limit of Blank = 3 U/L (0.05 µkat/L)

Limit of Detection = 3 U/L (0.05 µkat/L)

Limit of Quantitation = 5 U/L (0.08 µkat/L)

The Limit of Blank, Limit of Detection and Limit of Quantitation were determined in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP17-A2 requirements.

The Limit of Blank is the 95th percentile value from n ≥ 60 measurements of analyte-free samples over several independent series. The Limit of Blank corresponds to the concentration below which analyte-free samples are found with a probability of 95 %.

The Limit of Detection is determined based on the Limit of Blank and the standard deviation of low concentration samples.

The Limit of Detection corresponds to the lowest analyte concentration which can be detected (value above the Limit of Blank with a probability of 95 %).

The Limit of Quantitation is the lowest analyte concentration that can be reproducibly measured with a precision coefficient of variation of 20 %. It has been determined using low concentration of lipase samples.

Expected values[17]

Adults: 13-60 U/L (0.22-1.00 µkat/L)

Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.

Specific performance data

Representative performance data on the analyzers are given below. Results obtained in individual laboratories may differ.

Precision

Repeatability and intermediate precision were determined using human samples and controls in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP5 requirements (2 aliquots per run, 2 runs per day, 21 days). The following results were obtained:

LIP

Repeatability	*Mean* U/L (µkat/L)	*SD* U/L (µkat/L)	*CV* %
PCCC Multi 1	45.4 (0.76)	0.49 (0.01)	1.1
PCCC Multi 2	100 (1.67)	0.79 (0.01)	0.8
Human serum 1	12.0 (0.20)	0.28 (0.005)	2.3
Human serum 2	47.1 (0.79)	0.48 (0.01)	1.0
Human serum 3	74.5 (1.24)	1.12 (0.02)	1.5
Human serum 4	139 (2.32)	2.10 (0.04)	1.5
Human serum 5	286 (4.78)	3.23 (0.05)	1.1

Intermediate precision	*Mean* U/L (µkat/L)	*SD* U/L (µkat/L)	*CV* %
PCCC Multi 1	45.4 (0.76)	0.91 (0.02)	2.0
PCCC Multi 2	100 (1.67)	2.10 (0.04)	2.1
Human serum 1	12.0 (0.20)	0.41 (0.01)	3.5
Human serum 2	47.1 (0.79)	0.92 (0.02)	1.9
Human serum 3	74.5 (1.24)	1.71 (0.03)	2.3
Human serum 4	139 (2.32)	3.04 (0.05)	2.2
Human serum 5	286 (4.78)	5.85 (0.10)	2.0

S-LIP

Repeatability	*Mean* U/L (µkat/L)	*SD* U/L (µkat/L)	*CV* %
PCCC Multi 1	46.2 (0.77)	0.47 (0.01)	1.0
PCCC Multi 2	102 (1.70)	0.89 (0.01)	0.9
Human serum 1	12.3 (0.21)	0.29 (0.005)	2.3
Human serum 2	47.8 (0.80)	0.50 (0.01)	1.1
Human serum 3	75.4 (1.26)	0.96 (0.02)	1.3
Human serum 4	141 (2.35)	1.56 (0.03)	1.1
Human serum 5	290 (4.84)	2.46 (0.04)	0.8

Intermediate precision	*Mean* U/L (µkat/L)	*SD* U/L (µkat/L)	*CV* %
PCCC Multi 1	46.2 (0.77)	0.94 (0.02)	2.0
PCCC Multi 2	102 (1.70)	1.94 (0.03)	1.9
Human serum 1	12.3 (0.21)	0.37 (0.01)	3.0
Human serum 2	47.8 (0.80)	0.94 (0.02)	2.0
Human serum 3	75.4 (1.26)	1.55 (0.03)	2.1
Human serum 4	141 (2.35)	2.51 (0.04)	1.8
Human serum 5	290 (4.84)	4.93 (0.08)	1.7

PCCC = PreciControl ClinChem

Method comparison

Lipase values for human serum and plasma samples obtained on a **cobas c** 701 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 501 analyzer (x).

LIPC

Lipase colorimetric

LIP:

Sample size (n) = 102

Passing/Bablok[18]	Linear regression
y = 1.00x + 0.482 U/L	y = 0.997x + 0.792 U/L
r = 0.985	r = 1.000

The sample activities were between 4.2 and 294 U/L (0.07 and 4.91 µkat/L).

S-LIP:

Sample size (n) = 99

Passing/Bablok[18]	Linear regression
y = 1.00x + 0.153 U/L	y = 1.00x + 0.304 U/L
r = 0.984	r = 0.999

The sample activities were between 4.2 and 294 U/L (0.07 and 4.91 µkat/L).

References

1 Greiling H, Gressner AM, eds. Lehrbuch der Klinischen Chemie und Pathobiochemie, 3rd ed. Stuttgart/New York: Schattauer Verlag 1995.

2 Keller H, ed. Klinisch-chemische Labordiagnostik für die Praxis, 2nd ed. Stuttgart/New York: Georg Thieme Verlag 1991:354-361.

3 Kazmierczak S, Catrou P, Van Lente F. Diagnostic accuracy of pancreatic enzymes evaluated by use of multivariate data analysis. Clin Chem 1993;39:1960-1965.

4 Steinberg WM, Goldstein SS, Davies ND, et al. Diagnostic assays in acute pancreatitis [Review]. Ann Intern Med 1985;102:576-580.

5 Panteghini M, Pagani F, Bonora R, et al. Diagnostic value of four assays for lipase determination in serum: A comparative reevalution. Clin Biochem 1991;24:497-503.

6 Tietz NW, Shuey DF. Lipase in serum - the elusive enzyme: An overview. Clin Chem 1993;39(5):746-756.

7 Tietz NW, ed. Clinical Guide to Laboratory Tests, 3rd ed. Philadelphia PA: WB Saunders Company 1995;865.

8 Neumann U, Junius M, Batz HG, et al. New substrates for the optical determination of lipase. EP 207252 1987.

9 Borgström B. The action of bile salts and other detergents on pancreatic lipase and the interaction with colipase. Biochimica et Biophysica Acta 1977;488:381-391.

10 Gargouri Y, Julien R, Bois A, et al. Studies on the detergent inhibition of pancreatic lipase activity. J of Lipid Research 1983;24:1336-1342.

11 Leybold A, Junge W. Importance of colipase for the measurement of serum lipase activity. Adv Clin Enzymol 1986;4:60-67.

12 Guder W, Fonseca-Wollheim W, Heil O, et al. Maximum permissible transport and storage times for analysis of blood (serum, plasma), urine and cerebrospinal fluid. DG Klinische Chemische Mitteilungen 1995;26:207-224.

13 Glick MR, Ryder KW, Jackson SA. Graphical Comparisons of Interferences in Clinical Chemistry Instrumentation. Clin Chem 1986;32:470-475.

14 Breuer J. Report on the Symposium "Drug effects in Clinical Chemistry Methods". Eur J Clin Chem Clin Biochem 1996;34:385-386.

15 Sonntag O, Scholer A. Drug interference in clinical chemistry: recommendation of drugs and their concentrations to be used in drug interference studies. Ann Clin Biochem 2001;38:376-385.

16 Bakker AJ, Mücke M. Gammopathy interference in clinical chemistry assays: mechanisms, detection and prevention. Clin Chem Lab Med 2007;45(9):1240-1243.

17 Junge W, Abicht K, Goldmann J, et al. Evaluation of the Colorimetric Liquid Assay for Pancreatic Lipase on Hitachi Analyzers in 7 Clinical Centers in Europe, Japan and USA. Clin Chem Lab Med 1999;37(Special Suppl):469.

18 Bablok W, Passing H, Bender R, et al. A general regression procedure for method transformation. Application of linear regression procedures for method comparison studies in clinical chemistry, Part III. J Clin Chem Clin Biochem 1988 Nov;26(11):783-790.

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Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard (for USA: see navifyportal.roche.com for definition of symbols used):

CONTENT	Contents of kit
→	Volume for reconstitution
GTIN	Global Trade Item Number
Rx only	For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

FOR US CUSTOMERS ONLY: LIMITED WARRANTY

Roche Diagnostics warrants that this product will meet the specifications stated in the labeling when used in accordance with such labeling and will be free from defects in material and workmanship until the expiration date printed on the label. THIS LIMITED WARRANTY IS IN LIEU OF ANY OTHER WARRANTY, EXPRESS OR IMPLIED, INCLUDING ANY IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR PARTICULAR PURPOSE. IN NO EVENT SHALL ROCHE DIAGNOSTICS BE LIABLE FOR INCIDENTAL, INDIRECT, SPECIAL OR CONSEQUENTIAL DAMAGES.

CE 0123

For USA: Rx only

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com
+800 5505 6606

Distribution in USA by:
Roche Diagnostics, Indianapolis, IN
US Customer Technical Support 1-800-428-2336

LIPC

cobas®

Lipase colorimetric

Order information

REF	CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
03029590322	Lipase colorimetric (200 tests)	System-ID 07 5900 7	COBAS INTEGRA 400 plus

Materials required (but not provided):

10759350190	Calibrator f.a.s. (12 x 3 mL)	System-ID 07 3718 6	
10759350360	Calibrator f.a.s. (12 x 3 mL, for USA)	System-ID 07 3718 6	
12149435122	Precinorm U plus (10 x 3 mL)	System-ID 07 7999 7	
12149435160	Precinorm U plus (10 x 3 mL, for USA)	System-ID 07 7999 7	
12149443122	Precipath U plus (10 x 3 mL)	System-ID 07 8000 6	
12149443160	Precipath U plus (10 x 3 mL, for USA)	System-ID 07 8000 6	
05117003190	PreciControl ClinChem Multi 1 (20 x 5 mL)	System-ID 07 7469 3	
05947626190	PreciControl ClinChem Multi 1 (4 x 5 mL)	System-ID 07 7469 3	
05947626160	PreciControl ClinChem Multi 1 (4 x 5 mL, for USA)	System-ID 07 7469 3	
05117216190	PreciControl ClinChem Multi 2 (20 x 5 mL)	System-ID 07 7470 7	
05947774190	PreciControl ClinChem Multi 2 (4 x 5 mL)	System-ID 07 7470 7	
05947774160	PreciControl ClinChem Multi 2 (4 x 5 mL, for USA)	System-ID 07 7470 7	

English

New application

System information

Test LIP, test ID 0-052

Intended use

In vitro test for the quantitative determination of the catalytic activity of lipase (EC 3.1.1.3; triacylglycerol acyl-hydrolase) in human serum and plasma on COBAS INTEGRA systems.

Summary[1,2,3,4,5,6,7]

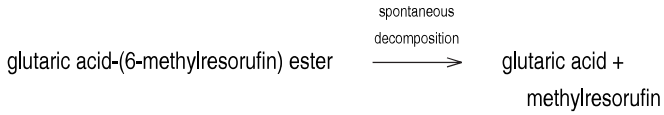
Lipases are glycoproteins with a molecular weight of 47000 daltons. They are defined as triglyceride hydrolases which catalyze the cleavage of triglycerides to diglycerides with subsequent formation of monoglycerides and fatty acids. In addition to α-amylase, pancreatic lipases have for many years been undeniably the most important clinical chemistry parameters for the differential diagnosis of diseases of the pancreas. The lipase activity determination has gained increasing international recognition because of its high specificity and rapid response. After acute pancreatitis the lipase activity increases within 4-8 hours, reaches a peak after 24 hours and decreases after 8 to 14 days. However, there is no correlation between the lipase activity determined in serum and the extent of damage to the pancreas. Numerous methods have been described for the determination of lipase which determine the decrease in substrate turbidimetrically or nephelometrically or determine degradation products.

This method is based on the cleavage of a specific chromogenic lipase substrate 1,2-O-dilauryl-rac-glycero-3-glutaric acid-(6-methylresorufin) ester emulsified with bile acids. The pancreatic enzyme activity is determined specifically by the combination of bile acid and colipase used in this assay. Virtually no lipase activity is detected in the absence of colipase. Colipase only activates pancreatic lipase, but not other lipolytic enzymes found in serum. The high amount of cholates ensures that the esterases present in the serum do not react with the chromogenic substrate due to the highly negative surface charge.

Test principle[8,9,10,11]

Enzymatic colorimetric assay with 1,2-O-dilauryl-rac-glycero-3-glutaric acid-(6-methylresorufin) ester as substrate.

The chromogenic lipase substrate 1,2-O-dilauryl-rac-glycero-3-glutaric acid-(6-methylresorufin) ester is cleaved by the catalytic action of alkaline lipase solution to form 1,2-O-dilauryl-rac-glycerol and an unstable intermediate, glutaric acid (6-methylresorufin) ester. This decomposes spontaneously in alkaline solution to form glutaric acid and methylresorufin. Addition of detergent and colipase increases the specificity of the assay for pancreatic lipase.



The color intensity of the red dye formed is directly proportional to the lipase activity and can be determined photometrically.

Reagents - working solutions

R1 BICIN[a] buffer: 50 mmol/L, pH 8.0; colipase (porcine pancreas): ≥ 0.9 mg/L; Na-deoxycholate: 1.6 mmol/L; calcium chloride: 10 mmol/L; detergent; preservative

SR Tartrate buffer: 10 mmol/L, pH 4.16; 1,2-O-dilauryl-rac-glycero-3-glutaric acid-(6-methylresorufin) ester: 0.27 mmol/L; taurodeoxycholate: 8.8 mmol/L; detergent; preservative

a) BICIN = N,N-bis(2-hydroxyethyl)glycine

R1 is in position B and SR is in position C.

Precautions and warnings

For in vitro diagnostic use for health care professionals. Exercise the normal precautions required for handling all laboratory reagents.

Infectious or microbial waste:
Warning: handle waste as potentially biohazardous material. Dispose of waste according to accepted laboratory instructions and procedures.

Environmental hazards:
Apply all relevant local disposal regulations to determine the safe disposal.

Safety data sheet available for professional user on request.

This kit contains components classified as follows in accordance with the Regulation (EC) No. 1272/2008:

Warning

H317	May cause an allergic skin reaction.

Prevention:

P261	Avoid breathing mist or vapours.
P272	Contaminated work clothing should not be allowed out of the workplace.
P280	Wear protective gloves.

LIPC

Lipase colorimetric

Response:

P333 + P313	If skin irritation or rash occurs: Get medical advice/attention.
P362 + P364	Take off contaminated clothing and wash it before reuse.

Disposal:

P501	Dispose of contents/container to an approved waste disposal plant.

Product safety labeling follows EU GHS guidance.

Contact phone: all countries: +49-621-7590, USA: 1-800-428-2336

Reagent handling

Ready for use

Storage and stability

Shelf life at 2-8 °C	See expiration date on **cobas c** pack label
COBAS INTEGRA 400 plus system	
On-board in use at 10-15 °C	4 weeks

Specimen collection and preparation

For specimen collection and preparation only use suitable tubes or collection containers.

Only the specimens listed below were tested and found acceptable:
Serum: collect serum using standard sampling tubes. Fresh serum is the specimen of choice.
Plasma: Li-heparin plasma

Do not use calcium complexing anticoagulants such as EDTA, citrate, and fluoride.

The sample types listed were tested with a selection of sample collection tubes that were commercially available at the time of testing, i.e. not all available tubes of all manufacturers were tested. Sample collection systems from various manufacturers may contain differing materials which could affect the test results in some cases. When processing samples in primary tubes (sample collection systems), follow the instructions of the tube manufacturer.

Centrifuge samples containing precipitates before performing the assay.

See the limitations and interferences section for details about possible sample interferences.

Sample stability claims were established by experimental data by the manufacturer or based on reference literature and only for the temperatures/time frames as stated in the method sheet. It is the responsibility of the individual laboratory to use all available references and/or its own studies to determine specific stability criteria for its laboratory.

Stability in serum:[12]	7 days at 20-25 °C
	7 days at 4-8 °C
	1 year at -20 °C (±5 °C)
Stability in plasma:	1 week at 15-25 °C
	1 week at 2-8 °C
	2 months at -20 °C (±5 °C)

Materials provided

See “Reagents – working solutions” section for reagents.

Assay

For optimum performance of the assay follow the directions given in this document for the analyzer concerned. Refer to the appropriate operator’s manual for analyzer-specific assay instructions.

Application for serum and plasma

COBAS INTEGRA 400 plus test definition

Measuring mode	Absorbance
Abs. calculation mode	Kinetic
Reaction mode	R1-S-SR
Reaction direction	Increase
Wavelength A/B	583/659 nm
Calc. first/last	40-46
Unit	U/L

Pipetting parameters

		Diluent (H_2O)
R1	80 µL	
Sample	2 µL	20 µL
SR	48 µL	
Total volume	150 µL	

Calibration

Calibrator	Calibrator f.a.s.
	Use deionized water as zero calibrator.
Calibration mode	Linear regression
Calibration replicate	Duplicate recommended
Calibration interval	Each lot and as required following quality control procedures

Calibration interval may be extended based on acceptable verification of calibration by the laboratory.

Traceability: This method has been standardized manually against Roche reagent using the substrate-specific absorptivity, ε.

Quality control

Reference range	Precinorm U plus or PreciControl ClinChem Multi 1
Pathological range	Precipath U plus or PreciControl ClinChem Multi 2
Control interval	24 hours recommended
Control sequence	User defined
Control after calibration	Recommended

For quality control, use control materials as listed in the “Order information” section. In addition, other suitable control material can be used.

The control intervals and limits should be adapted to each laboratory’s individual requirements. Values obtained should fall within the defined limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

Follow the applicable government regulations and local guidelines for quality control.

Calculation

COBAS INTEGRA analyzers automatically calculate the analyte activity of each sample. For more details, please refer to Data Analysis in the Online Help (COBAS INTEGRA 400 plus analyzers).

Conversion factor: U/L × 0.0167 = µkat/L

Limitations - interference

Criterion: Recovery within ±10 % of an initial value at a lipase activity of 60 U/L (1.00 µkat/L).

Icterus:[13] No significant interference up to an I index of 60 for conjugated and unconjugated bilirubin (approximate conjugated and unconjugated bilirubin concentration: 1026 µmol/L or 60 mg/dL).

Hemolysis:[13] No significant interference up to an H index of 100 (approximate hemoglobin concentration: 62 µmol/L or 100 mg/dL).

Lipemia (Intralipid):[13] No significant interference up to an L index of 2000. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

LIPC

Lipase colorimetric

Drugs: No interference was found at therapeutic concentrations using common drug panels.[14,15]

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[16]

For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

ACTION REQUIRED

Special Wash Programming: The use of special wash steps is mandatory when certain test combinations are run together on COBAS INTEGRA analyzers. Refer to the CLEAN Method Sheet for further instructions and for the latest version of the Extra wash cycle list.

Where required, special wash/carry-over evasion programming must be implemented prior to reporting results with this test.

Limits and ranges

Measuring range

3-300 U/L (0.05-5.01 µkat/L)

Determine samples having higher activities via the rerun function. Dilution of samples via the rerun function is a 1:10 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 10.

Lower limits of measurement

Limit of Blank, Limit of Detection and Limit of Quantitation

Limit of Blank	= 3 U/L (0.05 µkat/L)
Limit of Detection	= 3 U/L (0.05 µkat/L)
Limit of Quantitation	= 5 U/L (0.08 µkat/L)

The Limit of Blank, Limit of Detection and Limit of Quantitation were determined in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP17-A2 requirements.

The Limit of Blank is the 95th percentile value from n ≥ 60 measurements of analyte-free samples over several independent series. The Limit of Blank corresponds to the concentration below which analyte-free samples are found with a probability of 95 %.

The Limit of Detection is determined based on the Limit of Blank and the standard deviation of low concentration samples.

The Limit of Detection corresponds to the lowest analyte concentration which can be detected (value above the Limit of Blank with a probability of 95 %).

The Limit of Quantitation is the lowest analyte concentration that can be reproducibly measured with a precision coefficient of variation of 20 %. It has been determined using low concentration of lipase samples.

Expected values[17]

Adults	13-60 U/L	(0.22-1.00 µkat/L)

Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.

Specific performance data

Representative performance data on the analyzers are given below. Results obtained in individual laboratories may differ.

Precision

Repeatability and intermediate precision were determined using human samples and controls in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP5 requirements (2 aliquots per run, 2 runs per day, 21 days). The following results were obtained:

Repeatability	*Mean* U/L (µkat/L)	*SD* U/L (µkat/L)	*CV* %
PCCC Multi 1	46.4 (0.78)	0.64 (0.012)	1.4
PCCC Multi 2	97.8 (1.63)	1.46 (0.024)	1.5
Human serum 1	12.6 (0.21)	0.33 (0.006)	2.6
Human serum 2	47.4 (0.79)	0.63 (0.011)	1.3
Human serum 3	75.1 (1.25)	0.90 (0.015)	1.2
Human serum 4	139 (2.32)	1.59 (0.027)	1.1
Human serum 5	264 (4.41)	3.24 (0.054)	1.2

Intermediate precision	*Mean* U/L (µkat/L)	*SD* U/L (µkat/L)	*CV* %
PCCC Multi 1	46.4 (0.78)	0.86 (0.014)	1.8
PCCC Multi 2	99.5 (1.66)	1.98 (0.033)	2.0
Human serum 1	12.6 (0.21)	0.35 (0.006)	2.7
Human serum 2	47.4 (0.79)	0.95 (0.016)	2.0
Human serum 3	74.5 (1.24)	1.43 (0.024)	1.9
Human serum 4	138 (2.31)	2.74 (0.046)	2.0
Human serum 5	269 (4.49)	4.95 (0.083)	1.8

PCCC = PreciControl ClinChem

Method comparison

Lipase values for human serum and plasma samples obtained on a COBAS INTEGRA 400 plus analyzer with the COBAS INTEGRA Lipase colorimetric reagent (y) were compared with those determined using the corresponding reagent on a Roche/Hitachi MODULAR P analyzer (x).

Sample size (n) = 108

Passing/Bablok[18]	Linear regression
y = 1.01x - 0.643 U/L	y = 1.01x - 0.269 U/L
τ = 0.982	r = 0.999

The sample activities were between 4.93 and 293 U/L (0.08 and 4.89 µkat/L).

References

1 Greiling H, Gressner AM, eds. Lehrbuch der Klinischen Chemie und Pathobiochemie, 3rd ed. Stuttgart/New York: Schattauer Verlag 1995.

2 Keller H, ed. Klinisch-chemische Labordiagnostik für die Praxis, 2nd ed. Stuttgart/New York: Georg Thieme Verlag 1991:354-361.

3 Kazmierczak S, Catrou P, Van Lente F. Diagnostic accuracy of pancreatic enzymes evaluated by use of multivariate data analysis. Clin Chem 1993;39:1960-1965.

4 Steinberg WM, Goldstein SS, Davies ND, et al. Diagnostic assays in acute pancreatitis [Review]. Ann Intern Med 1985;102:576-580.

5 Panteghini M, Pagani F, Bonora R, et al. Diagnostic value of four assays for lipase determination in serum: A comparative reevalution. Clin Biochem 1991;24:497-503.

6 Tietz NW, Shuey DF. Lipase in serum - the elusive enzyme: An overview. Clin Chem 1993;39(5):746-756

7 Tietz NW, ed. Clinical Guide to Laboratory Tests, 3rd ed. Philadelphia PA: WB Saunders Company 1995;865.

8 Neumann U, Junius M, Batz HG, et al. New substrates for the optical determination of lipase. EP 207252 1987.

9 Borgström B. The action of bile salts and other detergents on pancreatic lipase and the interaction with colipase. Biochimica et Biophysica Acta 1977;488:381-391.

10 Gargouri Y, Julien R, Bois A, et al. Studies on the detergent inhibition of pancreatic lipase activity. J of Lipid Research 1983;24:1336-1342.

11 Leybold A, Junge W. Importance of colipase for the measurement of serum lipase activity. Adv Clin Enzymol 1986;4:60-67.

12 Guder W, Fonseca-Wollheim W, Heil O, et al. Maximum permissible transport and storage times for analysis of blood (serum, plasma), urine and cerebrospinal fluid. DG Klinische Chemische Mitteilungen 1995;26:207-224.

13 Glick MR, Ryder KW, Jackson SA. Graphical Comparisons of Interferences in Clinical Chemistry Instrumentation. Clin Chem 1986;32:470-475.

14 Breuer J. Report on the Symposium "Drug effects in Clinical Chemistry Methods". Eur J Clin Chem Clin Biochem 1996;34:385-386.

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CE 0123

For USA: Rx only

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+800 5505 6606

Distribution in USA by:
Roche Diagnostics, Indianapolis, IN
US Customer Technical Support 1-800-428-2336

05403669001V3.0

LIPC

cobas®

Lipase colorimetric assay

Order information

REF	CONTENT		Analyzer(s) on which kit(s) can be used
05401704190	Lipase colorimetric assay (2 x 50 tests)		**cobas c** 111

Materials required (but not provided):

10759350190	Calibrator f.a.s. (12 x 3 mL)	Code 401	
10759350360	Calibrator f.a.s. (12 x 3 mL, for USA)	Code 401	
12149435122	Precinorm U plus (10 x 3 mL)	Code 300	
12149435160	Precinorm U plus (10 x 3 mL, for USA)	Code 300	
12149443122	Precipath U plus (10 x 3 mL)	Code 301	
12149443160	Precipath U plus (10 x 3 mL, for USA)	Code 301	
05117003190	PreciControl ClinChem Multi 1 (20 x 5 mL)	Code 391	
05947626190	PreciControl ClinChem Multi 1 (4 x 5 mL)	Code 391	
05947626160	PreciControl ClinChem Multi 1 (4 x 5 mL, for USA)	Code 391	
05117216190	PreciControl ClinChem Multi 2 (20 x 5 mL)	Code 392	
05947774190	PreciControl ClinChem Multi 2 (4 x 5 mL)	Code 392	
05947774160	PreciControl ClinChem Multi 2 (4 x 5 mL, for USA)	Code 392	
04774248190	Cleaner	Code 947	

English

New application

System information

LIP: ACN 789

Intended use

Enzymatic in vitro test for the quantitative determination of lipase in human serum and plasma on the **cobas c** 111 system.

Summary[1,2,3,4,5,6,7]

Lipases are glycoproteins with a molecular weight of 47000 daltons. They are defined as triglyceride hydrolases which catalyze the cleavage of triglycerides to diglycerides with subsequent formation of monoglycerides and fatty acids. In addition to α-amylase, pancreatic lipases have for many years been undeniably the most important clinical chemistry parameters for the differential diagnosis of diseases of the pancreas. The lipase activity determination has gained increasing international recognition because of its high specificity and rapid response. After acute pancreatitis the lipase activity increases within 4-8 hours, reaches a peak after 24 hours and decreases after 8 to 14 days. However, there is no correlation between the lipase activity determined in serum and the extent of damage to the pancreas.

Numerous methods have been described for the determination of lipase which determine the decrease in substrate turbidimetrically or nephelometrically or determine degradation products.

This method is based on the cleavage of a specific chromogenic lipase substrate 1,2-O-dilauryl-rac-glycero-3-glutaric acid-(6-methylresorufin) ester emulsified with bile acids. The pancreatic enzyme activity is determined specifically by the combination of bile acid and colipase used in this assay. Virtually no lipase activity is detected in the absence of colipase. Colipase only activates pancreatic lipase, but not other lipolytic enzymes found in serum. The high amount of cholates ensures that the esterases present in the serum do not react with the chromogenic substrate due to the highly negative surface charge.

Test principle[8,9,10,11]

Enzymatic colorimetric assay with 1,2-O-dilauryl-rac-glycero-3-glutaric acid-(6-methylresorufin) ester as substrate.

The chromogenic lipase substrate 1,2-O-dilauryl-rac-glycero-3-glutaric acid-(6-methylresorufin) ester is cleaved by the catalytic action of alkaline lipase solution to form 1,2-O-dilauryl-rac-glycerol and an unstable intermediate, glutaric acid-(6-methylresorufin) ester. This decomposes spontaneously in alkaline solution to form glutaric acid and methylresorufin. Addition of detergent and colipase increases the specificity of the assay for pancreatic lipase.

1,2-O-dilauryl-rac-glycero-3-glutaric acid-(6-methylresorufin) ester $\xrightarrow{\text{lipase}}$ 1,2-O-dilauryl-rac-glycerol + glutaric acid-(6-methylresorufin) ester

glutaric acid-(6-methylresorufin) ester $\xrightarrow[\text{decomposition}]{\text{spontaneous}}$ glutaric acid + methylresorufin

The color intensity of the red dye formed is directly proportional to the lipase activity and can be determined photometrically.

Reagents - working solutions

R1 BICIN[a)] buffer: 50 mmol/L, pH 8.0; colipase (porcine pancreas): ≥ 0.9 mg/L; Na-deoxycholate: 1.6 mmol/L; calcium chloride: 10 mmol/L; detergent; preservative

SR Tartrate buffer: 10 mmol/L, pH 4.16; 1,2-O-dilauryl-rac-glycero-3-glutaric acid-(6-methylresorufin) ester: 0.27 mmol/L; taurodeoxycholate: 8.8 mmol/L; detergent; preservative

a) BICIN = N,N-bis(2-hydroxyethyl)glycine

Precautions and warnings

For in vitro diagnostic use for health care professionals. Exercise the normal precautions required for handling all laboratory reagents.

Infectious or microbial waste:
Warning: handle waste as potentially biohazardous material. Dispose of waste according to accepted laboratory instructions and procedures.

Environmental hazards:
Apply all relevant local disposal regulations to determine the safe disposal.

Safety data sheet available for professional user on request.

This kit contains components classified as follows in accordance with the Regulation (EC) No. 1272/2008:

Warning

H317 May cause an allergic skin reaction.

Prevention:

P261 Avoid breathing mist or vapours.

P272 Contaminated work clothing should not be allowed out of the workplace.

LIPC

Lipase colorimetric assay

P280	Wear protective gloves.

Response:

P333 + P313	If skin irritation or rash occurs: Get medical advice/attention.
P362 + P364	Take off contaminated clothing and wash it before reuse.

Disposal:

P501	Dispose of contents/container to an approved waste disposal plant.

Product safety labeling follows EU GHS guidance.

Contact phone: all countries: +49-621-7590, USA: 1-800-428-2336

Reagent handling

Ready for use

Storage and stability

Shelf life at 2-8 °C:	See expiration date on reagent
On-board in use and refrigerated on the analyzer:	4 weeks

Note: Store protected from light after opening.

Specimen collection and preparation

For specimen collection and preparation only use suitable tubes or collection containers.

Only the specimens listed below were tested and found acceptable.

Serum

Plasma: Li-heparin plasma

Do not use calcium complexing anticoagulants such as EDTA, citrate, and fluoride.

The sample types listed were tested with a selection of sample collection tubes that were commercially available at the time of testing, i.e. not all available tubes of all manufacturers were tested. Sample collection systems from various manufacturers may contain differing materials which could affect the test results in some cases. When processing samples in primary tubes (sample collection systems), follow the instructions of the tube manufacturer.

Centrifuge samples containing precipitates before performing the assay.

See the limitations and interferences section for details about possible sample interferences.

Sample stability claims were established by experimental data by the manufacturer or based on reference literature and only for the temperatures/time frames as stated in the method sheet. It is the responsibility of the individual laboratory to use all available references and/or its own studies to determine specific stability criteria for its laboratory.

Stability in serum:[12]	7 days at 20-25 °C
	7 days at 4-8 °C
	1 year at -20 °C (±5 °C)
Stability in plasma:	1 week at 15-25 °C
	1 week at 2-8 °C
	2 months at -20 °C (±5 °C)

Materials provided

See “Reagents – working solutions” section for reagents.

Materials required (but not provided)

See “Order information” section

General laboratory equipment

Assay

For optimum performance of the assay follow the directions given in this document for the analyzer concerned. Refer to the appropriate operator’s manual for analyzer-specific assay instructions.

The performance of applications not validated by Roche is not warranted and must be defined by the user.

Application for serum and plasma

cobas c 111 **test definition**

Measuring mode	Absorbance
Abs. calculation mode	Kinetic
Reaction direction	Increase
Wavelength A/B	583/659 nm
Calc. first/last	20/24
Unit	U/L
Reaction mode	R1-S-SR

Pipetting parameters

		Diluent (H_2O)
R1	80 µL	
Sample	2 µL	20 µL
SR	48 µL	
Total volume	150 µL	

Calibration

Calibrators	Calibrator f.a.s. Deionized water is used automatically by the instrument as the zero calibrator.
Calibration mode	Linear regression
Calibration interval	Each lot and as required following quality control procedures

Calibration interval may be extended based on acceptable verification of calibration by the laboratory.

Traceability: This method has been standardized manually against Roche reagent using the substrate-specific absorptivity, ε.

Quality control

For quality control, use control materials as listed in the "Order information" section.

In addition, other suitable control material can be used.

The control intervals and limits should be adapted to each laboratory’s individual requirements. Values obtained should fall within the defined limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

Follow the applicable government regulations and local guidelines for quality control.

Calculation

The **cobas c** 111 analyzer automatically calculates the analyte activity of each sample.

Conversion factor: U/L x 0.0167 = µkat/L

Limitations - interference

Criterion: Recovery within ±10 % of initial values at a lipase activity of 60 U/L (1.00 µkat/L).

Icterus:[13] No significant interference up to an I index of 60 for conjugated and unconjugated bilirubin (approximate conjugated and unconjugated bilirubin concentration: 1026 µmol/L or 60 mg/dL).

Hemolysis:[13] No significant interference up to an H index of 100 (approximate hemoglobin concentration: 62 µmol/L or 100 mg/dL).

Lipemia (Intralipid):[13] No significant interference up to an L index of 2000. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Drugs: No interference was found at therapeutic concentrations using common drug panels.[14,15]

In very rare cases, gammopathy, in particular type IgM (Waldenström’s macroglobulinemia), may cause unreliable results.[16]

LIPC

Lipase colorimetric assay

For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

ACTION REQUIRED

Special Wash Programming: The use of special wash steps is mandatory when certain test combinations are run together on the **cobas c** 111 analyzer. For information about test combinations requiring special wash steps, please refer to the latest version of the carry-over evasion list found with the CLEAN Method Sheet and the operator's manual for further instructions.

Where required, special wash/carry-over evasion programming must be implemented prior to reporting results with this test.

Limits and ranges

Measuring range

3-300 U/L (0.05-5.01 µkat/L)

Determine samples having higher activities via the rerun function. Dilution of samples via the rerun function is a 1:10 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 10.

Lower limits of measurement

Limit of Blank, Limit of Detection and Limit of Quantitation

Limit of Blank	= 3 U/L (0.05 µkat/L)
Limit of Detection	= 3 U/L (0.05 µkat/L)
Limit of Quantitation	= 5 U/L (0.08 µkat/L)

The Limit of Blank, Limit of Detection and Limit of Quantitation were determined in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP17-A2 requirements.

The Limit of Blank is the 95th percentile value from n ≥ 60 measurements of analyte-free samples over several independent series. The Limit of Blank corresponds to the concentration below which analyte-free samples are found with a probability of 95 %.

The Limit of Detection is determined based on the Limit of Blank and the standard deviation of low concentration samples.

The Limit of Detection corresponds to the lowest analyte concentration which can be detected (value above the Limit of Blank with a probability of 95 %).

The Limit of Quantitation is the lowest analyte concentration that can be reproducibly measured with a precision coefficient of variation of 20 %. It has been determined using low concentration of lipase samples.

Expected values[17]

Adults: 13-60 U/L (0.22-1.00 µkat/L)

Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.

Specific performance data

Representative performance data on the **cobas c** 111 analyzer are given below. Results obtained in individual laboratories may differ.

Precision

Repeatability and intermediate precision were determined using human samples and controls in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP5 requirements (2 aliquots per run, 2 runs per day, 21 days). The following results were obtained:

Repeatability	*Mean* *U/L (µkat/L)*	*SD* *U/L (µkat/L)*	*CV* *%*
PCCC Multi 1	47.5 (0.79)	0.78 (0.01)	1.6
PCCC Multi 2	103 (1.73)	1.20 (0.02)	1.2
Human serum 1	12.8 (0.21)	0.49 (0.01)	3.8
Human serum 2	48.8 (0.82)	0.83 (0.01)	1.7
Human serum 3	76.8 (1.28)	1.00 (0.02)	1.3
Human serum 4	144 (2.41)	1.80 (0.03)	1.3
Human serum 5	292 (4.88)	3.08 (0.05)	1.1

Intermediate precision	*Mean* *U/L (µkat/L)*	*SD* *U/L (µkat/L)*	*CV* *%*
PCCC Multi 1	47.5 (0.79)	1.04 (0.02)	2.2
PCCC Multi 2	103 (1.73)	2.11 (0.04)	2.0
Human serum 1	12.8 (0.21)	0.56 (0.01)	4.4
Human serum 2	48.8 (0.82)	1.23 (0.02)	2.5
Human serum 3	76.8 (1.28)	1.63 (0.03)	2.1
Human serum 4	144 (2.41)	3.10 (0.05)	2.2
Human serum 5	292 (4.88)	5.79 (0.1)	2.0

PCCC = PreciControl ClinChem

Method comparison

Lipase values for human serum and plasma samples obtained on the **cobas c** 111 analyzer (y) were compared with those determined using the same reagent on a COBAS INTEGRA 400 analyzer (x).

Sample size (n) = 108

Passing/Bablok[18]	Linear regression
y = 0.992x - 0.333 U/L	y = 0.992x - 0.296 U/L
τ = 0.984	r = 0.999

The sample activities were between 4.48 and 287 U/L (0.07 and 4.79 µkat/L).

References

1 Greiling H, Gressner AM, eds. Lehrbuch der Klinischen Chemie und Pathobiochemie, 3rd ed. Stuttgart/New York: Schattauer Verlag 1995.

2 Keller H, ed. Klinisch-chemische Labordiagnostik für die Praxis, 2nd ed. Stuttgart/New York: Georg Thieme Verlag 1991:354-361.

3 Kazmierczak S, Catrou P, Van Lente F. Diagnostic accuracy of pancreatic enzymes evaluated by use of multivariate data analysis. Clin Chem 1993;39:1960-1965.

4 Steinberg WM, Goldstein SS, Davies ND, et al. Diagnostic assays in acute pancreatitis [Review]. Ann Intern Med 1985;102:576-580.

5 Panteghini M, Pagani F, Bonora R, et al. Diagnostic value of four assays for lipase determination in serum: A comparative reevalution. Clin Biochem 1991;24:497-503.

6 Tietz NW, Shuey DF. Lipase in serum - the elusive enzyme: An overview. Clin Chem 1993;39(5):746-756

7 Tietz NW, ed. Clinical Guide to Laboratory Tests, 3rd ed. Philadelphia PA: WB Saunders Company 1995;865.

8 Neumann U, Junius M, Batz HG, et al. New substrates for the optical determination of lipase. EP 207252 1987.

9 Borgström B. The action of bile salts and other detergents on pancreatic lipase and the interaction with colipase. Biochimica et Biophysica Acta 1977;488:381-391.

10 Gargouri Y, Julien R, Bois A, et al. Studies on the detergent inhibition of pancreatic lipase activity. J of Lipid Research 1983;24:1336-1342.

11 Leybold A, Junge W. Importance of colipase for the measurement of serum lipase activity. Adv Clin Enzymol 1986;4:60-67.

12 Guder W, Fonseca-Wollheim W, Heil O, et al. Maximum permissible transport and storage times for analysis of blood (serum, plasma), urine and cerebrospinal fluid. DG Klinische Chemische Mitteilungen 1995;26:207-224.

13 Glick MR, Ryder KW, Jackson SA. Graphical Comparisons of Interferences in Clinical Chemistry Instrumentation. Clin Chem 1986;32:470-475.

14 Breuer J. Report on the Symposium "Drug effects in Clinical Chemistry Methods". Eur J Clin Chem Clin Biochem 1996;34:385-386.

15 Sonntag O, Scholer A. Drug interference in clinical chemistry: recommendation of drugs and their concentrations to be used in drug interference studies. Ann Clin Biochem 2001;38:376-385.

16 Bakker AJ, Mücke M. Gammopathy interference in clinical chemistry assays: mechanisms, detection and prevention. Clin Chem Lab Med 2007;45(9):1240-1243.

17 Junge W, Abicht K, Goldmann J, et al. Evaluation of the Colorimetric Liquid Assay for Pancreatic Lipase on Hitachi Analyzers in 7 Clinical Centers in Europe, Japan and USA. Clin Chem Lab Med 1999;37(Special Suppl):469.

18 Bablok W, Passing H, Bender R, et al. A general regression procedure for method transformation. Application of linear regression procedures for method comparison studies in clinical chemistry, Part III. J Clin Chem Clin Biochem 1988 Nov;26(11):783-790.

A point (period/stop) is always used in this Method Sheet as the decimal separator to mark the border between the integral and the fractional parts of a decimal numeral. Separators for thousands are not used.

Any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the Member State in which the user and/or the patient is established.

Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard (for USA: see navifyportal.roche.com for definition of symbols used):

CONTENT	Contents of kit
REAGENT	Reagent
→	Volume for reconstitution
GTIN	Global Trade Item Number
Rx only	For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

FOR US CUSTOMERS ONLY: LIMITED WARRANTY

Roche Diagnostics warrants that this product will meet the specifications stated in the labeling when used in accordance with such labeling and will be free from defects in material and workmanship until the expiration date printed on the label. THIS LIMITED WARRANTY IS IN LIEU OF ANY OTHER WARRANTY, EXPRESS OR IMPLIED, INCLUDING ANY IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR PARTICULAR PURPOSE. IN NO EVENT SHALL ROCHE DIAGNOSTICS BE LIABLE FOR INCIDENTAL, INDIRECT, SPECIAL OR CONSEQUENTIAL DAMAGES.

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