

REF		CONTENT		Analyzer(s) on which <b>cobas c</b> pack(s) can be used
05171962190*	05171962500	Fructosamine (250 tests)	System-ID 03 3756 9	<b>cobas c</b> 701/702
05171962214*	05171962500	Fructosamine (250 tests)	System-ID 03 3756 9	<b>cobas c</b> 701/702

Materials required (but not provided):

11098993122	Precimat Fructosamine (3 x 1 mL)	Code 581	
11098985122	Precinorm Fructosamine (3 x 1 mL)	Code 321	
11174118122	Precipath Fructosamine (3 x 1 mL)	Code 322	

\* Some kits shown may not be available in all countries.

## English

### System information

FRA: ACN 8667

### Intended use

In vitro test for the quantitative determination of glycated proteins (fructosamine) in human serum and plasma on **cobas c** systems.

### Summary

Fructosamine measurements performed with this assay in human serum and plasma can be used as an aid in the assessment of diabetes mellitus.

Fructosamine is formed by the non-enzymatic reaction (glycation) between a sugar (glucose or fructose) and the amino acid group of a serum protein (primarily albumin), therefore forming a ketoamine.<sup>1</sup> The formation of fructosamine is a two-step reaction, as a first step a Schiff base is formed by the reversible coupling of glucose and other sugars to a serum protein which, in a second step, is transformed by non-reversible Amadori rearrangement to the corresponding ketoamine (fructosamine). The formation of fructosamine increases with the level of blood glucose.<sup>2</sup> Metabolization occurs within 1 to 3 weeks, corresponding to the turnover of most serum proteins. The concentration of fructosamine thus reflects the average of the continuously varying blood glucose concentrations during this period, serving as a blood glucose memory.<sup>2,3,4</sup> Fructosamine can therefore be used as an indicator of glycemia in the assessment of diabetes mellitus, in particular in conjunction with glycated hemoglobin (HbA1c) or when measurement of HbA1c is invalid for monitoring of diabetes control.<sup>5,6,7</sup>

### Test principle

Colorimetric test by reaction with nitroblue tetrazolium.<sup>8,9,10</sup>

The colorimetric test for fructosamine (glycated protein) is based on the ability of ketoamines to reduce nitroblue tetrazolium in alkaline medium. The rate of formation of formazan is directly proportional to the fructosamine concentration and is measured photometrically.

### Reagents - working solutions

**R1** Nitroblue tetrazolium: 1.2 mmol/L; uricase (microbial): ≥ 12 µkat/L; pH 7.5; non-reactive buffer; stabilizer; surfactants

**R3** Carbonate buffer: 1.5 mol/L; pH 10.4

R1 is in position B and R3 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:



### Danger

H315 Causes skin irritation.

H318 Causes serious eye damage.

### Prevention:

P264 Wash skin thoroughly after handling.

P280 Wear protective gloves/ eye protection/ face protection.

### Response:

P302 + P352 IF ON SKIN: Wash with plenty of water.

P305 + P351 + P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do.  
+ P310 Continue rinsing. Immediately call a POISON CENTER/ doctor.

P332 + P313 If skin irritation occurs: Get medical advice/attention.

P362 + P364 Take off contaminated clothing and wash it before reuse.

Product safety labeling follows EU GHS guidance.

Contact phone: all countries: +49-621-7590

### Reagent handling

Ready for use

### Storage and stability

Shelf life at 2-8 °C: See expiration date on **cobas c** pack label.

On-board in use and refrigerated on the analyzer: 8 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: Collect serum using standard sampling tubes.

Plasma: Li-heparin and K<sub>2</sub>-EDTA 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.

Stability: 3 days at 15-25 °C<sup>11</sup>  
2 weeks at 2-8 °C<sup>11</sup>  
2 months at (-15)-(-25) °C<sup>12</sup>

Freeze only once.

#### 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	10/34-38	
Wavelength (sub/main)	700/546 nm	
Reaction direction	Increase	
Unit	µmol/L	
Reagent pipetting	Diluent (H <sub>2</sub> O)	
R1	60 µL	28 µL
R3	12 µL	20 µL

Sample volumes	Sample	Sample dilution	
		Sample	Diluent (H <sub>2</sub> O)
Normal	6 µL	–	–
Decreased	3 µL	–	–
Increased	12 µL	–	–

#### Calibration

Calibrators	S1: H <sub>2</sub> O S2: Precimat Fructosamine
Calibration mode	Linear
Calibration frequency	2-point calibration - every 4 weeks on board - 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 against fructose polylysine standard.

#### 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 concentration of each sample in the unit µmol/L.

#### Limitations – interference

Criterion: Recovery within ± 29 µmol/L of initial values of samples ≤ 285 µmol/L and within ± 10 % for samples > 285 µmol/L.

Icterus:<sup>13</sup> No significant interference up to an I index of 4 for conjugated and unconjugated bilirubin (approximate conjugated and unconjugated bilirubin concentration: 68 µmol/L or 4 mg/dL).

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

Lipemia:<sup>13</sup> No significant interference up to an L index of 1800. 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.<sup>14,15</sup>

Exception: Levodopa causes artificially high fructosamine results. Oxytetracycline causes artificially high fructosamine results.

As tested according CLSI recommendation Methyldopa causes artificially high fructosamine results.<sup>16</sup>

Ascorbic acid: No significant interference from ascorbic acid up to a concentration of 99.4 µmol/L (17.5 mg/L).

In hydremic states (pregnancy for instance) it may be favorable to relate fructosamine to protein using the following formula:

$$\text{Fructosamine}_{\text{corr}} = \frac{\text{measured fructosamine} \times 72}{\text{measured total protein (in g/L)}}$$

Dysproteinemic states may affect fructosamine values.<sup>17</sup>

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.<sup>18</sup>

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

14-1000 µmol/L

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:2 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 2.

##### Lower limits of measurement

*Lower detection limit of the test*

14 µmol/L

The lower detection limit represents the lowest measurable analyte level that can be distinguished from zero. It is calculated as the value lying 3 standard deviations above that of the lowest standard (standard 1 + 3 SD, repeatability, n = 21).

Values below the lower detection limit (< 14 µmol/L) will not be flagged by the instrument.

##### Expected values<sup>9,19</sup>

Fructosamine concentrations were determined in 555 apparently healthy subjects between the ages of 20 and 60. A reference range of 205 to 285 µmol/L was determined in this study for adults without diabetes. In a poorly controlled diabetic population, mean fructosamine values were reported to be 396 µmol/L (range 228-563 µmol/L). A fructosamine concentration above the established expected value is an indicator for hyperglycemia during the preceding 1-3 weeks or longer.

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**

Precision was determined using human samples and controls in an internal protocol with repeatability (n = 21) and intermediate precision (3 aliquots per run, 1 run per day, 21 days).

The following results were obtained on the **cobas c 701** analyzer:

Repeatability	Mean	SD	CV
	µmol/L	µmol/L	%
Precinorm Fructosamine	275	2	0.8
Precipath Fructosamine	515	3	0.5
Human serum A	220	2	1.0
Human serum B	315	2	0.7
Human serum C	748	4	0.6

Intermediate precision	Mean	SD	CV
	µmol/L	µmol/L	%
Precinorm Fructosamine	262	4	1.5
Precipath Fructosamine	489	6	1.2
Human serum 3	266	4	1.5
Human serum 4	210	4	1.8

Results for intermediate precision were obtained on the **cobas c 501** analyzer.

The data obtained on **cobas c 501** analyzer(s) are representative for **cobas c 701** analyzer(s).

**Method comparison**

Fructosamine values for human serum and plasma samples obtained on a **cobas c 701** analyzer (y) were compared with those determined on **cobas c 501** analyzers (x).

Sample size (n) = 98

Passing/Bablok <sup>20</sup>	Linear regression
y = 0.998x + 10.1 µmol/L	y = 0.992x + 11.8 µmol/L
r = 0.939	r = 0.998

The sample concentrations were between 104 and 765 µmol/L.

**References**

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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:

	Contents of kit
	Volume for reconstitution
	Global Trade Item Number

Rx only For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

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Fructosamine

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