

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE**

A. 510(k) Number:

k061093

B. Purpose for Submission:

New Device

C. Measurand:

Cholinesterase

D. Type of Test:

Quantitative

E. Applicant:

Roche Diagnostics Corp.

F. Proprietary and Established Names:

Cholinesterase Gen.2

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
DIH	I, reserved	21 CFR 862.3240	91 (Tox)

H. Intended Use:

1. Intended use(s):

The Cholinesterase Gen.2 Test System is an in vitro test for the quantitative determination of the catalytic activity of cholinesterase (EC 3.1.1.8; acylcholine acylhydrolase) in serum and plasma.

2. Indication(s) for use:

The Cholinesterase Gen.2 Test System is an in vitro test for the quantitative determination of the catalytic activity of cholinesterase (EC 3.1.1.8; acylcholine

acylhydrolase) in serum and plasma. Measurements obtained by this device are used in the diagnosis and treatment of cholinesterase inhibition disorders.

3. Special conditions for use statement(s):

For prescription use only.

4. Special instrument requirements:

In this submission, the Cholinesterase Gen.2 test system is being applied to the previously cleared COBAS INTEGRA family of analyzers including the COBAS INTEGRA 400/400 plus; COBAS INTEGRA 700, and COBAS INTEGRA 800 analyzers. The COBAS INTEGRA family of analyzers was cleared in k951595.

I. Device Description:

The Cholinesterase Gen.2 Test System is an in vitro test for the quantitative determination of the catalytic activity of cholinesterase in serum and plasma. The test consists of two ready-to-use liquid reagents. The calibrator is the Calibrator for automated systems (C.f.a.s) that was cleared under k033501. The recommended control materials are Precinorm U or Precinorm U Plus; and Precipath U or Precipath U plus which were cleared under k041227 and k042389 respectively. In this submission the reagents are being applied to the COBAS INTEGRA 400, 400 plus, 700 and 800 analyzers.

J. Substantial Equivalence Information:

Predicate	k951595 - Cholinesterase test system on the Integra Analyzer
Similarities	
Both the Cholinesterase and the Cholinesterase Gen.2 test systems are intended for the in vitro quantitative determination of the catalytic activity of cholinesterase in serum and plasma.	
Both test systems are run on the COBAS INTEGRA family of analyzers.	
The test principles are similar; both rely on spectrophotometric determination of reaction product after cholinesterase hydrolyzes a butyrylthiocholine derivative.	
Differences	
Cholinesterase Gen.2 test system measures the decrease in color while the predicate device measures an increase in color.	
The reagents for the new test system are provided in liquid ready-to-use format while the predicate device test system reagents require reconstitution	
There are slight differences in reagent stability, measuring range, and limit of detection.	

K. Standard/Guidance Document Referenced (if applicable):

None referenced.

L. Test Principle:

The Cholinesterase Gen.2 Test System is an in vitro test for the quantitative determination of the catalytic activity of cholinesterase in serum and plasma. The test is based on the butyrylthiocholine method. Cholinesterase catalyzes the hydrolysis of butyrylthiocholine to thiocoline and butyrate. Thiocoline reduces the yellow substrate hexacyanoferrate III to the almost colorless hexacyanoferrate II. The decrease in color is measured spectrophotometrically.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Within-run (n=21) and between-day precision was conducted for the Cholinesterase Gen.2 test system using two controls and two human serum pools on the Integra 800 Analyzer. The between-day precision samples were run in triplicate and the second of the three results were used for the precision determination. The precision summaries are listed in the tables below.

Within-run	Control 1	Control 2	Serum Pool 1	Serum Pool 2	Serum Pool 3
N	21	21	21	21	21
Mean (U/L)	6263	6015	4028	6374	561.4
SD	36.06	33.69	35.54	28.75	24.27
CV%	0.58	0.56	0.88	0.45	4.32
Min	6204	5948	3959	6316	510.0
Max	6331	6075	4094	6423	613.0

Between-day	Control 1	Control 2	Serum Pool 1	Serum Pool 2
N	21	21	21	21
Mean (U/L)	6213	5964	3152	6675
SD	70.34	55.66	39.69	95.92
CV%	1.13	0.93	1.26	1.44
Min	6093	5858	3065	6500
Max	6341	6053	3246	6838

b. *Linearity/assay reportable range:*

The measuring range for this assay is 200 – 14000 U/L.

The sponsor conducted two serial dilution linearity studies for the Cholinesterase Gen.2 test system on the Integra 800 analyzer. The samples were prepared by spiking a saline solution with pure cholinesterase from human plasma and diluting with saline. One study measured samples ranging from 404 – 4801 U/L (theoretical spiked concentration). The second study measured samples ranging from 2762 – 27621 U/L (theoretical spiked concentration). All samples were recovered within +/- 10% of the theoretical concentration. The extended measuring range from 14000 to 28000 (based on post dilution factor of 2) was also validated in the second set of samples.

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

The calibrators and controls for use with this device have been previously cleared. Their composition has not been modified for use with the Cholinesterase Gen.2 test system. The calibrators and controls are standardized against and traceable to a reference method using a manual application of the butyrlthiocholine/ hexacyanoferrate (III) method on a photometer and the published molar absorptivity of hexacyanoferrate (III)

Stability studies for the device were described. Studies supported the sponsor's 4-week on-board stability claim. The sponsor also described real-time and an accelerated studies to support the 15 month closed stability claim.

d. Detection limit:

Analytical sensitivity (Limit of Blank) was defined as the concentration at three standard deviations above the mean of repeated measurements (N=21) of the zero calibrator. The mean + (3xSD) was calculated to be 122.8 U/L. The sponsor claims a lower detection limit of 200 U/L.

e. Analytical specificity:

Human serum pools that contained 5817 – 9143 U/L cholinesterase was evaluated for endogenous interference by the Cholinesterase Gen.2 test system. The sponsor defined interference as percent recovery that exceeded +/- 10% of the expected 100% recovery. Human serum pools that contained approximately 4700 U/L cholinesterase were tested by the Cholinesterase Gen.2 test system for drug interference. The sponsor defined drug interference as results that deviated more than 10% from the reference value. A list of compounds tested can be found in the device labeling. There was no interference (<10%) from the 18 drug pharmaceuticals tested and also from the following substances:

Hemoglobin up to 347 mg/dL,

Bilirubin: conjugated up to 65 mg/dL and unconjugated up to 86 mg/dL and

Lipemia up to 997 U/L.

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

The sponsor conducted two sample method comparisons between the Integra cholinesterase test system and the Cholinesterase Gen.2 test system from samples collected from hospitals and blood donor clinics. See the table below for regression statistics (least squares linear regression).

	N	Range	Equation	Correlation coefficient
Study #1	51	1144 to 13527	$Y = 0.965(X) + 152.5$	0.99
Study #2	56 (5 spiked)	171 to 12995	$Y = 0.967(X) + 98.4$	0.99

Y= Integra Cholinesterase test system and X= Cholinesterase Gen.2 test system

b. Matrix comparison:

K2 EDTA and K3 EDTA plasma samples (N=27 of each) and lithium heparin (N=54) samples were compared to paired serum samples in a matrix comparison study with the Cholinesterase Gen.2 test system on the Integra 800. The linear regression equations, ranges and correlation constants are listed in the table below.

Comparator against serum	N	Range (U/L)	Slope	Intercept	R
K2-EDTA Plasma	27	5751 to 11115	0.964	156	0.995
K3-EDTA Plasma	27	6342 to 9789	0.922	29.5	0.994
Li-Heparin Plasma	54	5457 to 11129	0.970	29.8	0.995

3. Clinical studies:

a. *Clinical Sensitivity:*

Not Applicable

b. *Clinical specificity:*

Not Applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Not Applicable

4. Clinical cut-off:

Not Applicable

5. Expected values/Reference range:

The expected values/ reference intervals for cholinesterase were provided from literature as follows:

Children, men, women aged 40 and over:
5320-12920 U/L

Women age 16 to 39 that are not pregnant or using hormonal contraceptives:
4260-11250

Women age 18 to 41 that are pregnant or taking contraceptives:
3650-9120 U/L.

Reference:

denBlauween DH et al.. Cholinesterase (EC 3.1.1.8) with Butyrlthiocholine-iodide as substrate: reference values with dependence on age and sex, and with regards to hormonal influence and pregnancy. J. Clin Chem Clin Biochem 1983; 21:381-386.

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.