

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

A. 510(k) Number:

k110313

B. Purpose for Submission:

Addition of three additional anticoagulants (Na-heparin, NaF/K-Oxalate, and NaF/Na₂-EDTA) for use with a previously cleared device (k072714) and replacement of Lower Detection Limit (LDL) claims with Limit of Blank (LOB) and Limit of Detection (LOD) claim.

C. Measurand:

Glycosylated Hemoglobin (HgbA1C)

D. Type of Test:

Quantitative turbidimetric inhibition immunoassay

E. Applicant:

Roche Diagnostics Corporation

F. Proprietary and Established Names:

Tina-quant Hemoglobin A1c Gen.2 assay

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
LCP	Class II	21 CFR 864.7470	Chemistry 75

H. Intended Use:

1. Intended use(s):

See indications for use below.

2. Indication(s) for use:

The Tina-Quant hemoglobin A1c Gen.2 assay is an in vitro diagnostic reagent system intended for quantitative determination of mmol/mol hemoglobin A1c (IFCC) and % hemoglobin A1c (DCCT/NGSP) in hemolysate or whole blood on Roche clinical chemistry analyzers. HbA1c determinations are useful for monitoring of long-term blood glucose control in individuals with diabetes mellitus.

3. Special conditions for use statement(s):

Prescription use only.

There are two application methods: Whole Blood and Hemolysate. Hemolysate should be prepared and stored for analysis if whole blood cannot be analyzed within 8 hours of collection.

4. Special instrument requirements:

Performance was evaluated on the Roche Integra 800 Analyzer

I. Device Description:

The Roche Tina-quant Hemoglobin A1c Gen. 2 consists of two working reagents (R1 and R2) and an Hemolyzing reagent. The R1 reagent consists of antibody reagent, MES buffer: 0.025 mol/L; TRIS buffer: 0.015mol/L, ph6.2; HbA1c antibody (bovine serum): ≥ 0.5 mg/ml; stabilizers; preservatives (liquid). R2 reagent (Polyhapten reagent) consists of MES buffer: 0.025 mol/L; TRIS buffer: 0.015 mol/L, ph 6.2, HbA1c polyhapton: $\geq 8\mu\text{g/mL}$; stabilizers; preservatives (liquid)

The Roche Tina-quant Hemoglobin A1c Gen. 2 consists of two application types: The Whole Blood application uses an automated on-board sample pretreatment with hemolyzing reagent. The Hemolysate application consists of a manual pretreatment step which is performed using the hemolyzing reagent before the sample is placed on the analyzer.

J. Substantial Equivalence Information:

1. Predicate Device name(s):

Roche Tina-quant Hemoglobin A1c Gen.2 test system

2. Predicate 510(k) number(s)

k072714

3. Comparison with predicate

Similarities and Differences		
Item	Candidate Device (k110313)	Predicate Device (k072714)
Intended Use	In vitro test for the quantitative determination of hemoglobin A1c in hemolysate and whole blood on Roche clinical chemistry analyzers.	Same
Sample Types	Li-Heparin, K2-EDTA, K3-EDTA, KF/Na ₂ -EDTA, Na-Heparin, NaF/K-Oxalate, NaF/Na ₂ -EDTA	Li-heparin, K2-EDTA, K3-EDTA, KF/Na ₂ -EDTA
Calibrator	Cfas HbA1c	Same
Instrument Platform	Roche Integra analyzers	Same
Calibration Mode	Logit/log 5	Same
Controls	HbA1c Control N or PreciControl HbA1c norm; HbA1C Control P or PreciControl HbA1c path	Same
Measuring Range	Integra 400/400 plus Hb: 4-35 g/dL HbA1c: 4.3-19.5% Integra 800 Hb: 4-35 g/dL HbA1c: 4.3-24.8%	Same
Antibody	Polyclonal anti-HbA1c from sheep blood	Same

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

CLSI EP17-A, Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline

L. Test Principle:

Anticoagulated whole blood is hemolyzed prior to determination of HbA1c by a turbidimetric inhibition immunoassay (TINIA). Liberated hemoglobin (Hb) in the hemolyzed sample is converted to a derivative having a characteristic absorption spectrum and measured biochromatically. The instrument calculates the %HbA1c from the HbA1c/Hb ratio according to a user selected protocol.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

This tube type precision study was performed along with the matrix comparison study on the Roche Integra 800 analyzer with K₂-EDTA, Na-heparin, NaF/K-Oxalate, and NaF/Na₂-EDTA. K₂-EDTA was used as the reference anticoagulant since it was originally cleared in k072714. Duplicate samples from the matrix studies were calculated for average SD for 3 partitioned bins covering the ranges tested. The average SD and CV in each of the 3 bins for all tube types evaluated were summarized in the table below.

Precision Comparison with Full Tubes

K2-EDTA (predicate)	n	Mean (% A1c)	SD	%CV
Low Level	90	5.64	0.35	6.2
Medium Level	25	9.42	0.43	4.5
High Level	19	13.81	0.71	5.1
Na-Heparin (candidate)	n	Mean (% A1c)	SD	%CV
Low Level	90	5.64	0.35	6.2
Medium Level	25	9.40	0.39	4.2
High Level	19	13.80	0.77	5.6
NaF/K-Oxalate (candidate)	n	Mean (% A1c)	SD	%CV
Low Level	90	5.65	0.35	6.2
Medium Level	25	9.44	0.42	4.5
High Level	19	13.80	0.70	5.1
NaF/Na₂-EDTA (candidate)	n	Mean (% A1c)	SD	%CV
Low Level	90	5.64	0.35	6.1
Medium Level	25	9.44	0.41	4.3
High Level	19	13.79	0.74	5.4

Precision Comparison with Half Full Tubes

K2-EDTA (predicate)	n	Mean (% A1c)	SD	%CV
Low Level	90	5.65	0.34	6.0
Medium Level	25	9.42	0.43	4.5
High Level	19	13.77	0.69	5.0
Na-Heparin (candidate)	n	Mean (% A1c)	SD	%CV
Low Level	90	5.66	0.35	6.1
Medium Level	25	9.39	0.42	4.5
High Level	19	13.77	0.71	5.2
NaF/K-Oxalate (candidate)	n	Mean (% A1c)	SD	%CV
Low Level	90	5.68	0.35	6.2
Medium Level	25	9.42	0.42	4.5
High Level	19	13.83	0.71	5.1
NaF/Na₂-EDTA (candidate)	n	Mean (% A1c)	SD	%CV
Low Level	89	5.66	5.44	6.1

Medium Level	25	9.44	0.40	4.3
High Level	19	13.77	0.73	5.3

b. Linearity/assay reportable range:

Previously established in k072714

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

Previously established in k072714

Stability studies were conducted using all three candidate anticoagulants, Na-heparin, NaF/K-Oxalate, and NaF/Na₂-EDTA using the hemolysate and whole blood applications. The hemolysate is stable for 4 hours at 15-25°C, 24 hours at 2-8°C and 6 months at (-15) – (-25) °C when using Na-heparin, NaF/K-Oxalate, and NaF/Na₂-EDTA. Whole Blood samples should be analyzed within 8 hours of collection. The labeling indicates hemolysate should be prepared and stored for analysis if whole blood cannot be analyzed within 8 hours of collection. Frozen stability of HbA1c has not been determined for samples treated with anticoagulants Na-heparin, NaF/K-Oxalate, and NaF/Na₂-EDTA.

d. Detection limit:

The Limit of Blank (LoB) and Limit of Detection (LoD) were determined by assaying an analyte free sample (blank) and five low HbA1c samples according to CLSI guideline EP17A. Each sample was assayed twice a day for three days on two Roche Integra 800 Analyzers. The detection limits are summarized in the table below.

Platform/Method	LoB (%A1c)	LoD (%A1c)
Roche Integra 800 analyzer	2.3%	2.5%

The assay has a reportable range of 4.3-24.8% on the Roche Integra 800 analyzer.

e. Analytical specificity:

Previously established in k072714

Interference studies for Na-heparin, NaF/K-Oxalate, and NaF/Na₂-EDTA were not performed. See previously cleared interference data in k072714.

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. *Method comparison with predicate device:*

Previously established in k072714

b. *Matrix comparison:*

A matrix comparison study was performed using Na-heparin, NaF/K-Oxalate, and NaF/Na₂-EDTA. K2-EDTA was used as the reference anticoagulant. 132 total samples were analyzed for HbA1c. Each single set of samples were analyzed on the Roche Integra 800 analyzer and values obtained. Samples ranged from 4.97 – 15.97% HbA1c. The results using Passing/Bablok linear regression analysis are as follows:

Full Tubes		
Na-Heparin	NaF/K-Oxalate	NaF/Na ₂ -EDTA
$y=1.004x-0.026$	$y=1.005x-0.010$	$y=1.001x-0.011$

Half-Full Tubes		
Na-Heparin	NaF/K-Oxalate	NaF/Na ₂ -EDTA
$y=0.998x+0.006$	$y=0.994x +0.051$	$y=1.010x-0.057$

An additional comparison study was performed to evaluate the two application methods (whole blood versus hemolysate). 30 whole blood samples were collected in Na-Heparin, NaF/K-Oxalate, and NaF/ Na₂-EDTA. Each whole blood sample was hemolyzed manually per labeling instructions and then placed on the Integra analyzer for the automated hemolysate application. The results using simple regression analysis are as follows:

Hemolysate Application vs. Whole Blood Application

	Slope	Intercept	r	Sample range
Na-Heparin	1.0091	0.0590%	0.9994	5.14 – 13.15%
NaF/K-Oxalate	1.0122	0.0457%	0.9980	5.18 – 12.75%
and NaF/ Na ₂ -EDTA	1.0025	0.1135%	0.9994	5.17 – 13.0%

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 according to the literature cited are:

Protocol 1 (acc. to IFCC): 29-42 mmol/mol HbA1c*

Protocol 2 (acc. to DCCT/NGSP):4.8-5.9% HbA1c*

*Junge, W, Wilke B, Halabi A et al. Determination of reference levels in adults for hemoglobin A1c (HbA1c). Poster presentation EUROMEDLAB, Barcelona 2003

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.