

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

**A. 510(k) Number:**

k152464

**B. Purpose for Submission:**

New device

**C. Measurand:**

Not applicable.

**D. Type of Test:**

Saliva Collection Device for human genomic DNA testing

**E. Applicant:**

DNA Genotek Inc.

**F. Proprietary and Established Names:**

ORAcollect•Dx models OCD-100 and OCD-100A

**G. Regulatory Information:**

1. Regulation section:

21 CFR §862.1675 - Blood specimen collection device

2. Classification:

II

3. Product code:

OYJ - DNA specimen collection, saliva

4. Panel:

Chemistry (75)

**H. Intended Use:**

1. Intended use(s):

See indications for use below.

2. Indication(s) for use:

ORAcollect•Dx is intended for use in the non-invasive collection of saliva samples. Human DNA from the saliva sample is isolated, stabilized, and suitable for use in FDA cleared molecular diagnostic applications. Saliva samples collected using ORAcollect•Dx are stabilized and can be transported and/or stored long term at ambient conditions.

3. Special conditions for use statement(s):

For prescription use only.

For use in people 18 years of age or older.

The Oragene•Dx collection devices are only cleared for use with genotyping tests that have obtained FDA clearance for use with saliva samples obtained with these collection devices.

4. Special instrument requirements:

None.

**I. Device Description:**

ORAc collect·Dx are available in the following models; OCD-100 and OCD-100A. Both ORAc collect·Dx formats have the same collection principle in that saliva is collected using a sponge into a collection tube containing a stabilizing liquid. Both OCD-100 and OCD-100A are made from the same physical and chemical materials. Both device formats consist of the same double ended tube cap with an attached integrated sponge, the same collection tube and contain the same DNA stabilizing liquid. The attached integrated sponge is used to collect and transfer the saliva sample from a donor's mouth into the stabilizing liquid inside the collection tube.

OCD-100A includes a molded plastic insert inside the collection tube. The insert does not impact user experience or user collection instructions but rather is intended to facilitate or enable a more efficient physical handling of the sample in the laboratory.

**J. Substantial Equivalence Information:**

1. Predicate device name(s):

DNA Genotek Oragene•Dx

2. Predicate K number(s):

k110701

3. Comparison with predicate:

<b>Similarities</b>		
<b>Item</b>	<b>Proposed Device</b>	<b>Predicate Device (k110701)</b>
Intended use	Intended for use in the non-invasive collection of saliva samples. DNA from the saliva sample is isolated, stabilized and suitable for use in FDA cleared molecular diagnostic applications.	Same

<b>Similarities</b>		
<b>Item</b>	<b>Proposed Device</b>	<b>Predicate Device (k110701)</b>
	Saliva samples collected using the device are stabilized and can be transported and/or stored long term at ambient conditions.	
Indications for use	For use with molecular diagnostic applications	Same
Additive	Nucleic acid stabilization solution	Same

<b>Differences</b>		
<b>Item</b>	<b>Proposed Device</b>	<b>Predicate Device (k110701)</b>
Physical design	Consists of a tube cap with an attached integrated sponge and a collection tube containing a DNA stabilizing liquid.	Consists of a collection tube, a DNA stabilizing liquid and optional sponges for assisted collection.

**K. Standard/Guidance Document Referenced:**

- ISO 13485: Medical Device – Quality Management Systems
- ISO 14971: Medical Device – Application of Risk Management in Medical Devices

**L. Test Principle:**

Upon contacting saliva cells, the stabilizing liquid lyses cellular and nuclear membranes to release and stabilize nucleic acids (DNA). Samples can be immediately processed, transported or stored for future use. Samples can be shipped or transported at ambient temperature to the laboratory for processing. ORAcollect·Dx samples are stable at room temperature for up to 60 days. Device and sample integrity are preserved during typical ambient transport and storage conditions. DNA extraction from ORAcollect·Dx saliva samples should be performed using the QIAGEN QIAamp DNA Mini Kit.

## M. Performance Characteristics:

### 1. Analytical performance:

#### a. *Precision/Reproducibility:*

Three reproducibility studies were conducted.

The first reproducibility study was designed to show collection-to-collection, lot-to-lot and day-to-day reproducibility. Ten donors self-collected nine saliva samples each over 3 days using 3 reagent lots (OCD-100 format). The 10 donors had never used the product previously. One operator performed the DNA extraction (from one aliquot of each sample on each of two days) followed by testing for concentration, yield and  $A_{260}/A_{280}$  ratio. DNA testing using the eSensor Warfarin Sensitivity Test was performed over several days. A total of 120 aliquots from the 60 self-collected samples from the 10 donors were tested.

All specimens yielded a DNA concentration of 2 ng/ $\mu$ L or better, DNA purity ( $A_{260}/A_{280}$ ) between 1.2 and 2.3 and total DNA yield of at least 10 ng (0.010  $\mu$ g).

After the first round of testing, total percent agreement between the results of the eSensor Warfarin Sensitivity Saliva Test and genotype (by sequencing) was 100%.

A second reproducibility study was performed to evaluate operator-to-operator reproducibility. For this study, 3 of the samples collected by the ten donors for the first study were pooled and aliquoted into 3 tubes (and one reserve aliquot was stored). Each of 3 operators performed the DNA extraction (from one aliquot of each sample that they received on each of two days) followed by testing for concentration, yield and  $A_{260}/A_{280}$  ratio prior to testing each aliquot from each sample received on the eSensor® Warfarin Sensitivity Test. One lot of the collection device was used for this study. A total of 60 aliquots from 30 self-collected samples from 10 donors were tested.

All specimens yielded a DNA concentration of 2 ng/ $\mu$ L or better, DNA purity ( $A_{260}/A_{280}$ ) between 1.2 and 2.3 and total DNA yield of at least 10 ng (0.010  $\mu$ g).

After the first round of testing, total percent agreement between the results of the eSensor Warfarin Sensitivity Saliva Test and genotype (by sequencing) was 100%.

A third reproducibility study was conducted. Thirty (30) donors collected multiple saliva samples each from 3 sites; 2 of the 3 sites were in a professional setting and had supervised collections compared to unsupervised collections at the third site. The 30 donors were selected to encompass a diverse genotype distribution for CYP2C9 and VKORC1 genotype distribution. After sample collection, one sample from each donor was transported at ambient temperatures to three independent sites. Each site had

one operator for a study total of 3 operators. Following sample extraction, all purified genomic DNA samples were tested for DNA concentration and A<sub>260</sub>/A<sub>280</sub> at the sites where they were extracted. All purified genomic DNA samples were transported to Site 1 for testing on the eSensor Warfarin Sensitivity Saliva Test (k152612) where 1 extracted DNA aliquot from each sample from each site was tested on the Warfarin assay, excluding a single sample that did not meet assay input criteria. When data from all 3 sites are combined one sample did not meet the eSensor Warfarin Sensitivity Saliva Test DNA quality input requirements. In the first run there were 88/89 (98.9%) correct calls on the 89 testable samples of 90 total collected samples. In the second run there was 100% agreement (89/89) with bidirectional sequencing on the 89 testable samples of 90 total collected samples.

*b. Linearity/assay reportable range:*

Not applicable.

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

Shelf-life stability:

Stability testing protocols and simulated transport shelf-life studies were reviewed and found to be acceptable.

Current real-time data supports a shelf-life 24 months at ambient temperature.

Stability of samples post-saliva collection: A study was performed to evaluate the stability of samples after saliva collection. Two samples were collected from each of 30 donors (using 3 lots of the OCD-100 format). One was exposed to simulated transport conditions (3 freeze-thaw cycles, where each cycle was comprised of a minimum of 3 hours at -20°C and a minimum of 3 hours at 50°C). The second was stored at room temperature and processed after 30 days and 70 days of storage. At each time point, an aliquot of sample was extracted and the DNA was analyzed for concentration, yield and A<sub>260</sub>/A<sub>280</sub> ratio and percent bacterial content.

All specimens from all samples at all conditions (baseline, simulated transport, 30 days and 70 days) yielded a DNA concentration of 2 ng/μL or better, DNA purity (A<sub>260</sub>/A<sub>280</sub>) between 1.2 and 2.3 and total DNA yield of at least 10 ng (0.010 μg). There was also no significant difference from baseline in the bacterial content in the samples.

A subset of 10 donors was selected and all samples (baseline, transport, 30 days and 70 days) from those donors tested for agreement between genotyping results on the eSensor Warfarin Sensitivity Saliva Test and sequencing. There was 100% agreement (40/40) of the eSensor® Warfarin Sensitivity Test results to bidirectional sequencing.

Donor	CYP2C9	VKORC1
PCS2-03	*1/*1	A/A
PCS2-04	*1/*2	G/A
PCS2-07	*1/*1	G/A
PCS2-12	*1/*1	G/A
PCS2-14	*1/*2	A/A
PCS2-15	*1/*2	G/G
PCS2-17	*1/*3	G/G
PCS2-21	*1/*1	G/A
PCS2-26	*1/*1	G/G
PCS2-30	*1/*3	G/G

d. *Detection limit:*

The device is intended for the collection of a saliva sample by using the double ended tube cap with attached integrated sponge to collect and transfer saliva samples. The sample is collected using 10 sponge actions per each of the lower gum one each side of the mouth for a total of 20 sponge actions total. A study was conducted to evaluate the effect of over or under collecting a sample using the OCD-100 collection device.

Individuals collected a sample by one of the following methods: “recommended” (10 sponge actions per each lower gums one each side of the mouth for a total of 20 sponge actions total); “over-collection” (10 sponge actions per each upper and lower gums on each side of the mouth for a total of 40 sponge actions total); “Under-collection by 50%” (5 sponge actions per each lower gums for a total of 10 sponge actions total); “Under-collection by 75%” (5 sponge actions on a single lower gum for a total of 5 sponge actions total); and “no motion” (sponge placed in lower gutter region for 10 seconds for each side of the mouth).

A total of 10 donors were asked to collect 5 saliva samples using the different collection methods. A total of 50 DNA samples were analyzed for DNA concentration, yield and  $A_{260}/A_{280}$  ratio. In addition, 49 samples were processed on the eSensor Warfarin Sensitivity Test.

All specimens from the “recommended,” “over-collection,” and “under-collection” methods collected samples with sufficient DNA purity and yield. For the “no motion” group, only 90% of samples had sufficient DNA purity and yield. In addition, one sample (10%) from the “no motion” group did not collect a sufficient concentration of DNA.

DNA testing resulted in 4 no calls (45/49 or 91% agreement between genotyping results on the eSensor Warfarin Sensitivity Saliva Test and sequencing). Upon retesting there was 100% agreement of the eSensor® Warfarin Sensitivity Test results to bidirectional sequencing. One sample from the no motion group did not meet the concentration criteria and was not able

to be tested on the eSensor Warfarin Sensitivity Saliva Test.

Donor	CYP2C9	VKORC1
US01	*1/*1	G/G
US02	*1/*1	A/A
US03	*1/*3	A/A
US04	*1/*3	G/G
US05	*1/*1	G/A
US06	*1/*1	G/A
US07	*1/*1	G/G
US08	*1/*1	G/A
US09	*1/*1	G/A
US10	*1/*3	G/G

Effect of Incorrect Collection sites: The sample is collected using 10 sponge actions per each of the lower gum one each side of the mouth for a total of 20 sponge actions total. A study was conducted to evaluate the effect of collecting from incorrect collection sites using the OCD-100 collection device.

Individuals collected a sample by one of the following methods: “recommended” (10 sponge actions per each lower gums one each side of the mouth for a total of 20 sponge actions total); “cheek” (10 sponge actions per inside of cheek on each side of the mouth); “teeth” (10 sponge actions per each lower teeth on each side of the mouth); and “tongue” (10 sponge actions per each side of the top of the tongue).

A total of 10 donors were asked to collect 4 saliva samples using the different collection sites. A total of 40 DNA samples were analyzed for DNA concentration, yield and  $A_{260}/A_{280}$  ratio. In addition, 39 samples were processed on the eSensor Warfarin Sensitivity Test.

All specimens from the “recommended” collection site, collected from the “teeth” and the “tongue” had adequate DNA purity and yield. For the samples collected from the “cheek”, 90% of samples had adequate DNA purity and yield. In addition, one sample (10%) from the “cheek” group did not collect a sufficient concentration of DNA.

DNA testing resulted in 100% agreement (39/39) between genotyping results on the eSensor Warfarin Sensitivity Saliva Test and sequencing. One sample collected from the cheek did not meet the concentration criteria was not able to be tested on the eSensor Warfarin Sensitivity Saliva Test.

Donor	CYP2C9	VKORC1
US11	*1/*1	G/G
US12	*1/*1	G/G
US13	*1/*2	A/A
US14	*1/*2	G/G
US15	*1/*1	G/A
US16	*1/*1	G/A
US17	*1/*1	G/G
US18	*1/*1	G/A
US19	*1/*2	G/G
US20	*1/*2	A/A

Dry Mouth Study: 13 donors with dry mouth were recruited to participate in the study (based on answers to the modified Xerostomia Inventory which is used to evaluate dry mouth. The sponsor used at least 3 “yes” responses to the questions to select participants, and recruited participants with the most yes responses).

11 of 12 specimens had adequate DNA purity and yield.

DNA testing resulted in 2 no-calls (84.6% agreement - 11/13) between genotyping results on the eSensor Warfarin Sensitivity Saliva Test and sequencing. Upon retesting there was 100% agreement of the eSensor Warfarin Sensitivity Test results to bidirectional sequencing.

*e. Analytical specificity:*

Effect of Endogenous Interfering Substances: Interfering substances were spiked into saliva samples. 10 donors each provided five samples which were each spiked with one of the four interfering substances. A control sample was included. All samples were evaluated for effect on DNA concentration, purity,  $A_{260}/A_{280}$  ratio and testing on a genotyping device.

Three independent DNA extractions were performed on each spiked sample while one DNA extraction was performed for the control samples. No endogenous substances tested exhibited interference with the assay.

Donor	CYP2C9	VKORC1
INTF01	*1/*1	G/G
INTF02	*1/*2	G/A
INTF03	*1/*1	G/G
INTF04	*1/*1	G/A
INTF05	*1/*1	G/A
INTF06	*1/*1	G/G
INTF07	*1/*1	G/G
INTF08	*1/*3	A/A
INTF09	*1/*1	G/A
INTF10	*1/*1	A/A

Effect of Exogenous Interfering Substances: Potentially interfering exogenous substances introduced into saliva samples through various activities (eating, drinking, chewing gum, using mouthwash, smoking and brushing teeth) were tested. Each activity group was composed of five to nine donors who each provided samples immediately after activity, 10 minutes and 30 minutes post-activity. There was 100% agreement between the eSensor Warfarin Sensitivity Saliva Test results and bidirectional DNA sequencing for all activities tested in one run at the 30 minute time point, demonstrating no effect of any interfering substances on genotyping.

*f. Assay cut-off:*

Not applicable.

2. Comparison studies:

*a. Method comparison with predicate device:*

A method comparison study was performed in order to determine the accuracy of the genotype obtained on the eSensor® Warfarin Sensitivity Saliva Test (k110786) using saliva samples collected using the proposed collection device (3 lots of OCD-100) as compared to bi-directional DNA sequencing. Samples from 156 subjects were collected. Eighty percent of donors were naïve to the device. Twenty percent had used the device more than once.

All samples yielded a DNA concentration of 2 ng/μL or better, DNA purity ( $A_{260}/A_{280}$ ) between 1.2 and 2.3 and total DNA yield of at least 10 ng (0.010 μg).

Overall, there was 98.1% (153/156) first run agreement of the eSensor Warfarin Sensitivity Saliva Test to bidirectional sequencing. In the first run there were 2 incorrect results and one no-call result. After re-testing, there was 99.4% (155/156) agreement between the eSensor Warfarin Sensitivity Saliva Test results and DNA sequencing, including one no-call result.

No call result: There was one first and final run no-call, sample MC002. This sample was re-tested using the same purified DNA (retest 1) and upon a second no-call result, was re-extracted and re-tested on the eSensor Warfarin Sensitivity Saliva Test (retest 2). The original test, retest 1 and retest 2 all gave a no-call result (all \*3 indeterminate score). For investigation purposes, both the original and re-extracted DNA was diluted 1:10 and re-tested on the eSensor Warfarin Sensitivity Saliva Test. Both the 1:10 diluted samples gave a correct call of \*1/\*3, G/G, concordant with sequencing. The sponsor hypothesizes that there may be an inhibitor present in the sample that was not removed by the Qiagen QIAmp Mini Kit purification. Users should be aware of this potential failure mode.

Incorrect results: There were two first run incorrect calls (CYP2C9 \*2/\*2, VKORC1 G/G and CYP2C9 \*1/\*2, VKORC1 G/A). An investigation revealed that a sample mix-up had occurred. Both samples were re-tested on the and re-test 1 resulted in genotypes concordant with sequencing for both samples.

<b>Number (%) of genotypes of each allele in the OCD-100 Method Comparison Study (n=156)</b>			
<b>Polymorphism</b>	<b>*2</b>	<b>*3</b>	<b>VKORC1</b>
W	104 (67%)	130 (83%)	63(40%)
H	42 (27%)	16 (10%)	71 (46%)
M	5 (3%)	1 (1%)	22 (14%)
Compound HET (*2/*3) = 4 (3%)			

*b. Matrix comparison:*

The sponsor conducted a method comparison study between the two tube types, OCD-100 and OCD-100A. The collection of samples from 45 different donors was evaluated for DNA concentration, total DNA yield, A260/A280 and the warfarin sensitivity assay. All 45 samples collected had adequate DNA concentration, total DNA and A260/A280. Samples from the OCD-100A generated correct results on the warfarin sensitivity genotyping assay (95.6% in the first pass due to 2 no-call results, and 100% in the final pass).

Summary of Genotyping Results for the Matrix Comparison Study

	<b>Sample Tested</b>	<b>Correct Call</b>	<b>Incorrect Call</b>	<b>No-Call</b>	<b>% Agreement</b>	<b>95% LCB</b>
<b>First-Run</b>	45	43	0	2	95.6%	86.%
<b>Final Run</b>	45	45	0	0	100%	93.5%

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):

A user study was performed to evaluate usability and user understanding of the collection instructions. 101 naïve donors were recruited. After being provided oral instructions from the Package insert by a professional and handed an ORAclect·Dx collection kit, each donor was observed for their ability to complete the core tasks. Actions for each of the core tasks were recorded by the study observer. The overall pass rate for all tasks was 93.9%. All specimens from all samples at all conditions (baseline, simulated transport, 30 days and 70 days) yielded a DNA concentration of 2 ng/μL or better, DNA purity ( $A_{260}/A_{280}$ ) between 1.2 and 2.3 and total DNA yield of at least 10 ng (0.010 μg). However users misunderstood some instructions, summarized in the table below.

Task	Task description Acceptance criteria: Success rate $\geq$ 80% overall and $\geq$ 70% of each task	Total number of Observations	% Pass			% Fail
			Combined	Core Task	Accepted Variable action	
1	Do not eat, drink, smoke or chew gum for 30 minutes prior to collection	101	74%	74%	0%	26%
2	Opening the pouch and removing the ORAclectDx device using the non-sponge end	101	93%	93%	0%	7%
3	Place sponge against lower gums on one	101	100%	88%	12%	0%

	side of mouth					
4	Rub sponge along gums in back-and- forth motion 10 times	101	91%	90%	1%	9%
5	Place sponge against lower gums in opposite side of mouth	101	98%	89%	9%	2%
6	Rub sponge along gums in back-and- forth motion 10 times	101	91%	88%	3%	9%
7	Holding tube upright, unscrew blue cap and invert sponge into tube, close cap	101	98%	98%	0%	0%
8	Invert tube	101	100%	70%	30%	0%
9	Shake tube (while inverted) 10 times	101	100%	69%	31%	0%
Combined	Overall for all tasks	909	93.9%	84.5%	9.5%	6.1%

4. Clinical cut-off:

Not applicable.

5. Expected values/Reference range:

Not applicable for this device type.

**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.