ORAgene®·Dx

Product handbook

DNA genotek

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Superior samples
Proven performance

IVD CE

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Intended use

Oragene®•Dx is intended for use in the non-invasive collection of saliva samples for in vitro diagnostic testing of human DNA. Saliva may be collected by spitting directly into the Oragene®•Dx container or may be transferred into the Oragene®•Dx container using a sponge. Saliva samples may be collected by a healthcare professional or non-healthcare professional, such as a lay user. Saliva samples collected using Oragene®•Dx are stabilized and isolated for use in downstream diagnostic testing applications. Saliva samples collected using Oragene®•Dx can be transported and/or stored long term at ambient conditions.

Summary and explanation of use

Use Oragene•Dx for reliable collection, stabilization, transportation and long-term room temperature storage of human DNA from saliva.

Features

- Non-invasive, reliable self-collection or assisted collection of DNA from saliva
- Samples remain stable at room temperature for one year, reducing transportation and storage costs
- Samples can be exposed to temperatures from -20°C to 50°C during collection and transport
- Increase efficiency and minimize sample handling with a compatible tube format for high throughput processing
- Samples can be mailed using a postal system
- Oragene•Dx is an FDA cleared device intended for In Vitro Diagnostic Use

Materials

There are several formats in the Oragene•Dx family. The following chart summarizes the kit components. Each non-reusable Oragene•Dx kit includes the following:

Format	Stabilizing liquid volume	Tube	Funnel lid**	Small cap	Collection sponge	Instructions for use
OGD-500/ OGD-600	2 mL	✓	✓	✓	—	✓
OGD-510/ OGD-610	1 mL	✓	✓	✓	—	✓
OGD-575/ OGD-675	0.75 mL	✓	✓	✓	2	✓

** Lid contains stabilizing liquid.

Warnings and precautions

1. IVD In Vitro Diagnostic Medical Device.
2. For In Vitro Diagnostic Use.
3. For Prescription and Direct-to-Consumer Use.
4. Do NOT use if packaging is damaged or seal in the funnel lid is broken or leaking. Discard unused, damaged or leaking kits in accordance with appropriate regulations.
5. Do NOT use Oragene•Dx beyond the "collect saliva by" date indicated on the tube.
6. Only use the components and accessories provided with the kit.
7. Collection precautions:
   a. Do NOT eat, drink, smoke or chew gum for 30 minutes before sample collection.
   b. Do NOT remove plastic film from the funnel lid.
   c. Wash with water if stabilizing liquid comes in contact with eyes or skin.
   d. Do NOT ingest stabilizing liquid.
8. DNA concentration and yield may be affected if sample is collected after eating or chewing gum. To optimize performance ensure the donor follows the instructions for use.
9. Choking hazard:
   a. Small cap in collection kit.
   b. Plastic bag containing sponges (OGD-575/OGD-675 only).
10. For supervised collections:
    a. Do NOT leave donor unattended.
    b. Do NOT allow donor to handle the sponge, small cap or packaging.
    c. Caution should be used when inserting sponge into donor's mouth.
11. Genomic DNA isolated from oral samples collected using Oragene•Dx will contain a small amount of bacterial DNA (see page 13).
12. Decontaminate and dispose of all specimens, reagents, and other potentially contaminated materials in accordance with local, state, and federal regulations.
13. This product requires the handling of human saliva specimens.
14. Material Safety Data Sheet (MSDS) is available at: www.dnagenotek.com.

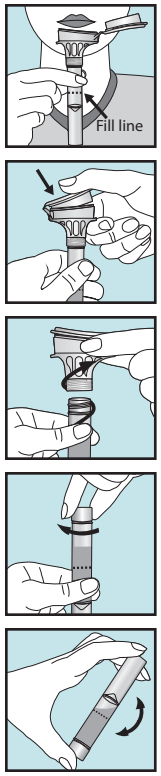
Product use limitations

1. Oragene•Dx is intended for collection and stabilization of human DNA from saliva, it is NOT intended for the collection and stabilization of RNA, protein or hormones.
2. Oragene•Dx has only been validated for use with germline testing.

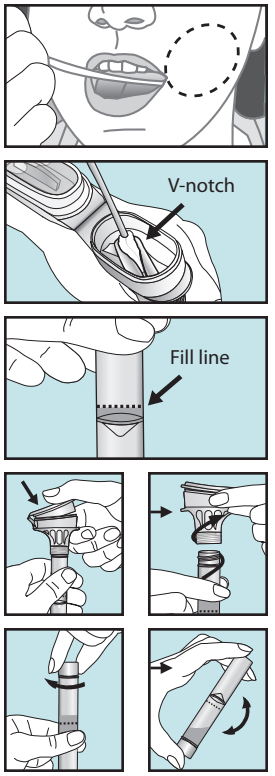
Donor collection instructions for use

Product number	Donor collection instructions for use document number
OGD-500/OGD-510	PD-PR-00151
OGD-600/OGD-610	PD-PR-00502
OGD-575	PD-PR-00152
OGD-675	PD-PR-00503

OGD-500/OGD-600
OGD-510/OGD-610†



OGD-575/OGD-675†



† For detailed instructions refer to the full instructions for use, as referenced in the table above. Available at www.dnagenotek.com.

Transportation of Oragene•Dx

Pre-collection

Oragene•Dx kits can be transported at temperatures ranging from -20°C to 50°C.

Post-collection

Oragene•Dx/saliva samples can be transported at temperatures ranging from -20°C to 50°C.

For domestic or international shipments, specimens should be packaged and labelled in compliance with applicable state, federal, and international regulations covering the transport of clinical, diagnostic, or biological specimens.

Storage of Oragene•Dx

Pre-collection

Store Oragene•Dx kits at room temperature for up to 30 months.

Post-collection

Store Oragene•Dx/saliva samples at room temperature for up to 12 months (OGD-500/OGD-600, OGD-510/OGD-610 and OGD-575/OGD-675).

To achieve optimal sample preservation kits must be closed tightly and stabilization liquid must be fully released from the funnel lid.

Purification and quantification

Oragene•Dx performance has been established using the following protocols:

1. Performance characteristics for the Oragene•Dx kits were established using DNA Genotek's manual purification protocol.
2. OGD-500/OGD-600, OGD-510/OGD-610 and OGD-575/OGD-675: *Manual purification protocol for 0.5 mL Oragene•Dx/saliva sample* (DNA Genotek).
3. We recommend quantifying DNA using fluorescent dyes specific for double stranded DNA (PicoGreen® or SYBR® Green I).

Purification protocols are available at www.dnagenotek.com.

Performance characteristics (representative data)

The following data are representative of Oragene•Dx performance and were generated using the purification and extraction methods described in purification and quantification section on page 4.

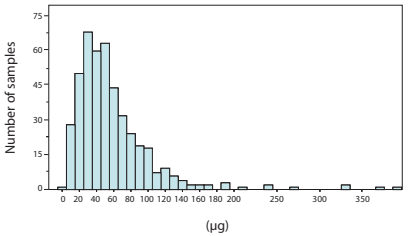
The results obtained during studies of product performance support the following claims.

Oragene•Dx device performance and format comparison

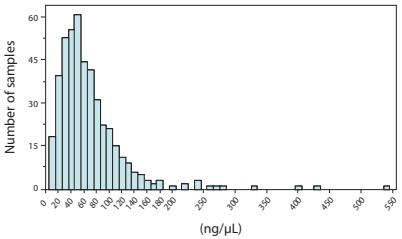
Data from a total of 450 samples from 245 unique donors is used in support of the performance characteristics for OGD-500/OGD-600. A subset of 43 donors is used in support of the performance characteristics for OGD-575/OGD-675. Data from 45 donors is used in support of the performance characteristics for OGD-510/OGD-610.

OGD-500/OGD-600

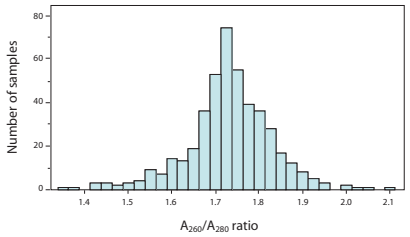
Summary for yield (µg)



Summary for DNA concentration



Summary for A_{260}/A_{280} ratio

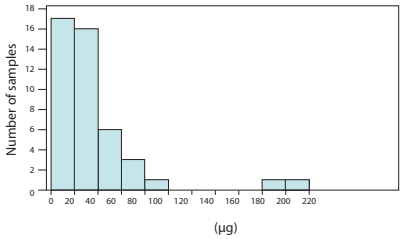


OGD-500/OGD-600 summary

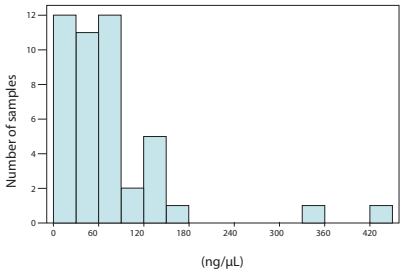
	Yield (µg)	Concentration (ng/µL)	A_{260}/A_{280} ratio
Mean ± SD	58.5 ± 47.0	68.1 ± 55.3	1.7 ± 0.1
Median	48.4	55.3	1.7
95% of samples	≥ 13.1	≥ 16.0	1.5 – 1.9

OGD-510/OGD-610

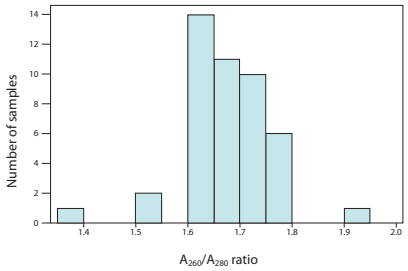
Summary for yield (µg)



Summary for DNA concentration



Summary for A_{260}/A_{280} ratio

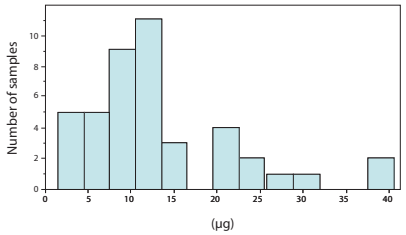


OGD-510/OGD-610 summary

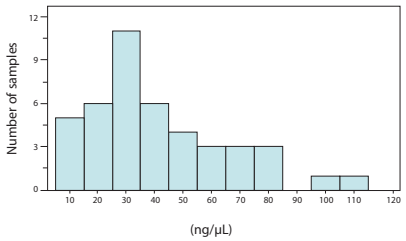
	Yield (µg)	Concentration (ng/µL)	A_{260}/A_{280} ratio
Mean ± SD	36.0 ± 41.1	76.3 ± 78.0	1.7 ± 0.1
Median	27.0	52.1	1.7
90% of samples	≥ 6.9	≥17.1	≥1.6

OGD-575/OGD-675

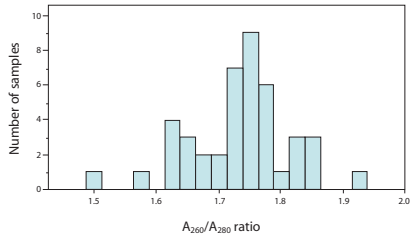
Summary for DNA yield



Summary for DNA concentration



Summary for A_{260}/A_{280} ratio



OGD-575/OGD-675 summary

	Yield (µg)	Concentration (ng/µL)	A_{260}/A_{280} ratio
Mean ± SD	13.5 ± 8.8	41.1 ± 24.6	1.7 ± 0.1
Median	11.0	33.2	1.7
95% of samples	≥ 3.8	≥ 11.2	1.6 – 1.9

Summary of eSensor® Warfarin Sensitivity Saliva Test results for Oragene•Dx format comparison

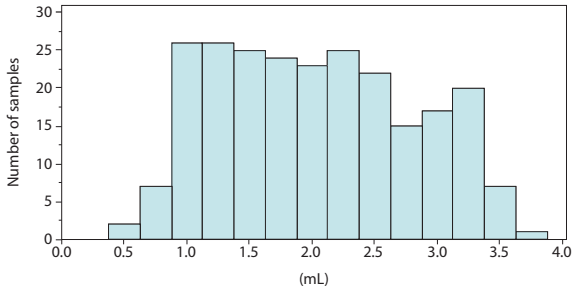
Format	SNP	Samples tested	Correct calls	Incorrect calls	No-calls	% Correct calls
OGD-500/ OGD-600	2C9*2	45	45	0	0	100%
	2C9*3	45	45	0	0	100%
	VKORC1	45	45	0	0	100%
OGD-510/ OGD-610	2C9*2	45	45	0	0	100%
	2C9*3	45	45	0	0	100%
	VKORC1	45	45	0	0	100%
OGD-575/ OGD-675	2C9*2	43	40	0	3†	93.0%
	2C9*3	43	40	0	3†	93.0%
	VKORC1	43	40	0	3†	93.0%
After re-test						
OGD-575/ OGD-675	2C9*2	43	43	0	0	100%
	2C9*3	43	43	0	0	100%
	VKORC1	43	43	0	0	100%

† First-pass no-call results were due to eSensor® control failures.

Volume tolerance

A total of 240 samples were collected using OGD-500/OGD-600 with modified fill lines in order to simulate both under and over spitting. Collected samples ranged from as low as 0.58 mL of saliva to as much as 3.64 mL of saliva with a median collection volume of 2.00 mL.

Collected saliva volume



As expected the DNA yield was dependent on collected volume and neither the A_{260}/A_{280} ratio or performance was affected by over or under spitting. All samples contained sufficient DNA with sufficient quality to be used on the eSensor® Warfarin Sensitivity Saliva Test. All 240 samples gave a correct call after re-testing.

Summary of eSensor® Warfarin Sensitivity Saliva Test results after re-testing for sample volume tolerance study

Range of collected saliva volume (mL)	Samples tested	Correct calls	Incorrect calls	No-calls†	% Correct calls
0.58 – 3.64	240	240	0	0	100%

† One first-pass no-call which was resolved upon re-testing.

Interfering substances

Both endogenous and exogenous potentially interfering substances were added separately to OGD-500/OGD-600/saliva samples from donors with known genotypes. Addition of tested substances had no effect as demonstrated through testing on the eSensor® Warfarin Sensitivity Saliva Test. All samples gave a correct call on the first-pass.

Summary of eSensor® Warfarin Sensitivity Saliva Test results for interfering substances

Endogenous substance	Samples tested	Correct calls	Incorrect calls	No-calls	% Correct calls
Control	30	30	0	0	100%
Amylase	30	30	0	0	100%
Hemoglobin	30	30	0	0	100%
IgA	30	30	0	0	100%
Total protein	30	30	0	0	100%

Exogenous substances	Collection time-point post activity	Samples tested	Correct calls	Incorrect calls	No-calls	% Correct calls
Eating	30 minutes	15	15	0	0	100%
Drinking	30 minutes	15	15	0	0	100%
Chewing gum	30 minutes	15	15	0	0	100%
Mouthwash	30 minutes	15	15	0	0	100%
Smoking	30 minutes	15	15	0	0	100%

Reproducibility

The device reproducibility study was conducted at three sites. Three samples (collected using three lots of OGD-500/OGD-600) from each of ten donors, covering all possible genotypes for three alleles for the eSensor® Warfarin Sensitivity Saliva Test, were tested in triplicate by four different operators at three different sites. Each operator extracted DNA from each sample using the same alcohol precipitation method, followed by determination of DNA concentration and A_{260}/A_{280} ratio for all samples by an independent operator at one of the sites. Four operators at three sites tested the extracted DNA samples on the eSensor® Warfarin Sensitivity Saliva Test.

The following table summarizes the DNA concentration, yield and A_{260}/A_{280} ratio results obtained by four operators at three sites.

Summary of device reproducibility DNA concentration, yield and A_{260}/A_{280} results

		Operator 1	Operator 2	Operator 3	Operator 4	Combined
Samples tested		87†	87†	90	90	354
Yield (µg)	Mean ± SD	74.89 ± 68.00	76.68 ± 61.76	69.59 ± 57.24	77.40 ± 68.36	74.62 ± 63.79
	Median	57.31	66.32	60.95	57.62	60.39
	95% of samples	≥ 23.23	≥ 26.56	≥ 18.13	≥ 26.02	≥ 23.47
Concentration (ng/µL)	Mean ± SD	86.76 ± 84.43	87.84 ± 70.76	80.21 ± 67.78	90.20 ± 86.69	86.24 ± 77.61
	Median	63.83	74.43	68.82	66.20	68.58
	95% of samples	≥ 25.87	≥ 29.58	≥ 20.42	≥ 28.98	≥ 26.74
A_{260}/A_{280}	Mean ± SD	1.9 ± 0.1	1.8 ± 0.1	1.9 ± 0.1	1.8 ± 0.1	1.9 ± 0.1
	Median	1.9	1.8	1.9	1.8	1.9
	95% of samples	1.6 – 2.3	1.6 – 2.1	1.7 – 2.0	1.5 – 2.0	1.6 – 2.2

† One sample [3 aliquots] from a donor was excluded due to failure to meet incoming study screening criteria.

Genotyping data was evaluated after first-pass results and after re-testing. Following re-testing and investigation, all samples gave 100% correct calls when compared with bi-directional sequencing. There were five first-pass no calls and one incorrect call which was determined to be due to operator error. The table on the following page summarizes the percent agreement between genotyping results and bi-directional sequencing obtained by four operators at three sites.

Summary of eSensor® Warfarin Sensitivity Saliva Test results for device reproducibility study stratified by site and operator

First-pass

Site	Operator	SNP	Samples tested	Correct calls	Incorrect calls	No-calls‡	% Correct calls
Site 1	Operator 1	2C9*2	87	86	0	1	98.9%
		2C9*3	87	86	0	1	98.9%
		VKOR	87	86	0	1	98.9%
	Operator 2	2C9*2	87	86	0	1	98.9%
		2C9*3	87	86	0	1	98.9%
		VKOR	87	86	0	1	98.9%
Site 2	Operator 3	2C9*2	90	87	1†	2	96.7%
		2C9*3	90	88	0	2	97.8%
		VKOR	90	87	1†	2	96.7%
Site 3	Operator 4	2C9*2	90	43	0	47	47.8%
		2C9*3	90	43	0	47	47.8%
		VKOR	90	43	0	47	47.8%

After re-testing and investigation

	Operator	SNP	Samples tested	Correct calls	Incorrect calls	No-calls	% Correct calls
Site 1	Operator 1	2C9*2	87	87	0	0	100%
		2C9*3	87	87	0	0	100%
		VKOR	87	87	0	0	100%
	Operator 2	2C9*2	87	87	0	0	100%
		2C9*3	87	87	0	0	100%
		VKOR	87	87	0	0	100%
Site 2	Operator 3	2C9*2	90	90	0	0	100%
		2C9*3	90	90	0	0	100%
		VKOR	90	90	0	0	100%
Site 3	Operator 4	2C9*2	90	90	0	0	100%
		2C9*3	90	90	0	0	100%
		VKOR	90	90	0	0	100%

† Incorrect call due to operator error resolved upon investigation.

‡ 46 first-run no-calls were due to two runs (23 samples per run) invalidated due to DNA Contamination Monitor (DCM) failures. The other five first-pass no calls were low signal for the 2C9*2 allele (three), positive control failure (one) and contradictory score at the 2C9*3 allele (one).

Sample stability

Thirty (30) donors each self-collected four saliva samples using Oragene•Dx format OGD-500/OGD-600 for a total of 120 samples. Samples were stored at room temperature (RT), 6°C ± 4°C or -20°C ± 5°C for 12 months, or at 50°C ± 5°C for 3 months. At the study time-point, DNA was extracted and analyzed for yield and A_{260}/A_{280} ratio. Samples stored at room temperature were analyzed for microbial content using a real-time PCR-based assay. A sub-population of samples (188 OGD-500/OGD-600 samples across all time-points) was tested on the eSensor® Warfarin Sensitivity Saliva Test.

Summary of post-collection (sample) stability study results

	Temperature	-20°C ± 5°C	6°C ± 4°C	RT	50°C ± 5°C	Freeze (-20°C)/ thaw (50°C)
	Time (months)	12	12	12	3	
OGD-500/ OGD-600	Yield	●	●	●	●	●
	A_{260}/A_{280} ratio	●	●	●	●	●

● Samples meet acceptance criteria (yield ≥ 10 ng, A_{260}/A_{280} ratio 1.2 – 2.3).

Summary of eSensor® Warfarin Sensitivity Saliva Test results for sample stability study

First-pass

Format	Samples tested	Correct calls	Incorrect calls	No-calls	% Correct calls
OGD-500/ OGD-600	188	183	1	4	97.3%

After re-testing

Format	Samples tested	Correct calls	Incorrect calls	No-calls	% Correct calls
OGD-500/ OGD-600	188	187	1†	0	99.5%

† After incorrect call investigation it was determined that there was a sample contamination due to user error during purification.

Microbial content of samples stored at room temperature for 12 months

Samples stored at room temperature for 12 months exhibited no significant change in microbial content.

OGD-500/OGD-600		Baseline	12 months
Samples tested		29‡	29‡
% Microbial content	Mean ± SD	7.3% ± 5.5%	7.9% ± 5.5%
	Median	6.0%	5.9%
	Min, Max	0.6%, 22.1%	1.6%, 24.8%
	p-value	0.72	

‡ Insufficient sample obtained from 1 donor.

Medical device symbol chart

	Consult package insert
	Collect saliva by (Use by)
IVD	In vitro diagnostic medical device
REF	Catalog number
CE	CE Marking
	Caution, consult instructions for use
15°C 30°C	Storage instructions
EC REP	Authorized Representative
	Manufacturer
LOT	Lot number

Patent information

Patent (www.dnagenotek.com/legalnotices)

Troubleshooting

Before collection

Observation	Action
There is no stabilizing liquid in the funnel lid or the funnel lid is leaking.	Do NOT allow donor to use the product; discard and request a replacement kit.
Stabilizing liquid comes into contact with eyes or skin.	Get donor to wash with water if stabilizing liquid comes in contact with eyes or skin. Do NOT allow donor to ingest stabilizing liquid. For safety data information consult the MSDS at www.dnagenotek.com. To close funnel lid properly, ask donor to firmly push the lid until it makes a loud click.
Sample has many bubbles.	Ask the donor to tap the tube on a flat surface to allow bubbles to settle in the tube.
When removing funnel from tube, the sample overflows onto tube exterior and/or donor's hands.	Ask donor to cap the tube with small cap, wipe the outside of the tube with a paper towel and wash hands.

Before purifying

Observation	Action
Volume of collected sample is below fill line.	Donor user error. Recollect sample. Possible causes: • Insufficient sample collected. • Stabilizing liquid not fully released.
Saliva sample is cloudy, discoloured, and/or has floating particles.	Sample appearance may indicate that the donor did NOT follow the instructions for use. However this is unlikely to affect sample quality or performance as evaluated on GenMark Diagnostics' eSensor® Warfarin Sensitivity Saliva Test. Interference studies have demonstrated that such samples should not impact the genotyping results. Substances outside the scope of the interference study have not been evaluated thus caution should be taken when testing samples of abnormal appearance, such samples may require re-collection in accordance to the instructions for use. According to donor instructions for use, ensure donor abstains from eating, drinking, smoking or chewing gum for 30 minutes prior to donating a sample.
Sample is difficult to pipette.	Prior to sample purification, heat the entire sample in its original container at 50°C for at least an hour.
Sample leaked.	Donor error. Recollect sample.

Oragene®•DNA is not available for sale in the United States.

Oragene®•DISCOVER is for research use only, not for use in diagnostic procedures.

All DNA Genotek protocols, white papers and application notes, are available in the support section of our website at www.dnagenotek.com.

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