Product handbook

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Subsidiary of OraSure Technologies, Inc.

Superior samples
Proven performance

CE IVD MD UKCA

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CE IVD MD UK CA

EC REP

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Intended use

ORAcollect®•RNA (ORE-100) is intended for the collection and stabilization of RNA from human saliva samples.

Summary and explanation of use

ORAcollect•RNA (ORE-100) is a self-collection kit that provides the materials and instructions for collection, stabilization, storage and transportation of saliva specimens suspected of containing SARS-CoV-2 ribonucleic acid (RNA).

Special conditions for use statement (Canada)

For In Vitro Diagnostic Use Only, and For Use Under Interim Order Respecting the Importation and Sale of Medical Devices for Use in Relation to COVID-19

- Users must validate the use of the ORAcollect•RNA (ORE-100) with their assay for SARS-CoV-2 testing.

Special conditions for use statement (United States)

For In Vitro Diagnostic Use Only, For Prescription Use Only, and For Use Under Emergency Use Authorization

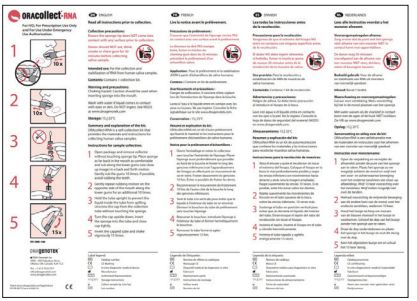
- This sample collection device has not been FDA cleared or approved.
- This sample collection device has been authorized by FDA under an EUA.
- This sample collection device has been authorized only to collect, stabilize, and maintain during transport, saliva specimens suspected of containing SARS-CoV-2 ribonucleic acid (RNA), not for any other viruses or pathogens.
- This sample collection device is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of medical devices during the COVID-19 outbreak under Section 564(b)(1) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

Features of ORAcollect•RNA (ORE-100)

- Non-invasive, reliable self-collection of saliva without the challenges associated with clinical or hospital settings.
- Stabilization of RNA from human saliva samples for up to 60 days at room temperature (20°C to 26°C/68°F to 79°F).
- Stabilization of saliva samples for the detection of SARS-CoV-2 viral RNA for up to 48 hours at room temperature.[1]
- Inactivates SARS-CoV-2 virus.[2]
- Pre- and post-collection, the device and chemistry can withstand expected transport (-20°C to 50°C/-4°F to 122°F) and up to 3 freeze-thaw cycles.
- Barcoded samples enable laboratory workflow efficiencies and sample traceability.

Materials

Each single-use ORAcollect•RNA (ORE-100) kit includes a sample collection device and multi-language Instructions for Use.



Warnings and precautions

Collection instructions must be strictly followed so that test results are not compromised, including, but not limited to, an elevated risk of false negative results.

1. IVD In Vitro Diagnostic Medical Device.
2. For IVD Use, For Rx Use and For Use under Emergency Use Authorization.
3. Do NOT use if packaging is damaged or device is broken or leaking. Discard unused, damaged or leaking kits in accordance with appropriate regulations.
4. Do NOT use ORAcollect•RNA (ORE-100) beyond the "use by" date indicated on the device.
5. Only use the components and accessories provided with the kit.

6. Collection precautions:
    - **Read all instructions carefully prior to sample collection; deviation may result in inadequate sample collected, which may lead to inaccurate test results including false negative results and delay in diagnosis.**
    - Do NOT eat, drink, smoke or chew gum for 30 minutes before sample collection.
    - Ensure the sponge tip does NOT come into contact with any surface prior to collection.
    - Choking hazard. Caution should be used when inserting the sponge into the donor's mouth.
    - Wash with water if stabilizing liquid comes in contact with eyes or skin.
    - Do NOT ingest stabilizing liquid.
7. Decontaminate and dispose of all specimens, reagents and other potentially contaminated materials in accordance with local, regional and federal regulations.
8. This product requires the handling of human saliva specimens.
9. Material Safety Data Sheet (MSDS) is available at www.dnagenotek.com.

Product use limitations

- **For SARS-CoV-2 testing: Saliva samples must be processed within 72 hours of collection. Saliva specimen must NOT be collected on the weekend. The specimen must be collected and shipped on the same day Monday through Friday (before the last pickup time for overnight shipping).**
- Performance characteristics of the ORAcollect•RNA (ORE-100) kits were established using the QIAGEN® miRNeasy® Mini extraction kit (Cat. No./ID: 217004), according to the manufacturer's instructions.
- Performance of ORAcollect•RNA (ORE-100) was demonstrated by the evaluation of total RNA yield and ribosomal RNA stability using the Agilent RNA 6000 Nano Kit (Cat. no./ID: 5067-1511) with the 2100 Bioanalyzer, according to the manufacturer's instructions.

Donor collection instructions

Catalog number	Donor collection instructions document number
ORE-100	PD-PR-00764

ORAcollect®•RNA

REF ORE-100

Collection precautions:

Ensure the sponge tip does NOT come into contact with any surface prior to collection.

Donor should NOT eat, drink, smoke or chew gum for 30 minutes before collecting saliva sample.

Intended use: For the collection and stabilization of RNA from human saliva samples

Contents: Contains 1 collection kit

Warnings and precautions: Choking hazard. Caution should be used when inserting sponge into the mouth.

Wash with water if stabilizing liquid comes in contact with eyes or skin. Do NOT ingest. See MSDS at www.dnagenotek.com

Storage: 15°C-25°C

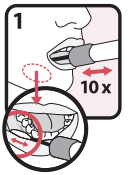
Summary and explanation of the kit: ORAcollect•RNA is a self-collection kit that provides the materials and instructions for collecting human saliva samples.

Label legend:

REF	Catalog number
Rx	For Prescription Use Only
IVD	In vitro diagnostic medical device
CE	CE marking
UK CA	UKCA marking
	Manufacturer
MD	Medical device
	Do not re-use
	Consult instructions for use
	Use by
LOT	Lot number
EC REP	Authorized Representative

ENGLISH

Instructions for sample collection:



Open package and remove collector without touching sponge tip. Place sponge as far back in the mouth as comfortable and rub along the lower gums (see close-up image) in a back and forth motion. Gently rub the gums 10 times. If possible, avoid rubbing the teeth.

Gently repeat rubbing motion on the opposite side of the mouth along the lower gums for an additional 10 times.

Hold the tube upright to prevent the stabilizing liquid inside the tube from spilling. Unscrew the cap from the collection tube without touching the sponge.

Turn the cap upside down, insert the sponge into the tube and close cap tightly.

Invert the capped tube and shake vigorously 15 times.

Instructions in other languages are available at www.dnagenotek.com

Transportation of ORAcollect•RNA (ORE-100)

Pre-collection

ORAcollect•RNA (ORE-100) kits can be transported at temperatures ranging from -20°C to 50°C/-4°F to 122°F.

Post-collection

Samples collected with ORAcollect•RNA (ORE-100) can be transported at temperatures ranging from -20°C to 50°C/-4°F to 122°F.

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

Storage of ORAcollect•RNA (ORE-100)

Pre-collection

ORAcollect•RNA (ORE-100) kits are validated for storage between 15°C and 25°C (59°F and 77°F) for up to 24 months.

Post-collection

Room temperature storage: Saliva samples collected in ORAcollect•RNA (ORE-100) are validated for storage at room temperature (20°C to 26°C/68°F to 79°F) for up to 60 days after sample collection.

Important: Storing at 4°C (39°F) is NOT recommended for saliva samples collected in ORAcollect•RNA (ORE-100).

For SARS-CoV-2 testing: Saliva samples collected in ORAcollect•RNA (ORE-100) for SARS-CoV-2 testing can be stored at room temperature (20°C to 26°C/68°F to 79°F) for up to 48 hours after sample collection.[1]

Freeze-thaw cycles: ORAcollect•RNA (ORE-100) will maintain RNA integrity for up to 3 freeze-thaw cycles.

Purification

Preprocessing step

Saliva samples collected in ORAcollect•RNA (ORE-100) should be incubated at 50°C (122°F) for one hour in a water bath or two hours in an air incubator (in the original tube), and mixed well by inversion.

ORAcollect•RNA (ORE-100) performance has been established using the following protocol:

RNA purification: ORAcollect•RNA (ORE-100) RNA purification was performed using the QIAGEN miRNeasy Mini extraction kit, according to the manufacturer's instructions.

Sample stability

Room temperature stability

To evaluate the performance of ORAcollect•RNA (ORE-100) to stabilize RNA from human saliva, stability testing was performed on ORAcollect•RNA (ORE-100) collected samples.

Post-collection stability of samples was assessed by quantifying RNA yield both immediately following sample collection (Baseline) and after a 60-day hold (60 days) of those samples at room temperature (20°C to 26°C/68°F-79°F) (Table 1).

In addition to RNA yield quantification, stability of ribosomal RNA during room temperature hold was also assessed using the Agilent RNA Nano 6000 Kit, where integrity of 16S and 23S ribosomal RNA bands was visualized to compare baseline and 60-day hold RNA extracts (Figure 1).

Table 1. RNA yield quantification of collected samples. *Total RNA yield from baseline extraction and following 60-day hold of collected samples at room temperature (20°C to 26°C/68°F to 79°F).*

		Baseline (N = 20)	60 days (N = 20)
RNA yield (µg) Acceptable minimum: 0.1 µg	Mean ± SD	5.94 ± 2.85	6.85 ± 3.49
	Median	4.86	5.94
	Min, Max	2.16, 12.42	1.98, 15.84
	% within acceptable range	100%	100%

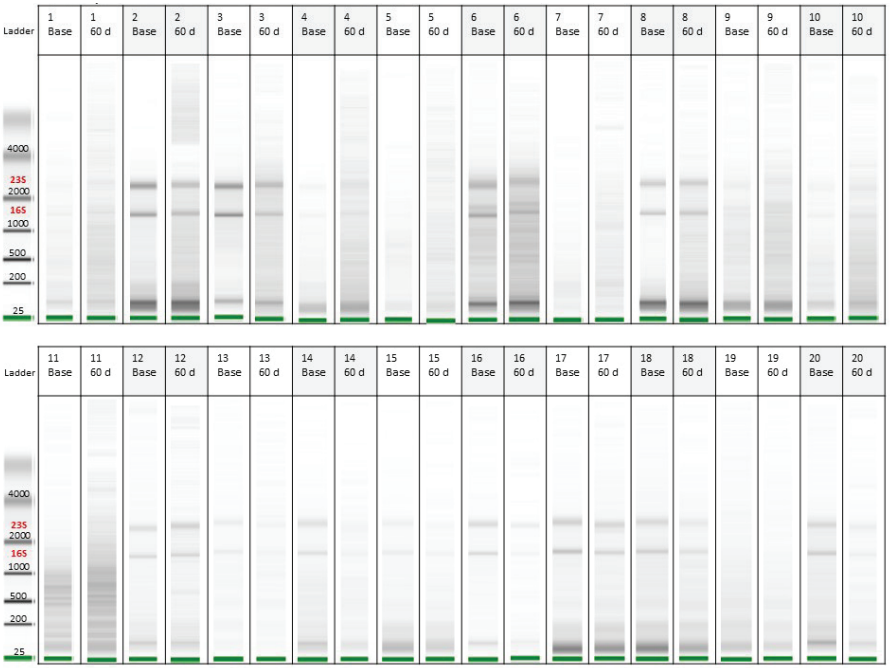


Figure 1. Room temperature post-collection RNA stability. *Bioanalyzer images for each of N = 20 samples collected in ORAcollect•RNA devices aged for 13 months at 27°C ± 2°C pre-collection, showing baseline extraction (Base) and 60-day post-collection extraction (60 d) side by side for each collected sample. Ladder fragment sizes are shown as total number of bases. Approximate location of 16S and 23S ribosomal RNA bands is indicated on the ladder in red font.*

Simulated transport stability

To assess stability of ORAcollect•RNA (ORE-100) during expected transport conditions, devices were cycled through extreme temperatures, in excess of what is expected to occur during transport (three cycles of -20°C (-4°F) for ≥ 3 hours to 50°C (122°F) for ≥ 3 hours). Following exposure of the devices to the simulated transport conditions, 20 donors each collected one sample. From each sample, RNA was extracted immediately following sample collection (Baseline). The collected samples were then subjected to the simulated transport conditions. Following exposure of the collected samples to simulated transport conditions, RNA was extracted (Transport).

Stability of samples was assessed through RNA quantification (Table 2) and through the evaluation of ribosomal RNA stability using the Agilent Bioanalyzer RNA Nano 6000 Kit, where integrity of 16S and 23S ribosomal RNA bands was visualized (Figure 2).

Table 2. RNA yield quantification after simulated transport conditions. *Using devices exposed pre-collection to transport simulation, total RNA yield from baseline extraction (Baseline) and following 60-day hold at room temperature, which included additional exposure of collected samples to simulated transport (Transport).*

		Baseline (N = 20)	Transport (N = 20)
RNA yield (µg) Acceptable minimum: 0.1 µg	Mean ± SD	7.31 ± 5.66	5.62 ± 3.68
	Median	6.48	4.59
	Min, Max	0.90, 26.28	0.36, 14, 22
	% within acceptable range	100%	100%

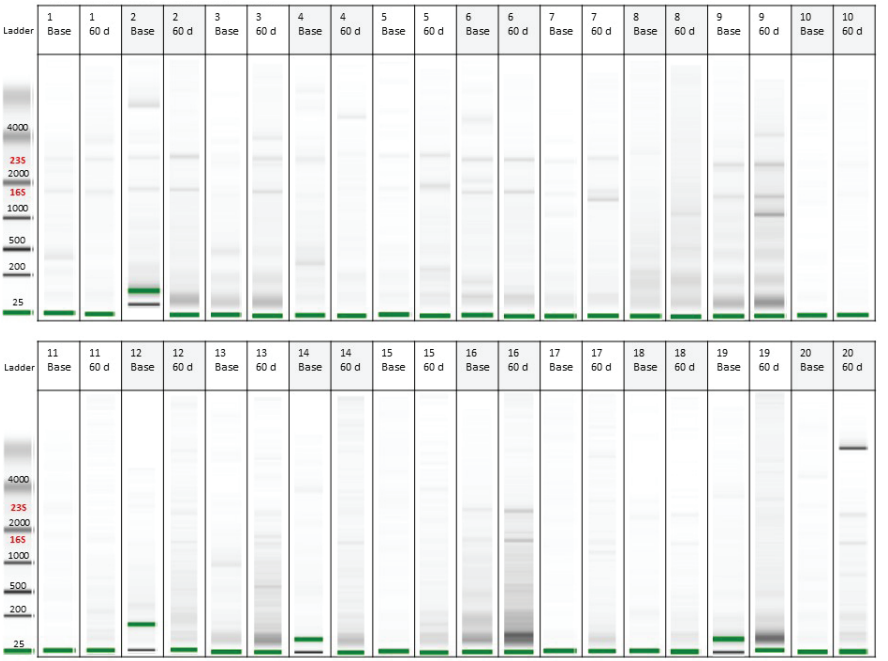


Figure 2. Simulated transport post-collection stability. *Bioanalyzer images for each of N = 20 samples, showing baseline extraction (Base) and 60-day post-collection extraction (60 d) side by side for each collected sample. Ladder fragment sizes are shown as total number of bases. Approximate location of 16S and 23S ribosomal RNA bands is indicated on the ladder in red font.*

Viral RNA stability (clinical SARS-CoV-2 evaluation)

A study was performed to evaluate the use of saliva collected with ORAcollect•RNA (OR-100) as a specimen type for detection of SARS-CoV-2 in patients who were suspected of having COVID-19. The study is included in the EUA provided to the FDA for the Clarifi COVID-19 Test Kit.[1] The study was conducted with symptomatic patients who were each swabbed within 0-5 days of having provided comparative nasopharyngeal (NP) swabs (32 negative, 31 positive) from an EUA authorized SARS-CoV-2 RT-PCR assay. Samples were collected by health care providers with ORAcollect•RNA (OR-100) collection devices, which are identical in both physical format and function to ORE-100 collection devices. The Instructions for Use provided with the collection device were followed.[1] Samples were labelled with the patient's ID number and the date and time the sample was collected; they were then packaged, shipped and transported according to the current edition of the International Air Transport Association (IATA) Dangerous Goods Regulations, following shipping regulations for UN 3373 Biological Substance, Category B when sending potential SARS-CoV-2 specimens. Samples were stored at ambient temperature and shipped overnight.

There was 100% positive and negative agreement between the results obtained from testing of saliva and those obtained from NP swab. Of the 31 previously reported positive NP swab samples, all 31 paired NP and saliva specimens produced positive results (31/31; 100%); all 32 paired NP and saliva specimens produced negative results (32/32; 100%), as shown in Table 3. The results of the clinical evaluation with paired NP swabs and saliva specimens were therefore considered acceptable.

Table 3. Clinical evaluations. *Summary of results obtained from parallel testing of nasopharyngeal swab samples and saliva from patients suspected of having COVID-19. Adapted from "Emergency Use Authorization (EUA) Clarifi COVID-19 Test Kit Instructions for Use" by Quadrant Biosciences Inc, 2020.*

		EUA authorized comparator (NP swab)		Total
		Positive	Negative	
Clarifi COVID-19 Test Kit (Saliva)	POSITIVE	31	0	**31**
	NEGATIVE	0	32	**31**
	Total	**31**	**32**	**63**
Positive percent agreement (PPA): 31/31 = 100% (95% CI) **Negative percent agreement (NPA): 32/32 = 100% (95% CI)**				

SARS-CoV-2 inactivation

A study was conducted to demonstrate the ability of the stabilizing solution contained in DNA Genotek® collection devices to inactivate the SARS-CoV-2 virus.[2] ORAcollect•RNA (ORE-100) contains the same chemistry as OMNIgene®•ORAL (OME-505) but at 50% of the concentration, due to the very small amount of saliva that is collected using the ORAcollect•RNA (ORE-100) device. This reduction of the concentration allows for approximately the same working concentration of the chemistry across both products. Therefore, the inactivation data collected for OMNIgene•ORAL (OME-505) stabilization chemistry supports inactivation of SARS-CoV-2 for both products.

Briefly, in this study, saliva samples collected from healthy subjects were spiked with a known quantity of infective SARS-CoV-2 virus in parallel with PBS (phosphate-buffered saline) as a positive control and unspiked samples as a negative control. Aliquots of spiked saliva or PBS were added to OMNIgene•ORAL (OME-505) collection devices and mixed with the stabilizing solution. An endpoint dilution assay was performed in Vero E6 cultured cells to quantify the amount of remaining infective virus in each sample, which is represented as TCID50/mL. There was > 99% reduction in infective virus in OMNIgene•ORAL (OME-505) with no observable difference with unspiked negative controls (Figure 3).

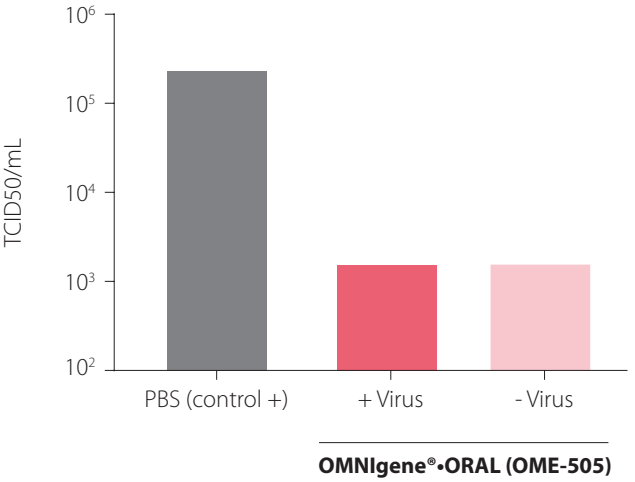


Figure 3. Quantification of infective SARS-CoV-2 in virus-spiked, unstabilized PBS (control +) and OMNIgene•ORAL (OME-505) stabilized saliva (+ Virus). *Unspiked PBS mixed with OMNIgene•ORAL (OME-505) stabilizing solution was used as a negative control (- Virus). Note that ORAcollect•RNA (OR-100 and ORE-100) contains the same chemistry as OMNIgene•ORAL (OME-505) but at 50% to maintain approximately the same working concentration of the chemistry across both products. Therefore, the inactivation data collected for OMNIgene•ORAL (OME-505) stabilization chemistry supports inactivation of SARS-CoV-2 for both products.*

Collection tolerances

Flex studies

ORAcollect•RNA design is based on the same platform as the ORAcollect•Dx saliva collection device in that they use an integrated sponge to collect oral or saliva samples. ORAcollect•Dx is FDA cleared for IVD use and suitable for self-collection by naive users (see K152464).[3]

Using the equivalent ORAcollect•Dx device, the usability and human factors studies evaluated the effect of sampling variability due to use collection error. The study evaluated the effects of incorrect collection methods and the effect of collection from an incorrect site.

In summary:

- Multiple samples were collected from each of ten (10) donors, with each donor using one of the pre-identified collection sites for each sample collection.
- DNA was extracted from each sample using the QIAamp® DNA Mini Kit (QIAGEN) and performance was evaluated by measuring DNA concentration, total sample DNA yield, A_{260}/A_{280} ratio and agreement between genotyping results on the eSensor® Warfarin Sensitivity Saliva Test (GenMark Diagnostics) and bidirectional sequencing. Study success was evaluated against predefined acceptance criteria and performance claims determined based on study data.
- Robustness of the ORAcollect•Dx collection device was demonstrated with all samples collected using the varied collection methods meeting the acceptance criteria of DNA concentration ≥ 2 ng/µL; total DNA yield ≥ 0.01 µg and A_{260}/A_{280} ratio between 1.2 and 2.3.
- Robustness of the ORAcollect•Dx collection device was also demonstrated with samples collected from an incorrect site in the mouth meeting acceptance criteria of DNA concentration ≥ 2 ng/µL; total DNA yield ≥ 0.01 µg and A_{260}/A_{280} ratio between 1.2 and 2.3, except in the case of an atypical collection site (cheek), where only 90% of samples had a DNA concentration ≥ 2 ng/µL.
- After final pass, there was 100% agreement irrespective of using alternative incorrect collection methods or incorrect collection sites.
- Overall, study data supports the robustness of ORAcollect•Dx, even in the hands of naive users and/or when instructions for use are not followed properly.

Usability studies

Home collection and mailing the sample to a CLIA-certified lab

Usability testing was done using the FDA guidance document *Applying Human Factors and Usability Engineering to Medical Devices* (February 2016).

The ORAcollect•RNA device contains the same physical components and collection procedure as the ORAcollect•Dx (OCD-100) device. Testing of ORAcollect•Dx (OCD-100) is referenced to fulfil usability performance requirements. See K152464 for usability and human factors data.[3] It is well demonstrated that samples can be mailed to a CLIA-certified lab for testing.

ORAcollect•Dx (OCD-100) usability study (K152464):

- 101 naive participants were observed completing the sample collection process.
- Study observers completed an observational checklist for each participant to document how each core task was performed.
- Each of the individual core tasks was performed correctly by ≥ 74% of the participants; the overall task success rate was 93.9%.
- Specimen adequacy across the entire study population:
  - 99% of samples had a concentration of DNA ≥ 2 ng/µL.
  - 100% of samples had an A_{260}/A_{280} ratio between 1.2 and 2.3.
- All acceptance criteria, predefined in the study protocol, were met successfully.

Biocompatibility

Biocompatibility testing of the materials included in ORAcollect•RNA was completed.[3] This testing was conducted on ORAcollect•Dx (OCD-100), a representative product that has equivalent components.

In summary, the results of the biocompatibility studies showed that:

- Based on the criteria of the test protocol and ISO 10993-5 guidelines, the device is not considered to have a cytotoxic effect.
- Based on the criteria of the test protocol and ISO 10993-10 guidelines, the device elicited no reaction at the challenge (0% sensitization) following an induction phase and therefore can be classified as non-sensitizers.
- Based on the criteria of the test protocol and the ISO 10993-10 guidelines, the device did not produce any primary buccal irritation following exposure (minimum of five minutes per hour for four hours) and therefore can be considered to be a non-irritant to buccal tissues.

Medical device symbol chart

REF	Catalog number
Rx	For Prescription Use Only
IVD	In vitro diagnostic medical device
CE	CE marking
UKCA	UKCA marking
	Manufacturer
MD	Medical device
	Do not re-use
	Consult instructions for use
	Use by
LOT	Lot number
EC REP	Authorized Representative

Patent information

Patent (www.dnagenotek.com/legalnotices)

Troubleshooting

Pre-collection

Observation	Action
There is no stabilizing liquid in the device or the device 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.	Wash with water if stabilizing liquid comes in contact with eyes or skin. For safety data information, consult the MSDS at www.dnagenotek.com.

Post-collection (before RNA extraction)

Observation	Action
Saliva sample is cloudy, discoloured and/or has floating particles.	Sample appearance may indicate that the donor did NOT follow the Instructions for Use. Caution should be taken when testing samples of abnormal appearance; such samples may require re-collection in accordance with the instructions for use.
Sample is difficult to pipette.	Prior to sample extraction, heat the entire sample in its original tube at 50°C for at least one hour in a water bath or two hours in an air incubator.
Sample leaked.	Donor error. Re-collect sample.

1 Quadrant Biosciences Inc. Emergency Use Authorization (EUA) Clarifi COVID-19 Test Kit Instructions for Use.
2 DNA Genotek. Inactivation of SARS-CoV-2 in samples collected using Oragene®, ORAcollect® and OMNIgene® products from DNA Genotek™ (MK-01430). https://www.dnagenotek.com/us/pdf/MK-01430.pdf
3 510(k) Substantial Equivalence Determination Decision Summary Assay Only Template (510(k) number K152464). https://www.accessdata.fda.gov/cdrh_docs/reviews/K152464.pdf

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