Abstract

Molecular diagnostic tests allow for the rapid and accurate detection of biomarkers. Achieving high sensitivity and specificity of a diagnostic test requires a reliable and high-quality sample. While traditionally blood was considered the preferred sample type for diagnostic applications, DNA from saliva is non-invasive and is now proven to be a viable and beneficial alternative. DNA from saliva improves patient care and convenience with point-of-care sample collection while enabling efficient storage and transportation of stable samples at ambient temperature. DNA from saliva is reliably and easily collected using ORAcollect®•Dx. ORAcollect®•Dx OCD-100 is a device for the collection, stabilization and transportation of DNA from saliva and offers a non-invasive, reliable method for collection of samples. A 510(k) validation study was performed to demonstrate the safety, effectiveness and robustness of the product.

Validation studies demonstrated that prior to collection the ORAcollect-Dx kits can be transported at temperatures ranging from -20°C to 50°C and can be stored at room temperature for up to 24 months. Once saliva is collected, ORAcollect®•Dx/saliva can be transported at temperatures ranging from -20°C to 50°C and can be stored at room temperature for up to 60 days without compromising the quality of the DNA present in the sample. DNA from 156 unique donors was extracted using the QIAamp® DNA Mini Kit and used to demonstrate performance characteristics for ORAcollect®Dx (DNA yield, DNA concentration and A260/A280 ratio). Performance of DNA extracted from ORAcollect®•Dx/saliva was also demonstrated in a molecular diagnostic assay, the eSensor® Warfarin Sensitivity Saliva Test (GenMark Diagnostics).

Device stability

Shelf life conditions were evaluated by testing devices that had been stored at room temperature (RT) for more than 24 months pre-collection. Additionally, separate devices were used to test simulated transportation conditions where the devices were subjected to multiple freeze/thaw cycles pre-collection. At study time-points, a subset of devices was evaluated for physical and chemical properties to ensure the product specifications remained within acceptable limits. Interfering substances were assessed through additional experiments, there was no effect of endogenous and exogenous potentially interfering substances (e.g., amylase, hemoglobin, eating, drinking, chewing gum) on performance. Product robustness was demonstrated through user studies which showed samples collected under variable conditions still met performance characteristics for the product. In conclusion, these studies validated the safety and effectiveness of ORAcollect®•Dx and demonstrated it is a reliable alternative to blood for use in molecular diagnostic applications.

Sample stability

Test OCD-100 samples were collected from each of 30 donors for a total of 60 samples. Samples were stored at room temperature (RT) for 60 days or subjected to 3 freeze/thaw cycles. At the study time-point, DNA was extracted and analyzed for yield/concentration and A260/A280 ratio. Reproducibility studies were conducted to evaluate sample, device lot, operator and processing site variability. Replicate samples were tested on the eSensor® Warfarin Sensitivity Saliva Test and 100% concordance with bidirectional sequencing was observed for all samples. Interfering substances were assessed with additional experiments; there was no effect of endogenous and exogenous potentially interfering substances (e.g., amylase, hemoglobin, eating, drinking, chewing gum) on performance. Product robustness was demonstrated through user studies which showed samples collected under variable conditions still met performance characteristics for the product. In conclusion, these studies validated the safety and effectiveness of ORAcollect®•Dx and demonstrated it is a reliable alternative to blood for use in molecular diagnostic applications.

Device stability

Pre-collection condition

OAD-100

Long-term storage (RT, 24 months)

Simulated transport (Freeze, 20°C / Thaw 50°C)

ODC-100

Chemical properties

DNA concentration (ng/µL)

A260/A280 ratio

Post-collection condition

OAD-100

Long-term storage (RT, 60 days)

Simulated transport (Freeze, 20°C / Thaw 50°C)

WST

100% agreement

100% agreement

Microbial content of samples stored at room temperature for 60 days

OAD-100

Baseline

60 days

Samples tested

30

30

% microbial content

Mean ± SD

5.5 ± 3.79

5.15 ± 3.79

Median

Mean

Max

Min

p-value

Microbial content of samples stored at room temperature for 60 days

OAD-100

Baseline

60 days

Samples tested

30

30

% microbial content

Mean ± SD

5.5 ± 3.79

5.15 ± 3.79

Median

Mean

Max

Min

p-value

Reproducibility

Three samples (collected using three lots of OCD-100) from each of ten donors, were processed by three different operators on multiple days. Each operator extracted DNA from each sample using the QIAamp® DNA Mini Kit, followed by determination of DNA concentration and A260/A280 ratio for all samples. Three operators tested the extracted DNA samples on the eSensor® Warfarin Sensitivity Saliva Test. Genotyping data was evaluated after fast-pass results and all samples were concordant with bi-directional sequencing.

Summary of results stratified by operator

<table>
<thead>
<tr>
<th>Sample type</th>
<th>Operator 1</th>
<th>Operator 2</th>
<th>Operator 3</th>
<th>Combined</th>
</tr>
</thead>
<tbody>
<tr>
<td>DNA yield (ng/µL)</td>
<td>Mean ± SD</td>
<td>13.9 ± 3.7</td>
<td>13.9 ± 3.7</td>
<td>13.9 ± 3.7</td>
</tr>
<tr>
<td>A260/A280 ratio</td>
<td>Mean ± SD</td>
<td>1.25 ± 0.08</td>
<td>1.25 ± 0.08</td>
<td>1.25 ± 0.08</td>
</tr>
</tbody>
</table>

For multi-site debris reproducibility a total of 90 ORAcollect®•Dx samples were extracted by three operators at three sites for a total of 270 sample aliquots extracted (90 aliquots per operator). Each operator analyzed the 90 extracted DNA samples for DNA concentration and A260/A280 ratio.

Interfering substances

Both endogenous and exogenous potentially interfering substances were tested with ORAcollect®•Dx/saliva samples from donors with known genotyping. Endogenous substances were added separately to the ORAcollect®•Dx samples post-collection. ORAcollect®•Dx/saliva samples containing potentially interfering endogenous substances were collected 30 minutes after completion of the assigned activity. Addition of tested substances had no effect as demonstrated through testing on the eSensor® Warfarin Sensitivity Saliva Test. All samples gave a correct call after the final pass.

Product robustness

Human factor studies demonstrated greater than 99% compliance to ORAcollect®•Dx user instructions. Additionally, it was demonstrated through various studies that following the instructions for use, the ORAcollect®•Dx product characteristics for DNA concentration, yield and A260/A280 ratio were met and the samples collected with the device were able to successfully perform on the eSensor® Warfarin Sensitivity Saliva Test (WST).

ORAcollect®•Dx is 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. Saliva samples collected using ORAcollect®•Dx are stabilized and can be transported and/or stored long-term at ambient conditions.