Copan Italia S.p.A.
Elena Simeonato
Regulatory Affairs Manager
Via F. Perotti 10
Brescia, Brescia 25125
Italy

September 17, 2020

Re: K201849
Trade/Device Name: eNAT molecular collection and preservation medium
Regulation Number: 21 CFR 866.2950
Regulation Name: microbial nucleic acid storage and stabilization device
Regulatory Class: Class II
Product Code: QBD
Dated: June 30, 2020
Received: July 6, 2020

Dear Elena Simeonato:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR

803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Kristian Roth, Ph.D.
Chief
Bacterial Respiratory and Medical Counter Measures Branch
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
and Radiological Health
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

# Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
*See PRA Statement below.*

510(k) Number *(if known)*
K201849

Device Name
eNAT - molecular collection and preservation medium-

Indications for Use *(Describe)*
Copan eNAT- molecular collection and preservation medium- is intended for the stabilization, transportation and inactivation of an unprocessed upper respiratory clinical specimen suspected of containing influenza A virus RNA. eNAT- molecular collection and preservation medium- is intended for use with compatible molecular assays.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

**CONTINUE ON A SEPARATE PAGE IF NEEDED.**

This section applies only to requirements of the Paperwork Reduction Act of 1995.

***DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.***

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# 5. 510 (K) SUMMARY

## I. SUBMITTER


| | |
|---|---|
| Applicant Name: | Copan Italia S.p.A.<br>Via F. Perotti 10<br>25125 Brescia, Italy |
| Contact Person: | Elena Simeonato<br>Via F. Perotti, 10<br>Brescia, Italy |
| Telephone: | +39 030 2687212 |
| Establishment Registration Number: | 3002444944 |
| Date Prepared: | June 30, 2020 |

## II. DEVICE – CLASSIFICATION

| | |
|---|---|
| Proprietary Name | eNAT® - molecular collection and preservation medium |
| Common/Usual Name | eNAT® |
| Device | Transport device for the stabilization of microbial nucleic acids |
| Classification Number | 21 CFR 866. 2950 |
| Product Code | QBD |
| Device Class | Class II |
| Review Panel | Microbiology |

## III. PREDICATE DEVICE – CLASSIFICATION

| | |
|---|---|
| Device Name | PrimeStore™ MTM |
| 510(k) Number | DEN170029 |
| Device | Transport device for the stabilization of microbial nucleic acids |
| Classification Number | 21 CFR 866. 2950 |
| Product Code | QBD |
| Device Class | Class II |
| Review Panel | Microbiology |

## IV. INTENDED USE OF THE DEVICE

Copan eNAT - molecular collection and preservation medium - is intended for the stabilization, transportation and inactivation of an unprocessed upper respiratory clinical specimen suspected of containing influenza A virus RNA. eNAT- molecular collection and preservation medium- is intended for use with compatible molecular assays.

## V. DEVICE DESCRIPTION

The primary purpose of nucleic acids amplification techniques is to screen for a wide range of infectious diseases, so nucleic acid integrity of clinical specimens during transport and storage should be preserved.

eNAT® medium contains a detergent and a protein denaturant to prevent microbial proliferation and to maintains the integrity of the nucleic acids from cells or pathogens collected from patients and inactivates pathogen viability, thus eNAT® is not intended to be used for culture-based techniques.

Copan eNAT® has 3 different configurations:

- Ref. 6U072S: a plastic screw-cap tube filled with 2 ml of Molecular Preservation and Transport medium.

- Ref. 6U073S01: a plastic screw-cap tube filled with 2 ml of Molecular Preservation and Transport medium and a regular size tip nylon flocked swab for sample collection.

- Ref. 6U074S01: a plastic screw-cap tube filled with 2 ml of Molecular Preservation and Transport and a minitip nylon flocked swab for sample collection.

## VI. COMPARISON OF TECHNOLOGICAL CHARACTERISTICS WITH THE PREDICATE DEVICE

Copan eNAT® Molecular Collection and Preservation Medium is substantially equivalent in intended use and overall function to the commercially distributed device PrimeStore™ Molecular Transport Medium® by Longhorn Vaccines and Diagnostics LLC.

PrimeStore MTM™ by Longhorn Vaccines and Diagnostics LLC consists of a polypropylene tube containing 1 mL or 1.5 mL of a medium.

Copan eNAT® is provided ready to use in a polypropylene tube with a leak-proof screw-cap closure, containing 2mL of medium for the inactivation of influenza A (Flu A) and the stabilization of the Flu A RNA.

eNAT® and PrimeStore MTM™ medium show similar composition including the two active ingredients: guanidine thiocyanate and N-lauroylsarcosine (detergent). These components inactive Flu A, denature and lyse cells, and stabilize Flu A virus RNA.

eNAT® is also supplied in kit format consisting of the media-filled tube with either a regular nylon flocked swab or a minitip nylon flocked swab (Copan FLOQSwabs®), while PrimeStore MTM™ is supplied in tube format only. See Table 1: Side-by-Side Comparison of Copan eNAT® - molecular collection and preservation medium

**Table 1: Side-by-Side Comparison of Copan eNAT® and Predicate Device.**

# Traditional 510(k) Premarket Notification for Copan eNAT® - molecular collection and preservation medium

| Characteristics | Copan eNAT® Molecular Collection and Preservation Medium | PrimeStore Molecular Transport Medium® DEN170029 (Longhorn Vaccines and Diagnostics LLC) |
|---|---|---|
| Collection device intended use | Copan eNAT® is intended for the collection, inactivation and transport of clinical specimens containing influenza A viruses from the collection site to the testing laboratory. eNAT® can be processed and used with compatible molecular assays the require stabilization of nucleic acids from influenza A viruses | The **PrimeStore MTM (#DEN170029)** is intended for the stabilization, transportation and inactivation of infectious unprocessed nasal washes suspected of containing *Influenza A* virus RNA and is also intended for the stabilization, transportation and inactivation of infectious unprocessed sputum samples suspected of containing *Mycobacterium tuberculosis* DNA from human samples |
| Indication for use | eNAT® medium is a 'ready to use' system that allows for the stabilization and safe transport of clinical samples at ambient temperature for viral RNA detection | PrimeStore MTM is a self-contained 'ready to use' system that allows for the stabilization and safe transport of clinical samples at ambient temperature from the collection site to the laboratory |
| Specimen Type | Respiratory specimens | Nasal washes and sputum samples |
| Microorganism nucleic acids preserved | Influenza A virus | Influenza A virus and *Mycobacterium tuberculosis* |
| Specimen stability | eNAT® medium preserves influenza A RNA for up to 28 days at 2-25°C. | Primestore MTM® medium preserves influenza A RNA for up to 8 days at 27°C and 29 days at 4°C. |
| Inactivation tested on Flu A | >4.0 log reduction in concentration at 10 seconds | Same |
| Container | Tube; plastic, conical bottom, | Same |

| | | |
|---|---|---|
| | self-standing with a screw cap | |
| Medium Formulation | Tris-EDTA<br>Guanidine thiocyanate<br>Detergent<br>HEPES<br>Distilled water | TRIS<br>EDTA<br>Guanidine thiocyanate<br>N-lauroylsarcosine sodium<br>Antifoam A<br>TCEP<br>Sodium citrate<br>Ethanol<br>HCl<br>Water |
| Medium Volume | 2 mL | 1 mL or 1.5 mL |
| Storage Temperature | 2-25ºC | Same |
| Shelf-life | 18 months | 24 months |

## VII. PERFORMANCE DATA

An inactivation study was conducted to verify that Copan eNAT® inactivates Flu A virus as efficiently as the predicate device PrimeStore MTM following the study design described by Longhorn in the PrimeStore MTM Decision Summary, DEN170029.

High concentrations of Flu A in nasal matrix were inoculated in eNAT® using Copan's regular nasal-type FLOQSwabs®. In particular, the swab was dipped into the infected matrix and used to transfer the sample into eNAT®.

The viability of the virus was measured after 10 seconds in eNAT® medium by inoculating aliquots onto MDCK (Madin-Darby Canine Kidney) cell lines, incubating for four days and measuring the cytopathic effect (CPE).

The results for the inactivation study (Table 2) confirmed > 4.0 log reduction in Flu A titer in 10 seconds and demonstrates equivalent performance of eNAT® with PrimeStore MTM™ in the inactivation of influenza A.

**Table 2: Summary of influenza A inactivation study results**

| *Sample* | *Viral load after 10s incubation* | *Log. reduction* |
|---|---|---|
| CTRL+ (Flu A only) | $3.16*10^7$ $TCID_{50}$/ml | n/a |
| Flu A in eNAT® | $\leq 10^3$ $TCID_{50}$/ml | 4.5 |

An analytical sensitivity study was conducted to determine the Flu A limit of detection (LoD) obtained by eNAT® in combination with the Cepheid Xpert® Xpress Flu/RSV assay. eNAT® medium in combination with the Cepheid assay has reached the same LoD than UTM (reference device for the assay) and LoD has fallen within the range of TCID 50/ml declared by the Cepheid assay (0.75 – 0.006 TCID50/ml in the matrix) for Flu A detection (Table 3) (Flu A 1 channel results shown).

**Table 3: Summary of results obtained at the dilution corresponding to 0.180 $TCID_{50}$/ml (in the matrix) during the Analytical Sensitivity Study using Xpert® Xpress Flu/RSV assay**

| | **eNAT® samples** |
|---|---|
| **N° of positive replicates** | 24/24 |
| **Average PCR Ct obtained** | 34.4 |
| **Standard deviation** | 0.93 |
| **CV%** | 2.7% |

A stability study was designed to demonstrate that RNA from Flu A is preserved and stable in eNAT® medium. The stability of Flu A RNA in eNAT® was tested with the Cepheid Xpert® Xpress Flu/RSV Assay. The results of eNAT® influenza A RNA Stability Study (Table 4) (Flu A 1 channel results shown) confirmed that RNA stability in eNAT® met the acceptance criteria of +/- 3.0 Ct after 4 weeks storage at both 2-8°C and 25°C storage. The stability of RNA from Flu A spiked into nasal wash and stored in Longhorn PrimeStore MTM™ is 29 days at 4°C and 8 days at 27°C. This study demonstrates at least equivalent performance of eNAT® with PrimeStore MTM™ in the influenza A RNA stability.

**Table 4: Flu A data in eNAT® at time zero and after 4 weeks at 2-8°C and 25°C**

| eNAT® samples | | Results |
|---|---|---|
| Time zero | N° of positive replicates | 24/24 |
| | Average of PCR CTs | 30.8 |
| | St. Dev | 0.40 |
| | CV% | 1.3% |
| | PASS | yes |
| 4 weeks @ 2-8°C | N° of positive replicates | 24/24 |
| | Average of PCR CTs | 30.6 |
| | St. Dev | 0.20 |
| | CV% | 0.6% |
| | ΔCt 4w-T0 | -0.2 |
| | PASS | yes |
| 4 weeks @ 25°C | N° of positive replicates | 24/24 |
| | Average of PCR CTs | 30.7 |
| | St. Dev | 0.28 |
| | CV% | 0.9% |
| | ΔCt 4w-T0 | -0.1 |
| | PASS | yes |

## VIII. CONCLUSIONS

Based on the above, Copan Italia S.p.A. believes that Copan eNAT® is substantially equivalent to the commercially distributed product PrimeStore MTM™ for the stabilization, inactivation and transportation of clinical specimens containing influenza A viruses from the collection site to the testing laboratory. No new issues of safety or effectiveness were found for Copan eNAT®.