June 11, 2024

FertiPro NV
℅ Gregor Kleinert
Official Correspondent
Ducks in a Row Compliance LLC
1447 Bentley Drive
Warrington, Pennsylvania 18976

Re: K221547
Trade/Device Name: InActiv Blue
Regulation Number: 21 CFR 866.2950
Regulation Name: Microbial nucleic acid storage and stabilization device
Regulatory Class: Class II
Product Code: QBD
Dated: May 26, 2022
Received: May 27, 2022

Dear Gregor Kleinert:

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 (the 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 available 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.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

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 Part 803) for devices or postmarketing safety reporting (21 CFR Part 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 Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 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,

Noel J. Gerald -S

Noel J. Gerald, Ph.D.
Branch Chief
Bacterial Respiratory and Medical Countermeasures Branch
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
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: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K221547

Device Name
InActiv Blue

Indications for Use *(Describe)*
InActiv Blue is intended for the stabilization, transportation and inactivation of upper respiratory specimens suspected of containing SARS-CoV-2. These devices can be used for collection, transport and storage of specimens at refrigerated (2-8°C) or ambient temperatures (20-25°C). SARS-CoV-2 RNA in the specimens is stabilized for 7 days at these specified temperatures. Specimens collected and stored in an InActiv Blue collection tube are suitable for use with legally marketed molecular diagnostic devices.

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.

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510(k) Summary – K221547

Applicant:	FertiPro NV Industriepark Noord 32 8730 Beernem Belgium
Establishment Registration No.:	3003272500
Primary correspondent:	Gregory P. Kleinert Ducks in a Row Compliance LLC. 1447 Bentley Drive Warrington, PA 18976 Phone: 215-858-2429 Email: DucksComplianceLLC@gmail.com
Summary Date:	14 March 2024
Device Proprietary Name:	InActiv Blue
Classification Name:	Microbial Nucleic Acid Storage and Stabilization Device
Regulation:	866.2950
Class:	Class II
Panel:	Microbiology
Product code:	QBD
Predicate Device:	K202641 – DNA/RNA Shield™ Collection Tube (Manufacturer: Zymo Research)

Intended Use/Indication for Use:
InActiv Blue is intended for the stabilization, transportation and inactivation of upper respiratory specimens suspected of containing SARS-CoV-2. These devices can be used for collection transport and storage of specimens at refrigerated (2-8°C) or ambient temperatures (20-25°C). SARS-CoV-2 RNA in the specimens is stabilized for 7 days at these specified temperatures. Specimens collected and stored in an InActiv Blue collection tube are suitable for use with legally marketed molecular diagnostic devices.

Device Description:
InActiv Blue is a virus-inactivating and lysis solution that abrogates the infectious potential of the collected material without affecting the integrity of the RNA. Two milliliters of InActiv Blue solution are provided in a polypropylene flat bottom collection tube with a high-density polyethylene (HDPE) cap (product code IB_TUB). The device is non-sterile, single use. Secondary Packaging for the collection tube configuration includes racks of 50 collection tubes and cardboard boxes with either 400 or 1200 collection tubes.

Sample types intended for collection with the device include upper respiratory swab samples. Swabs are not provided with the InActiv Blue collection tubes.

The active components of the InActiv Blue solution are guanidine thiocyanate, N-lauroylsarcosine sodium salt and EDTA. These components are formulated in a sodium phosphate buffered solution containing methylene blue.

Principles of Operation:

InActiv Blue main active components are guanidine thiocyanate, N-lauroylsarcosine and EDTA.

Guanidine thiocyanate is a chaotropic salt acting as a denaturing agent for macromolecules leading to virus inactivation. Additionally, guanidine acts as a ribonuclease (RNase) inhibitor, therefore preventing RNA degradation in samples and so keeping the virus RNA detectable for a longer period of time.

N-lauroylsarcosine (LS) is an anionic surfactant capable of reducing viral infection by interfering with the initial binding of the virus to the cells. Inactivation of SARS-CoV-2, is accomplished by disrupting the viral envelope, making it unable for the virus to enter cells. Additionally, LS is able to inhibit RNase and so protecting RNA from degradation, keeping the virus RNA detectable for a longer period of time.

EDTA is a chelating agent and nuclease inhibitor. Due to the high affinity of EDTA to divalent cations, such as Ca2+, Mn2+ and Mg2+, which act as cofactors for nucleases it could inhibit the degradation of RNA by RNases.

Comparison to Predicate Device

InActiv Blue has similar intended use, design and technological characteristics as the predicate device, DNA/RNA Shield Collection Tube (K202641). Below is a comparison table showing similarities and differences between InActiv Blue and predicate device K202641:

Device & Predicate Device(s):	Device: K221547	Predicate: K202641
Device Trade Name	InActiv Blue	DNA/RNA Shield Collection Tube
General Device Characteristic Similarities		

Intended Use/Indications For Use	InActiv Blue is intended for the stabilization, transportation and inactivation of upper respiratory specimens suspected of containing SARS-CoV-2. These devices can be used for collection transport and storage of specimens at refrigerated (2-8°C) or ambient temperatures (20-25°C). SARS-CoV-2 RNA in the specimens is stabilized for 7 days at these specified temperatures. Specimens collected and stored in an InActiv Blue collection tube are suitable for use with legally marketed molecular diagnostic devices.	The DNA/RNA Shield collection tube is intended for the stabilization and inactivation of upper and lower respiratory human specimens suspected of containing SARS-CoV-2. These devices can be used for collection transport and storage of specimens at ambient temperatures (20-25°C). Specimens collected and stored in a DNA/RNA Shield collection tube are suitable for use with legally marketed molecular diagnostic devices.
Inactivation	RNA virus particles	Same
Analyte	RNA	Same
General Device Characteristic Differences		
Sample Source	Human upper respiratory	Human lower and upper respiratory
Sample storage Temperature	7 days at refrigerated (2-8°C) or ambient temperatures (20-25°C)	28 days at 20-25˚C

Performance Characteristics:

Shelf-Life Stability:

Shelf-life stability of InActiv Blue was evaluated to ensure product integrity over the complete shelf-life of the product. Completed real-time stability studies included at least eight lots of InActiv Blue which have been stored at room temperature for different periods of time, with performance testing conducted at regularly spaced timepoints to support a 21-month shelf-life stability claim.

At each time points, appearance by visual inspection pH (6+/- 0.6), osmolarity **(**mOsm/kg 4200+/-420) and evaporation were assessed. The product met all stability specifications for the duration of the study, supporting 21 months of shelf life. The results are summarized below (Table 1).

Table 1: Shelf-life Stability of InActiv Blue when stored at 15-25°C

InActiv Blue lots stored at 15-25^{0}C	Lot number	Sample age	pH ^	Osmolality (mOsm/kg) ^^	Appearance *	Evaporation**
Recently produced	FP23IB06	38 days	6.02	435	PASS	PASS
Intermediate aged	FP23IB03	12 months	6.03	438	PASS	PASS
	FP23IB02	12 months	6.06	449	PASS	PASS
	FP23IB01	12 months	6.07	448	PASS	PASS
Expired batches	FP21IB06	> 21 months	5.97	460	PASS	PASS
	FP21IB04	> 21 months	5.90	459	PASS	PASS
	FP21IB03	> 21 months	5.95	461	PASS	PASS
	FP20IB06	> 21 months	6.02	452	PASS	PASS

^ Mean of three determinations. At production, pH values range from 5.98 to 6.03
^^ Mean of three determinations. At production osmolarity values range from 396 to 441 mOsm/kg. Determinations were made on product diluted 1:10
* Criteria: labeling does not show decreased quality and adheres well to the tube, and liquid is clear
** Criterium: >1.5 mL of InActiv Blue

Limit of Detection:

The limit of detection (LOD) of SARS-CoV-2 in InActiv Blue was established through preliminary and confirmatory LOD studies. The LOD was determined for InActiv Blue with nasopharyngeal swab samples, using the Roche cobas SARS-CoV-2 assay (EUA200009) on the cobas 6800 system.

The preliminary LOD was determined by spiking InActiv Blue with nasopharyngeal clinical matrix and SARS-CoV-2 at concentrations of 5, 15, 45, 135, and 405 particles/mL, with each determination performed in triplicate. The LOD was found to be within the range of 5-45 particles/mL.

Table 1. Preliminary LOD Study Results

SARS-CoV-2 (particles/mL)	Number of Positive Replicates	Number of Negative Replicates	% Positive
5	1	2	33%
15	3	0	100%
45	3	0	100%

135	3	0	100%
405	3	0	100%

The confirmatory LOD was established by spiking a swab with negative clinical nasopharyngeal matrix containing either 15 or 45 SARS-CoV-2 particles/mL, into InActiv Blue media. A total of 20 replicates were evaluated for each concentration. The nasopharyngeal swabs in InActiv Blue, containing 45 particles/mL, showed that 100% of the replicates were positive, and at a concentration of 15 particles/mL 90% of the replicates were positive.

Table 2. Confirmatory LOD Study Results

SARS-CoV-2 (particles/mL)	**Number of Positive Samples**	**Number of Negative Samples**	**% Positive**
15	19	2	90%
45	21	0	100%

The LOD for nasopharyngeal swab specimen in InActiv Blue was determined to be 45 particles/mL of SARS-CoV-2.

Sample Stability Study:

Stability of SARS-CoV-2 in nasopharyngeal specimens stored InActiv Blue was evaluated using product lots of different ages to ensure that there is no decrease in the performance of the product over its claimed shelf-life. Lots of InActiv Blue from different ages (newly manufactured, middle aged and near/recently expired lots), spanning the claimed shelf-life were evaluated. Six replicate samples containing nasopharyngeal matrix were collected and stored in each of the lots of InActiv Blue. Each replicate was spiked with 135 particles/mL (= 3x LOD). Three of the replicates from each lot were stored at 2-8°C while the other 3 replicates were stored at 20-25°C for at least 7 days. Each sample was evaluated using the cobas SARS-CoV-2 assay (EUA200009) on the 6800 system at day 0, day 4 and day 7. All samples collected in the four lots and stored at both temperatures remained within 3 Ct of the initial reading, supporting the sample stability claim for InActiv Blue of 7 days at a temperature between 2-8 and 20-25°C. The following table summarizes the results obtained.

Table 3. SARS-CoV-2 RNA stability after 4 and 7 days of incubation at 2-8°C and 20-25°C

Storage Temperature	Lot manufacturing age	Lot #	Target 1 (ORF 1Ab) Delta Ct's		Target 2 (E gene) Delta Ct's	
			Ct Day4 - Ct Day 0	Ct Day7 - Ct Day 0	Ct Day4 - Ct Day 0	Ct Day7 - Ct Day 0
4°C	new	FP23IB01	-0.12	0.00	0.74	0.80
	middle aged	FP21IB04	0.09	0.20	0.80	0.37
	after expiry date	FP21IB01	-0.36	0.05	0.13	0.12
	stressed	FP21IB01	-0.30	0.84	0.42	0.97
20°C	new	FP23IB01	-0.55	-0.22	-0.87	-0.49
	middle aged	FP21IB04	-0.23	0.47	0.33	0.45
	after expiry date	FP21IB01	0.02	-0.41	1.10	-0.42
	stressed	FP21IB01	-0.27	-0.37	0.63	-0.05

Viral Inactivation:

Inactivation was evaluated by measuring the presence of residual infective SARS-CoV-2 viral particles spiked into InActiv Blue. Inactivation studies were conducted in two phases. First a 1:1000 dilution of InActiv Blue was established to eliminate the cytotoxicity of the medium. Higher concentrations of medium were found to render the cultured cells nonviable and unusable for the viral inactivation study. The second phase of viral inactivation evaluated cytotoxicity of SARS-COV-2 spiked into a 1:1000 dilution of the transport media for 1, 2.5 and 5 minutes after inoculation.

The second phase of the study used a high concentration of infectious viral particles ($TCID_{50}$/mL=$10^{7.5}$ or $10^{7.39}$). Briefly, 100 µL of virus stock was mixed 1:1 with InActiv Blue and incubated for 1, 2.5 and 5 minutes. Negative and positive controls were prepared similarly. The virus and InActiv Blue (as well as positive and negative control samples) were then diluted 1:1000 before each replicate was added to cell culture plates containing adherent Vero E6 cells to determine the minimal incubation time required to inactivate virus. Cultures were incubated for several minutes and observed for presence or absence of cytopathic effect and $TCID_{50}$ was calculated by the Reed and Muench method. Virus inactivation was evaluated using 3 lots near the expiration of InActiv Blue (approximately 21 months old). Inactivation performance of InActiv Blue after 1 minute exposure was comparable to 2.5 and 5 minutes of exposure for each of the three batches of InActiv Blue evaluated.

Since the starting viral concentration was 7.5 logs ($TCID_{50}$/mL=$10^{7.5}$) for two of the lots examined and 7.39 logs ($TCID_{50}$/mL=$10^{7.39}$) for the third lot, the log infectivity reduction factor was calculated to be at least 3.89 logs for the virus exposed to InActiv Blue medium. Negative

control (without virus) demonstrated minimal cellular toxicity and positive control (virus in DMEM) showed no meaningful loss of viral recovery (data not shown). The study results are summarized in Table 4 below.

Table 4: SARS-CoV-2 Viral Inactivation when exposed to InActiv Blue

Lot	exposure time	log (TCID50 control) - log (TCID50 test)	virus log reduction factor
1	1 min	7.50-3.50	4
	2.5 min	7.50-3.50	4
	5 min	7.50-3.50	4
2	1 min	7.50-3.50	4
	2.5 min	7.50-3.50	4
	5 min	7.50-3.50	4
3	1 min	7.39-3.50	3.89
	2.5 min	7.39-3.50	3.89
	5 min	7.39-3.50	3.89