DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

Hologic, Inc.
Ron Domingo
Manager, Regulatory Affairs
10210 Genetic Center Drive
San Diego CA 92121

December 9, 2015

Re: K153223
Trade/Device Name: ProParaflu+ Assay
Regulation Number: 21 CFR 866.3980
Regulation Name: Respiratory viral panel multiplex nucleic acid assay
Regulatory Class: II
Product Code: OOU
Dated: November 5, 2015
Received: November 10, 2015

Dear Mr. Domingo:

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. 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 Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. 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 http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Tamara V. Feldblyum -S for

Uwe Scherf
Director
Division of Microbiology Devices
Office of In Vitro Diagnostics
and Radiological Health
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: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K153223

Device Name
Prodesse® ProParaFlu®+ Assay

Indications for Use *(Describe)*

The Prodesse® ProParaflu®+ Assay is a multiplex Real-Time PCR (RT-PCR) in vitro diagnostic test for the qualitative detection and discrimination of Parainfluenza 1 Virus, Parainfluenza 2 Virus and Parainfluenza 3 Virus (HPIV-1, HPIV-2 and HPIV-3) nucleic acids isolated and purified from nasopharyngeal (NP) swab specimens obtained from individuals exhibiting signs and symptoms of respiratory tract infections. This Assay targets the conserved regions of the Hemagglutinin-Neuraminidase (HN) gene of HPIV-1, HPIV-2 and HPIV-3, respectively. The detection and discrimination of HPIV-1, HPIV-2 and HPIV-3 nucleic acids from symptomatic patients aid in the diagnosis of human respiratory tract parainfluenza infections if used in conjunction with other clinical and laboratory findings. This test is not intended to detect Parainfluenza 4a or Parainfluenza 4b Viruses.

Negative test results are presumptive and should be confirmed by cell culture. Negative results do not preclude Parainfluenza 1, 2 or 3 virus infections and should not be used as the sole basis for treatment or other management decisions.

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.

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510(k) Summary

Contact

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Name of Device

Trade Name:	Prodesse® ProParaFlu®+ Assay
Regulation Number:	21 CFR 866.3980
Classification Name:	Parainfluenza Multiplex Nucleic Acid Assay
Product Code:	OOU

Predicate Devices

K132238 – ProParaFlu®+ Assay, Hologic, Inc.

K091053 – ProParaFlu®+ Assay, Prodesse Inc.

Intended Use

The Prodesse® ProParaflu®+ Assay is a multiplex Real-Time PCR (RT-PCR) in vitro diagnostic test for the qualitative detection and discrimination of Parainfluenza 1 Virus, Parainfluenza 2 Virus and Parainfluenza 3 Virus (HPIV-1, HPIV-2 and HPIV-3) nucleic acids isolated and purified from nasopharyngeal (NP) swab specimens obtained from individuals exhibiting signs and symptoms of respiratory tract infections. This Assay targets the conserved regions of the Hemagglutinin-Neuraminidase (HN) gene of HPIV-1, HPIV-2 and HPIV-3, respectively. The detection and discrimination of HPIV-1, HPIV-2 and HPIV-3 nucleic acids from symptomatic patients aid in the diagnosis of human respiratory tract parainfluenza infections if used in conjunction with other clinical and laboratory findings. This test is not intended to detect Parainfluenza 4a or Parainfluenza 4b Viruses.

Negative test results are presumptive and should be confirmed by cell culture. Negative results do not preclude Parainfluenza 1, 2 or 3 virus infections and should not be used as the sole basis for treatment or other management decisions.

Product Description

The ProParaflu+ assay enables detection and differentiation of Parainfluenza 1 Virus, Parainfluenza 2 Virus, Parainfluenza 3 Virus and Universal Internal Control nucleic acids. Nasopharyngeal swab specimens are collected from symptomatic patients using a polyester, rayon or nylon tipped swab and placed into viral transport medium.

A Universal Internal Control (UIC) is added to each sample prior to nucleic acid isolation to monitor for inhibitors present in the specimens. The isolation and purification of the nucleic acids is performed using either a MagNA Pure LC Instrument (Roche) and the MagNA Pure Total Nucleic Acid Isolation Kit (Roche) or a NucliSENS® easyMAG™ System (bioMérieux) and the Automated Magnetic Extraction Reagents (bioMérieux).

The purified nucleic acids are added to ProParaflu+ Supermix along with enzymes included in the ProParaFlu+ Assay Kit. The ProParaflu+ Supermix contains oligonucleotide primers and target-specific oligonucleotide probes. The primers are complementary to highly conserved regions of genetic sequences for these respiratory viruses. The probes are dual-labeled with a reporter dye and a quencher.

Reverse transcription of the RNA in the sample into complementary DNA (cDNA) and subsequent amplification of DNA is performed in a Cepheid SmartCycler® II instrument. In this process, the probe anneals specifically to the template followed by primer extension and amplification. The ProParaFlu+ Assay is based on Taqman chemistry, which utilizes the 5' – 3' exonuclease activity of the Taq polymerase to cleave the probe thus separating the reporter dye from the quencher. This generates an increase in fluorescent signal upon excitation from a light source. With each cycle, additional reporter dye molecules are cleaved from their respective probes, further increasing fluorescent signal. The amount of fluorescence at any given cycle is dependent on the amount of amplification products present at that time. Fluorescent intensity is monitored during each PCR cycle by the SmartCycler II instrument.

Substantial Equivalence

The Intended Use and Warnings and Precautions of the modified device as described in the labeling have not changed compared to the predicate device. The modifications detailed in the table below had not had any effect or caused any changes to the fundamental scientific technology of the device.

Similarities		
Element	**Modified Prodesse ProParaflu+ Assay**	**Current Prodesse ProParaflu+ Assay (K091053)**
Organisms Detected	Same	HPIV-1, HPIV-2, and HPIV-3
Analyte	Same	RNA
Technological Principles	Same	Multiplex nucleic acid amplification
Specimen Types	Same	Nasopharyngeal Swab
User Complexity	Same	High
Sample Preparation Method	Same	Up front sample processing is required to extract nucleic acid.
Instrumentation	Same	bioMérieux NucliSENS easyMAG or Roche MagNA Pure and Cepheid SmartCycler II Instrument
Time to result	Same	Approximately 4 hours
Controls	Same	Internal control in each sample. External control processed with each batch of samples. (see below for differences)

Differences		
Element	**Modified Prodesse ProParaflu+ Assay**	**Current Prodesse ProParaflu+ Assay (K091053)**
Limitations	Limited reactivity with the 2014 CAP sample ID2-08 and the 2015 CAP sample ID2-02.	Did not include information regarding limited reactivity with the 2014 CAP sample ID2-08 and the 2015 CAP sample ID2-02.

Limitations

The ProParaflu+ assay has limited reactivity with the 2014 CAP sample ID2-08 and the 2015 CAP sample ID2-02. Sequencing analysis of the CAP samples revealed that the HPIV3 target sequences of the CAP samples match the sequence of HPIV3/Homo sapiens/ PER/FLU8889/2007 strain in GenBank (GenBank Accession # KJ672604), and the limited reactivity is most likely due to a viral mutation in the probe binding region. Negative results may be obtained for samples containing this variant especially at low titers. If the ProParaflu+ assay does not indicate a positive result when an HPIV-3 infection is suspected, the specimen should be retested for HPIV-3 using an independent method (e.g. cell culture or molecular IVD).