SPECIAL 510(k): Device Modification
OIR Decision Summary

To: Hologic, Inc. RE: DOCUMENT NUMBER K153219

This special 510(k) submission contains information/data on modifications made to the SUBMITTER'S own Class II device requiring 510(k). The following items are present and acceptable:

1. The name and 510(k) number of the SUBMITTER'S previously cleared device.

   Trade Name: Prodesse® ProFlu™+ Assay
   510(k) number: K132129

2. Submitter's statement that the **INDICATION/INTENDED USE** of the modified device as described in its labeling **HAS NOT CHANGED** along with the proposed labeling which includes instructions for use and package labeling.

   The submitter states the intended use remains the same (510k summary). The intended use included for the new device is the same as the intended use in the predicate (k132129).

3. A description of the device **MODIFICATION(S).**

   The modification presented in this special 510(k) is the inclusion of one additional viral strain to the table of analytical reactivity in the labeling. The submitter tested the ability of the Prodesse ProFlu+ Assay to detect the Influenza A/H3N2 strain, A/New York/1/2015. A clinical isolate with a confirmed identity and titer was diluted in negative nasopharyngeal swab matrix to a concentration ($2x10^1$ TCID50/ml) near the estimated LoD. The reactivity of the strain at this concentration was tested with three replicate samples. The assay detected each of the three replicates. This strain was added to the table of reactive strains in the package insert.

   The predicate included an equivalency study to claim two extraction methods (Roche MagNA Pure LC and bioMérieux NucliSENS easyMAG), but the predicate used only the Roche instrument in the analytical reactivity study. The new device modification used the bioMérieux NucliSENS easyMAG to extract the additional strain for reactivity. Therefore, the analytical reactivity section of the new package insert labeling was revised to include the statement "Viral strains were extracted using the Roche MagNA Pure LC or bioMérieux NucliSENS easyMAG and tested in triplicate in each assay." This statement is a new revision of the package insert.

   The analytical reactivity section of the new package insert was revised to include the statement "Viruses present at concentrations below those tested for Reactivity may not be detected by the ProFlu+ Assay." This statement is not included in the predicate labeling, but it does not change the safety or effectiveness of the device.

   During interactive review, the labeling (instructions for use) was revised to include "Rx only" on the front page. The predicate had no "Rx only" in the package insert.

   In this submission, there were two new versions of package insert that are identical except that each had a different order number and different number of reactions included in the kit (either 100 and 1500 Rxns, or 2000 Rxns). The predicate had only one version of package insert (100 and 1500 Rxns).

4. The **FUNDAMENTAL SCIENTIFIC TECHNOLOGY** of the modified device has not changed.

   The product description in the labeling of the device is the same as the predicate and the submitter stated that the scientific technology is unchanged compared to the predicate.

5. **Comparison Information** (similarities and differences) to applicant's legally marketed predicate device including labeling, intended use, other characteristics.

Similarities and Differences		
Element	Modified Prodesse ProFlu+ Assay	Current Prodesse ProFlu+ Assay (K132129)
Similarities		
Intended Use	Same	The Prodesse® ProFluTM+ Assay is a multiplex Real-Time PCR (RT-PCR) in vitro diagnostic test for the rapid and qualitative detection and discrimination of Influenza A Virus, Influenza B Virus, and Respiratory Syncytial Virus (RSV) nucleic acids isolated and purified from nasopharyngeal (NP) swab specimens obtained from symptomatic patients. This test is intended for use to aid in the differential diagnosis of Influenza A, Influenza B and RSV viral infections in humans and is not intended to detect Influenza C. Negative results do not preclude influenza or RSV virus infection and should not be used as the sole basis for treatment or other management decisions. Conversely, positive results do not rule out bacterial infection or co-infection with other viruses. The agent detected may not be the definite cause of disease. The use of additional laboratory testing and clinical presentation must be considered in order to obtain the final diagnosis of respiratory viral infection. Performance characteristics for Influenza A Virus were established when Influenza A/H3 and A/H1 were the predominant Influenza A viruses in circulation (2006 – 2007 respiratory season). Performance characteristics for Influenza A were confirmed when Influenza A/H1, Influenza A/H3, and Influenza A/2009 H1N1 were the predominant Influenza A viruses in circulation (2008 and 2009). When other Influenza A viruses are emerging, performance characteristics may

		vary. If infection with a novel Influenza A virus is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, specimens should be collected with appropriate infection control precautions for novel virulent Influenza viruses and send to state or local health department for testing. Viral culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.
Organisms Detected	Same	Influenza A virus, Influenza B virus, Respiratory Syncytial Virus
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.
Differences		
Analytical reactivity with new Influenza A strain	Influenza A/H3N2 strain, A/New York/1/2015	Influenza A/H3N2 strain, A/New York/1/2015 was not listed in the Reactivity Table of the PI

6. A Design Control Activities Summary which includes:
    1. Reactivity testing was conducted as described in Section 3, Device Modifications.
    2. Risk Analysis

       The method used for the Risk Analysis for the Prodesse ProFlu+ Assay was the Failure Mode Effects Analysis (FMEA). This method is consistent with 21 CFR 820.30. The following table summarizes the risk analysis.

Assay	No.	Potential Cause of Failure	Risk	Risk Priority Number (RPN)	Justification
ProFlu+	30	New strain emerges and its nucleic acid sequence is undetectable by the device	Original	30	Ongoing Risk Control activities include continued monitoring of all complaints, tracking circulating strains and any pertinent sequence information at least annually. Testing showed that nucleic acid of the new strain, A/New York/1/2015, is detectable by the ProFlu+Assay at a concentration comparable to other H3N2 strains listed in Reactivity section of the IFU (2x101 TCID50/mL).

The risk of a false negative result was identified as a potential hazard that could occur if a new strain emerges and its nucleic acid sequence is undetectable by the device. This risk was addressed by conducting reactivity testing of an additional viral strain with the ProFlu+ assay and through updating the package insert.

3. Declaration of Conformity to Design Controls
   A "Declaration of Conformity" statement was submitted for the Hologic manufacturing facility. It was signed by an R&D Scientist, and the Regulatory Affairs Manager. The statements indicate that:
   a. "To the best of my knowledge, the verification activities for the modification were performed by the designated individual(s) and the results demonstrated that the predetermined acceptance criteria were met."
   b. The manufacturing facility, Hologic, Inc. is in conformance with the design control requirements as specified in 21 CFR 820. 3 0 and the records are available for review.

7. A Truth and Accurate Statement, a 510(k) Summary and the Indications for Use enclosure were included in the submission.

8. Conclusion
   The labeling for this modified subject device has been reviewed to verify that the indication/intended use for the device is unaffected by the modification. In addition, the submitter's description of the particular modification(s) and the comparative information between the modified and unmodified devices demonstrate that the fundamental scientific technology has not changed. The submitter has provided the design control information as specified in The New 510(k) Paradigm and on this basis, I recommend the device be determined substantially equivalent to the previously cleared (or their preamendment) device.