# SPECIAL 510(k): Device Modification
# OIR Decision Summary

**To:** Focus Diagnostics, Inc. **RE:** K152408

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This special 510(k) submission contains information/data on modifications made to the SUBMITTER'S own Class II device requiring a 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:
   Simplexa™ Flu A/B & RSV Direct Assay and
   Simplexa™ Flu A/B & RSV Positive Control Pack

   510(k) number:
   K142365

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.

3. A description of the device **MODIFICATION(S).** The modification presented in this special 510(k) is the inclusion of 37 influenza A strains, 9 influenza B strains, and 7 respiratory syncytial virus (RSV) strains to the Analytical Reactivity/Cross-Reactivity Section of the Simplexa™ Flu A/B & RSV Direct Assay package insert. A list of the strains tested is included below.

   Influenza A Virus (37 Strains)
   (H1N1) pdm09 - A/California/4/2009
   (H1N1) pdm09 - A/Massachusetts/15/2013
   (H1N1) pdm09 - A/Mexico/4108/2009
   (H1N1) pdm09 - A/New York/18/2009
   H1N1 - A/Hawaii/15/2001
   H2N2 - A/Japan/305/57
   H3N2 - A/California/02/2014
   H3N2 - A/New York/55/2004
   H3N2 - A/Rhode Island/01/2010
   H3N2 - A/Santiago/7981/2006
   H3N2 - A/Switzerland/9715293/2013
   H5N1 - A/Egypt/N03072/2010(H5N1)-PR8-IDCDC-RG29
   H5N1 - A/Hubei/1/2010(H5N1)-PR8-IDCDC-RG30
   H5N1 - A/India/NIV/2006(H5N1)-PR8-IBCDC-RG7
   H9N2 - A/Hong Kong/33982/2009(H9N2)-PR8-IDCDC_RG26
   H1N3 - A/shorebird/Delaware Bay/211/1994
   H1N8 - A/red knot/Delaware Bay/240/1994
   H3N6 - A/redhead/Alberta/192/2002
   H3N8 - A/duck/Chabarovsk/1610/1972
   H4N6 - A/duck/Czechoslovakia/1956
   H4N6 - A/red knot/Delaware/541/1988
   H5N1 - A/chicken/Vietnam/NCVD-016/2008(H5N1)-PR8-IDCDC-RG12
   H5N2 - A/pheasant/New Jersey/1355/1998(H5N2)-PR8-IBCDC-4
   H6N2 - A/turkey/Massachusetts/3740/1965
   H7N2 - A/turkey/Virginia/4529/2002(H7N2)xPR8-IBCDC-5
   H7N7 - A/mallard/Netherlands/12/2000(H7N7)/PR8-IBCDC-1

H10N1 - A/mallard/Wisconsin/4230/2009
H10N7 - A/chicken/Germany/N/49
H10N7 - A/mallard/Illinois/10OS4334/2010
H10N8 - A/quail/Italy/1117/1965
H11N9 - A/American green-winged teal/Mississippi/300/2010
H12N5 - A/mallard/Wisconsin/4218/2009
H12N6 -A/duck/Wisconsin/480/1979
H13N6 - A/black-legged kittiwake/Quebec/02838-1/2009
H16N3 - A/shorebird/Delaware/172/2006
H1N2 - A/swine/Ohio/09SW1477/2009
H3N2 - A/swine/Ohio/09SW83E/2009

Influenza B Virus (9 Strains)
Victoria - B/Brisbane/33/2008
Yamagata - B/Christchurch/33/2004
Yamagata - B/Guangdong-Liwan/1133/2014
Yamagata - B/Massachusetts/2/2012
Victoria - B/Nevada/03/2011
Yamagata - B/Phuket/3073/2013
Victoria - B/Texas/02/2013
Yamagata - B/Utah/9/2014
Victoria - B/Victoria/304/2006

RSV (7 Strains)
ATCC-2012-10
A 1997/12-35
A 1998/12-21
A 1998/3-2
A 2000/3-4
A 2001/2-20
A 2001/3-12

The submitter tested the ability of the Simplexa™ Flu A/B & RSV Direct Assay to detect these 53 additional viral strains. Viral stocks were spiked into negative nasopharyngeal swab matrix and tested in triplicate at a single concentration. All strains were appropriately detected by the Simplexa™ Flu A/B & RSV Direct Assay.

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

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

Similarities:

| Features | Predicate<br>Simplexa™ Flu A/B & RSV Direct Assay (K142365) | New Assay<br>Simplexa™ Flu A/B & RSV Direct Assay (K152409) |
|---|---|---|
| Intended Use | The Focus Diagnostics Simplexa™ Flu A/B & RSV | Same |

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|---|---|---|
| | Direct assay is intended for use on the 3M Integrated Cycler instrument for the *in vitro* qualitative detection and differentiation of influenza A virus, influenza B virus, and respiratory syncytial virus (RSV) RNA in nasopharyngeal swabs (NPS) from human patients with signs and symptoms of respiratory tract infection in conjunction with clinical and epidemiological risk factors. This test is intended for use as an aid in the differential diagnosis of influenza A, influenza B, and RSV viral infections in humans and is not intended to detect influenza C.<br><br>Negative results do not preclude influenza virus or RSV infection and should not be used as the sole basis for treatment or other patient management decisions.<br><br>Performance characteristics for influenza A were established with clinical specimens collected during the 2010/2011 influenza season when 2009 H1N1 influenza and H3N2 were the predominant influenza A viruses in circulation. When other influenza A viruses are emerging, performance characteristics may vary.<br><br>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 | |

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|---|---|---|
| | for novel virulent Influenza viruses and sent to the 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.<br><br><u>Simplexa™ Flu A/B & RSV Control Pack</u><br>Focus Diagnostics' Simplexa™ Flu A/B & RSV Positive Control Pack is intended to be used as a control with the Simplexa™ Flu A/B & RSV Direct kit. This control is not intended for use with other assays or systems. | |
| Technology | The Simplexa™ Flu A/B & RSV Direct assay system is a real-time RT-PCR system that enables the direct amplification, detection and differentiation of human influenza A (Flu A) virus RNA, human influenza B (Flu B) virus RNA and RSV RNA from unprocessed nasopharyngeal swabs that have not undergone nucleic acid extraction. The system consists of the Simplexa™ Flu A/B & RSV Direct assay, the 3M Integrated Cycler (with Integrated Cycler Studio Software), the Direct Amplification Disc and associated accessories.<br><br>In the Simplexa™ Flu A/B & RSV Direct assay, bi functional fluorescent probe-primers are used together with corresponding reverse primers to amplify Flu A, Flu B, RSV and internal control RNA. The assay provides three results; conserved regions of influenza A viruses (matrix gene), influenza B | Same |

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| | viruses (matrix gene) and RSV (M gene) are targeted to identify these viruses in the specimen. An RNA internal control is used to detect RT-PCR failure and/or inhibition. | |
| Instrument | 3M Integrated Cycler | Same |
| Specimen Types | Unprocessed nasopharyngeal swabs that have not undergone nucleic acid extraction | Same |
| Flu A Target | Matrix gene | Same |
| Flu B Target | Matrix gene | Same |
| RSV Target | M gene | Same |
| Assay Type | Qualitative | Same |

Differences:

1) The package insert for the Simplexa™ Flu A/B & RSV Direct Assay has been updated to include detection of 37 influenza A strains, 9 influenza B strains, and 7 respiratory syncytial virus (RSV) strains to the Analytical Reactivity/Cross-Reactivity Section.

2) The following wording was changed in the Warnings and Precautions Section of the Simplexa™ Flu A/B & RSV Direct Assay package insert:
"Contamination of patient specimens or reagents can produce erroneous results. Use aseptic techniques."

   The new language is as follows:
"Treat all specimens and discs as capable of transmitting infectious agents. Contamination of patient specimens or reagents can produce erroneous results. Use good laboratory practices and control workflow.[7,8]"

3) The words "Rx Only" were moved from the Limitations Section to the front page of the of the Simplexa™ Flu A/B & RSV Direct Assay package insert.

4) The word "reaction mix" was changed to "Reaction Mix" throughout the Simplexa™ Flu A/B & RSV Direct Assay package insert.

6. A **Design Control Activities Summary** which includes:

1) Cross-reactivity testing was conducted as described in Section 3, Device Modifications.

2) Risk Analysis

The method used for the Risk Analysis for the Simplexa™ Flu A/B & RSV Direct Assay was the Failure Mode Effects Analysis (FMEA). This method is consistent with 21 CFR 820.30. The following table summarizes the risk analysis:

| Risk Type | Failure Mode | Potential Hazard (Harm) | Severity (SEV) | Potential Cause of Failure | OCC Before RCM | RAL Before RCM | Risk Control Measures (RCM) | Verification of RCM Implementation | OCC After RCM | RAL After RCM |
|---|---|---|---|---|---|---|---|---|---|---|
| Product Design | Additional viruses with sequence variations could be encountered in the future that MOL2650 is unable to detect. | False Negative | 3 | Genetic mismatches to the primers and scorpions. | 2 | III | 1.A validation was performed and included additional strains. 53 additional strains were detected at clinically relevant levels.<br>2.PI lists additional strains in the Analytical Reactivity / Cross Reactivity section. | 1.PROT.215.00090 /VALR.215.00090<br>2.PI.MOL2650.IVD | 1 | IV |

The risk of a false negative result was identified as a potential hazard that could occur if target viral sequences contained genetic mismatches with the primers and scorpion probes. This risk was addressed by conducting cross-reactivity testing on an additional 53 viral strains with the Simplexa™ Flu A/B & RSV Direct Assay and through updating the package insert (PI).

3) Declaration of Conformity to Design Controls

A "Declaration of Conformity" statement was submitted for the Focus Diagnostics manufacturing facility. It was signed by the Senior Project Manager, an R&D Scientist, and the R&D Technical Director. The statements indicate that:

3a) "All development activities for the Simplexa™ Flu A/B & RSV REF MOL2650 expanded claims for the addition of the following analytical reactivity strains have been completed, including risk analysis, verification and validation. Activities were performed by designated individuals and the results demonstrated that the pre-determined acceptance criteria were met." Viral strains tested were listed in the Declaration of Conformity (see Section 3 for a complete list).

3b) "The Focus Diagnostics manufacturing facility is in conformance with the Design Control Procedure requirement as specified in 21 CFR 820.30 and the records are available for review."

In conclusion, based on the Risk Analysis and the results of the analytical cross-reactivity testing, the modified labeling is truthful and accurate. The changes do not affect the performance of the Simplexa™ Flu A/B & RSV Direct Assay and, therefore, it is substantially equivalent to the currently cleared test.

**7.** A **Truthful and Accurate Statement**, a **510(k) Summary**, and the **Indications for Use Enclosure**.

The labeling for the 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 and the comparative information between the modified and unmodified device demonstrates that the fundamental scientific technology has not changed. On this basis, I recommend that the device is determined to be substantially equivalent to the previously cleared device.