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Appendix C
Safety and Effectiveness Summary for ViraZyme® Culture Confirmation Screen for Influenza and Parainfluenza

This information is provided as a summary of the safety and effectiveness of the ZymeTx, ViraZyme® Culture Confirmation Screen for Influenza and Parainfluenza Viruses. For more detailed information please refer to the product package insert.

The ViraZyme® Culture Confirmation Screen for Influenza and Parainfluenza is intended for use as a screening test for respiratory viral cultures infected with influenza type A and B and parainfluenza types 1, 2, 3, and 4. This test will screen culture fluids for the presence of these viruses, but it is not indented for the definitive typing of these viruses.

Influenza and parainfluenza viruses posses surface glycoproteins with neuraminidase activity, that hydrolyze substrates which contain alpha-ketosidically linked N-acetylneuraminic acid (Neu5Ac). A modified Neu5Ac molecule has been synthesized and coupled to a chromogen to produce the neuraminidase substrate. In the presence of influenza and parainfluenza the chromogenic substrate is then cleaved by the action of viral neuraminidase, releasing a free chromogen. This free chromogen is then precipitated by combining with a diazonium salt to produce a red color. The red precipitate is then concentrated and collected from the solution onto a filter device.

Performance Characteristics

Viral studies were performed using the ViraZyme® Culture Confirmation Screen for Influenza and Parainfluenza at four separate locations throughout the United States. These studies compared the ViraZyme® Culture Confirmation Screen results to results obtained from standard culture confirmation with monoclonal antibodies.

At a Southern medical center, 177 previously identified patient specimens from freeze were examined in the ViraZyme® Culture Confirmation Screen for Influenza and Parainfluenza. A total of 98/177 specimens were positive in the ViraZyme® Culture Confirmation Screen. Of these 98, ViraZyme® was positive in 100% (23/23) of influenza A IFA confirmed positives, 100% (22/22) of influenza B IFA confirmed positives, 94.4% (17/18) of parainfluenza 1 IFA confirmed positives, 100% (8/8) parainfluenza 2 IFA confirmed positives, and 63.4% (26/41) of parainfluenza 3 IFA confirmed positives. The test site reported two virus-negative specimens by IFA as appearing weakly positive in ViraZyme®. The reminder of the specimens were IFA-negative specimens and these were all negative in ViraZyme®.

At a Southwestern medical center, 97 previously identified patient specimens from freeze were examined in the ViraZyme® Culture Confirmation Screen for Influenza and Parainfluenza. A total of 37/97 specimens were positive in the ViraZyme® Culture Confirmation Screen. Of these 37, ViraZyme® was positive in 100% (36/36) of influenza A IFA confirmed positive and 1.9% (1/53) of Parainfluenza 3 IFA confirmed positives. The remainder of the specimens at this site were virus-negative by IFA and likewise negative in ViraZyme®.

The low ViraZyme® sensitivity for parainfluenza 3 at this site is believed to be related to the presence of bovine serum in the feed medium used at this site. This site routinely used a commercial medium containing 2% bovine serum to feed the inoculated PRMK cultures. It has been shown, in our in-house studies that presence of serum at this concentration will result in a reduced ViraZyme® result. It has been observed that parainfluenza 3 typically gives a lower ViraZyme® result relative to a typical influenza result. Due to the results of our own in-house evaluation with serum and those seen at this test site, we have defined the ViraZyme® culture procedure to exclude serum from virus culture medium.

At a Midwestern medical center, 123 previously identified patient specimens from freeze were examined in the ViraZyme® Culture Confirmation Screen for Influenza and Parainfluenza. A total of 62/123 specimens were positive in the ViraZyme® Culture Confirmation Screen. Of these 62, ViraZyme® was positive in 100% (11/11) of influenza A IFA confirmed positives, 100% (16/16) of influenza B IFA confirmed positives, 100% (5/5) of parainfluenza 1 IFA confirmed positives, 77.8% (7/9) of parainfluenza 2 IFA confirmed positives and 55.6% (5/9) of parainfluenza 3 IFA confirmed positives. Eighteen specimens, which were originally identified as virus positive by IFA at the time of isolation from the patient as being influenza A (five), parainfluenza 1 (four) and parainfluenza 3 (nine), were ViraZyme®-positive, but IFA negative, when tested for these same viruses. The remainder of the specimens were virus-negative by IFA and appropriately negative in ViraZyme®

In an in-house evaluation, in the Southwest, a total of 403 previously identified frozen as well as fresh patient specimens were examined in the ViraZyme® Culture Confirmation Screen for Influenza and Parainfluenza. A total of 185/403 specimens were positive in the ViraZyme® Culture Confirmation Screen. Of these 185, ViraZyme® was positive in 100% (49/49) of influenza A IFA confirmed positives.

100% (99/99) of influenza B IFA confirmed positives, 85.7% (12/14) of parainfluenza 1 IFA confirmed positives, 100% (7/7) of parainfluenza 2 IFA confirmed positives, and 77.8% (14/18) of parainfluenza 3 IFA confirmed positives. Two other ViraZyme®-positives were IFA confirmed for parainfluenza 4 along with two additional ViraZyme®-positives which were

mumps virus strains. Mumps, being the other human virus, besides the influenza and parainfluenzas to produce neuraminidase, gave predictably positive in ViraZyme® as well as by IFA confirming MAb. The reminder of the specimens were IFA-negative for influenza and parainfluenza and these were also all negative in ViraZyme®.

Numerous lots of uninoculated Primary Rhesus Monkey Kidney were also included as negative culture controls to establish that there was no indication of false positive ViraZyme® results associated with either the cells or breakthrough endogenous simian virus. ViraZyme® was shown to be negative in all of these culture controls.

Technical Information

For technical information and comments regarding this product, you may contact the ViraZyme® Product Manager at (405) 271-1383.

This Safety and Effectiveness Summary has been provided as a part of the 510(k) notification for the ViraZyme® Culture Confirmation Screen for Influenza and Parainfluenza.

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Date