SPECIAL 510(k): Device Modification
ODE Review Memorandum

To: THE FILE **RE:** DOCUMENT NUMBER K033982

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

1. The name [**Vysis® UroVysion Bladder Cancer Recurrence Kit**] and 510(k) number of the SUBMITTER'S previously cleared device [**K013785**].

2. Submitter's statement that the INDICATION/INTENDED USE of the modified device as described in its labeling HAS NOT CHANGED. A copy of the proposed labeling which includes instructions for use, and package labeling, edited to reflect the modification, was provided.

   The submitter provided a description of the device **modifications** to demonstrate that the fundamental **scientific technology** of the modified device **has not changed**. **This change was for** the addition of an alternative preservative/transport solution that is commercially available, i.e., PreservCyt® (manufactured by Cytyc, Inc.), to collect urine specimens for testing with the UroVysion Kit. This will allow the end user to choose from two preservative/transport solutions listed in the Package Insert (PI). The preservatives are not included in the test kit.

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

   a. **Test system**: The system has not changed.

   b. **Comparison studies**: To demonstrate the comparability of the current Carbowax™ preservative and the PreservCyt® reagent the applicant performed two studies. Comparability of performance was assessed in a validation study where the hybridization quality of the UroVysion test on urine specimens using either preservative was measured. Concordance between classification results and the average signals per nuclei were used as validation criteria. In addition, a microbial challenge study was performed to (1) validate the use of the PreservCyt® preservative as a microbial inhibitory agent, and (2) assess test performance with both preservatives in urine samples spiked with a specific microbial load. Average signals per nuclei were used for comparison. Specimens used in the study were placed in simulated shipping conditions, i.e., standard shipment packaging and storage), for zero, one, two, 3 and 7 days.

   Data and relevant statistical analyses, including overall quality rating histograms, and graphs showing cell counts as a function of time, are provided. The information provided establishes similar test performance with both the PreservCyt® and the Carbowax™ preservatives. These results are summarized below:

   1. **Validation Study Results**: An 82% (14/17) concordance was observed between specimens incubated with both preservatives. Discordant cases were evenly split

between PreservCyt® (n=4) and Carbowax™ (n=3). In addition, a maximum of 39% variation (mean 7.3%) in average signals per nucleus was seen among all CEP probes. This result meets the acceptance criterion, i.e., the value for each probe should not vary by > 50% between each preparation set. Overall quality measurements showed that in all but two ratings both preservatives met the "pass" criterion. The results showed that both preservatives perform similarly when used in *"a 2:1 (v.v., urine: preservative) dilution and stored in blue ice."*

2. Microbial Challenge Results: Urine specimens, divided into each preservative solution and spiked with a specified microbial challenge dose, were stored at 2-8°C and 20-25 °C. The test was considered negative if there was no increase of $>1.3 \times 10^4$ cfu/mL of the challenge organism between t_0 and 24, 48, and 72 h incubation. All test met this criterion and slight differences in counts between preservatives were not significant. In addition, the average signals per nucleus counts between t_0 and 24, 48, and 72 h incubation showed less variation when samples were stored at 2-8°C. However, the results of the UroVysion assay were acceptable and similar with both preservatives.

3. **Transportability/storage**: The results of the two studies, performed under shipping conditions, established that storage of urine sample at 25°C for one week with either a PreservCyt® or a Carbowax™ is adequate.

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

   a) Identification of Risk Analysis method(s) used to assess the impact of the modification on the device and its components, and the results of the analysis

   b) Based on the Risk Analysis, an identification of the verification and/or validation activities required, including methods or tests used and acceptance criteria to be applied

   c) A **declaration of conformity with design controls** provided on **p.56** includes:

      i) A statement signed by the individual responsible, that, as required by the risk analysis, all verification and validation activities were performed by the designated individual(s) and the results demonstrated that the predetermined acceptance criteria were met, and
      ii) A statement signed by the individual responsible, that the manufacturing facility is in conformance with design control procedure requirements as specified in 21 CFR 820.30 and that the records are available for review.

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

The labeling for this modified subject device has been reviewed. The indication/intended use for the device is identical to the wording in the original clearance.

The submitter's description of the particular modification 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.

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(Reviewer's Signature) (Date)