EVALUATION OF AUTOMATIC CLASS III DESIGNATION FOR NP SCREEN DECISION SUMMARY

A. DEN Number:

DEN190031

B. Purpose for Submission:

De Novo request for evaluation of automatic class III designation for the NP Screen assay

C. Measurand:

Epstein-Barr Virus DNA

D. Type of Test:

Real-Time PCR

E. Applicant:

Advance Sentry Corporation

F. Proprietary and Established Names:

NP Screen

G. Regulatory Information:

1. Regulation section:

   21 CFR 866.3236

2. Classification:

   Class II

3. Product code:

   OJY

4. Panel:

   Microbiology (83)

H. Intended Use:

1. Intended use(s):

   NP Screen is a semi-quantitative in vitro diagnostic test that uses real-time PCR to determine the level of Epstein-Barr Virus Nuclear Antigen-1 (EBNA-1) DNA in nasopharyngeal cellular specimens collected using the NP Screen Trans-Oral Nasopharyngeal Brush. The test is intended for use in conjunction with endoscopy and other clinical information to assess the likelihood that EBV-associated nasopharyngeal carcinoma (NPC) is present. The test is indicated for use in adults of Chinese descent with signs and symptoms of nasopharyngeal carcinoma.
   The NP Screen assay is a single-site assay performed at Primex Clinical Laboratories, Inc.

2. Indication(s) for use:

   Same as Intended Use

3. Special conditions for use statement(s):

   For prescription use only.

   For *in vitro* diagnostic use.

4. Special instrument requirements:

   - Roche MagNA Pure 96 System (for nucleic acid extraction)
   - Thermo Scientific Fluoroskan Ascent (for pre-analytical DNA standardization)
   - Applied Biosystems QuantStudio 12K Flex Real-Time PCR System (for EBV DNA amplification)

I. Device Description:

NP Screen is a semi-quantitative *in vitro* test for the detection of Epstein-Barr Virus Nuclear Antigen-1 gene (EBNA-1) in nasopharyngeal epithelial specimens. Specimens are collected by the clinician, using the NP Screen Trans-Oral Collection Brush, and placed into the Transport Medium for shipping. The test is performed in a single laboratory, Primex Clinical Laboratories, Inc. Total nucleic acid is extracted from the specimen and the dsDNA is then quantitated. If the amount of extracted DNA does not meet the minimum required for testing, the specimen is rejected, and a new specimen must be collected. Extracted specimen DNA that meets the specification is normalized to a pre-defined concentration. The standardized

DNA is tested in duplicate using real-time Polymerase Chain Reaction (real-time PCR) and nucleic acid hybridization for the detection of target EBV EBNA-1 DNA. Simultaneous amplification and detection of human RNAse P DNA serves as the internal control for assessing all steps of the NP Screen assay. Low and High Positive External Controls are included with each run.

The NP Screen assay requires the following reagents and materials:

- Specimen Collection and Transport
  - Trans-Oral Nasopharyngeal Specimen Collection Kit
    - Instruction sheet
    - Trans-Oral Collection Brush, packaged separately (sterile)
    - Vial with Transport Medium – 0.5 mL
    - Vial labels for patient information and specimen identification
    - Biohazard specimen transport bag
    - Disposable scissors

- DNA Extraction
  - MagNA Pure 96 DNA and Viral NA Small Volume Kit

- DNA Standardization
  - Quant-iT dsDNA Assay Kit, broad range

- Real-Time PCR
  - EBV DNA TaqMan Primers and Probe
  - TaqMan RNase P Detection Kit
  - TaqMan Universal Master Mix II with UNG
  - External Controls
    - Low Positive
    - High Positive

J. Standard/Guidance Document Referenced (if applicable):

CLSI EP05-A3: Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline – Third Edition

K. Test Principle:

Target sequences located in the EBV EBNA-1 gene and the human RNase P gene are detected and co-amplified during the real-time PCR reaction. For patient samples, EBNA-1 is the clinically relevant analyte, while RNase P serves as the internal control.

Uracil-N-glycosylase is included in each reaction to prevent amplification of products from previous PCR reactions. The Low Positive Control and High Positive Control are extracted

and tested in duplicate with each run. A negative (no-template control) is tested in duplicate with each run.

For each specimen, the duplicate Ct results are averaged and then converted to an NP Screen-specific unit of Epstein-Barr Virus DNA Detection Level (EDL). Results of the NP Screen assay are reported as Positive, Equivocal, or Negative. The cut-off points for Negative and Positive results represent EBV DNA levels relevant in assessing the likelihood of nasopharyngeal carcinoma in adult patients of Chinese descent with signs and symptoms of nasopharyngeal carcinoma. The NP Screen result is intended to be used as a supplement to endoscopy, along with other clinical information. Result interpretation for the NP Screen assay is shown in Table 1.

Table 1: NP Screen Result Interpretation

NP Screen Result	Interpretation
Positive	EBV DNA was detected at a significantly elevated level.
Equivocal	EBV DNA was detected at a low level.
Negative	EBV DNA was not detected or was detected at a very low level.
Insufficient	Amount of DNA was not sufficient for testing. Collect and submit a new specimen.

L. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision:

A panel of (b)(4) samples consisting of High Positive, Low Positive, Equivocal, High Negative and Negative levels of EBV DNA was tested at (b)(4) site. The panel was tested in (b)(4) runs per day (b)(4) operators per day x (b)(4) runs per operator), in (b)(4) replicates per sample, on 20 days, for a total of (b)(4) replicates per sample. The study included (b)(4) reagent lots. Results are shown in Table 2.

Table 2: Precision of the NP Screen assay

			Repeatability		Between Run		Between Lot		Between Day		Within Lab	
Sample	**Mean EDL**	**N**	**SD**	**% CV**	**SD**	**% CV**	**SD**	**% CV**	**SD**	**% CV**	**SD**	**% CV**
High Positive	(b)(4)											

			Repeatability		Between Run		Between Lot		Between Day		Within Lab	
Sample	**Mean EDL**	**N**	**SD**	**% CV**	**SD**	**% CV**	**SD**	**% CV**	**SD**	**% CV**	**SD**	**% CV**
Low Positive	(b)(4)											
Equivocal												
High Negative												
Negative												

* (b)(4) results are excluded from calculations because they were (b)(4)
† (b)(4) invalid result was excluded due to a failed Internal Control signal.

b. *Linearity/assay reportable range:*
Not applicable

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
Traceability
The concentrations of EBV DNA detected at the NP Screen cut-off points for Negative and Positive result interpretations were determined using an EBV virus preparation traceable to the 1st WHO International Standard for Epstein-Barr Virus for Nucleic Acid Amplification Techniques, NIBSC code: 09/260. The Low and High Positive Controls are also traceable to the 1st WHO International Standard.

Reagent Stability
The reagents and the Controls used in the NP Screen assay are purchased from commercial vendors. Advance Sentry Corporation verified that the NP Screen reagents and Low and High Positive Controls are stable for up to seven months within the expiration date specified by the manufacturer of each reagent and control.

Specimen stability
(b)(4) samples with EBV concentrations slightly above the cut-off for Positive results of the NP Screen assay were prepared from pooled NP Screen-negative clinical samples spiked with EBV. Immediately after preparation, (b)(4) replicates of each sample were tested to establish the baseline results. All remaining aliquots were placed into storage. Storage conditions reflected temperature extremes that might be encountered during specimen transport as well as controlled temperatures in a laboratory setting. At each test time point, (b)(4) replicates of each of (b)(4) samples were used for NP Screen testing.

Results of the study support the stability of specimens and extracted DNA stored under the following conditions:

Specimen storage prior to extraction with the NP Screen assay:

- Up to 3 weeks, from time of collection, at either at 2 – 8°C or at Room Temperature 22 – 25°C

Extracted DNA storage:

- Up to 2 weeks at 2 – 8°C after storage of the specimen for up to 3 weeks, from time of collection, either at 2 – 8°C or at Room Temperature 22 – 25°C

Controls

- Run controls
  - Low Positive Control (purified EBV) is run in (b)(4) For each replicate, the Ct (FAM) must fall within the established range.
  - High Positive Control (purified EBV) is run in (b)(4) For each replicate, the Ct (FAM) must fall within the established range.
  - Negative (no-template) PCR control (sterile, molecular grade water replaces DNA template) is run in (b)(4) Results must show no amplification.

- Sample-specific controls – patient samples are run in (b)(4)
  - Internal Control – Detection of human RNase P. The Ct (VIC) of each replicate must fall within the established range and the difference between the Ct values must be within the established acceptable limit.
  - EBV EBNA-1 result. The Ct (FAM) of each replicate must fall within the established range and the difference between the Ct values must be within the established acceptable limit.

d. *Detection limit:*

The Limit of Detection (LoD) was determined by testing a panel of (b)(4) samples. The samples were prepared from quantified EBV diluted in a matrix of pooled negative clinical specimens. The samples were tested in (b)(4) replicates per run, (b)(4) runs per day, over (b)(4) days, for a total of (b)(4) replicates per sample. The LoD determined by the study is well below the established EBV concentration detected at the clinically validated NP Screen cut-off point for discriminating Negative from Equivocal specimen results.

e. *Analytical specificity:*

Cross-reactivity

Cross-reactivity studies were performed with a panel of (b)(4) microorganisms. For microorganisms sourced as viable virus or bacteria, the samples were thawed, or re-suspended in sterile water if lyophilized, and extracted. For microorganisms sourced as purified DNA or RNA, the nucleic acid was added directly to the PCR reaction. For each panel member, (b)(4) uL of purified nucleic acid from the microorganism plus (b)(4) uL of purified nucleic acid from a pool of NP Screen-negative samples were added to the PCR reaction. Each microorganism was tested in (b)(4) with the NP Screen

assay. No cross-reactivity was observed with the microorganisms tested at the concentrations shown in Table 3.

Table 3: Microorganisms tested for cross-reactivity in the NP Screen assay

Microorganism	Sample Type	Concentration*
Adenovirus (HAdv)	DNA	(b)(4)
Bordetella pertussis	culture	
Chlamydia pneumoniae	culture	
CMV (HHV5)	culture	
Corynebacterium sp.	culture	
E. coli	DNA	
Enterovirus D68	RNA	
Haemophilus influenzae	DNA	
HHV6	culture	
Human coronavirus 229E	RNA	
Human parainfluenza	RNA	
HPV Type 16‡	DNA	
HPV Type 18‡	DNA	
HSV I	culture	
HSV II	culture	
Influenza A (H1N1)‡	culture	
Influenza A (H3N2)‡	culture	
Influenza B‡	culture	
Klebsiella pneumoniae	DNA	
Lactobacillus sp.	culture	
Legionella pneumophila	culture	
Mumps virus	RNA	
Mycobacterium sp.	DNA	
Neisseria meningitidis	DNA	
Pseudomonas aeruginosa	DNA	
Respiratory syncytial virus	RNA	
Rhinovirus	RNA	
Staphylococcus aureus	DNA	
Staphylococcus epidermidis	DNA	
Streptococcus pneumoniae	DNA	
Streptococcus pyogenes	DNA	
Streptococcus salivarius	DNA	

* For culture samples, this is the concentration of the sample input to the extraction step. For nucleic acid samples, this is the concentration of DNA or RNA input to the PCR reaction.

† Concentration information was not available.
‡ 10 uL of microorganism DNA were added to the PCR reaction without the addition of nucleic acid from a pool of NP Screen-negative samples.

In addition, an *in silico* analysis was performed using the NP Screen assay primers and probe as input sequences for BLAST searches against the NCBI Public DNA Database. No significant sequence matches were detected in the *in silico* analysis.

Interfering Substances

A study was performed to evaluate the performance of the NP Screen assay in the presence of potentially interfering substances that might be found in the nasopharynx. A matrix of pooled NP Screen specimens was divided and spiked with EBV to obtain samples at two EBV concentrations, one just above the cutoff for Positive results and one in the range of Negative results for the NP Screen assay. An NP Screen Trans-Oral Collection Brush was submerged in the full-strength interfering substance and then placed in an aliquot of each sample. A control sample was prepared with Phosphate Buffered Saline (PBS), in place of the interfering substance. The samples were extracted and tested with the NP Screen assay. The potentially interfering substances evaluated are listed in Table 4.

Table 4: Potentially Interfering Substances Tested in the NP Screen Assay

Potentially Interfering Substances
Drixoral Nasal Spray
Taro-Mupirocin Antibiotic, nasal ointment
Mylan Belco AQ - nasal corticosteroid
Avamys Fluticasone - nasal corticosteroid
Lidodan - topical anesthetic
Relenza - inhaled antiviral medication
Blood

No interference was observed with the substances listed in Table 4, i.e., all positive replicates produced positive results and all negative replicates produced negative results.

f. Assay cut-off:

The EBV concentrations detected at the cut-off points for Positive and Negative results were determined by testing dilutions of a material traceable to the 1st WHO International Standard for Epstein-Barr Virus for Nucleic Acid Amplification Techniques, NIBSC code: 09/260. The cut-off points for Positive and Negative results of the NP Screen assay indicate clinically relevant levels of EBV DNA and

were validated in the clinical study.

g. *Analytical accuracy:*
Samples prepared from the pooled negative clinical specimens spiked with quantified EBV traceable to the 1st WHO International Standard were tested (see 1.d above).

h. *Carryover*

A series of EBV negative samples, with EDL=0, and high positive samples, with EDL (b)(4) were tested in a checkerboard pattern with the NP Screen assay. A total of (b)(4) high positive and (b)(negative samples were processed on each of (b)(4) plates by different operators in separate runs. All negative samples produced negative NP Screen results with EDL=0. No carryover was observed.

2. Comparison studies:

a. *Method comparison:*

Not applicable

b. *Matrix comparison:*

Not applicable; the NP Screen assay is intended for use only with the NP Screen Trans-Oral Nasopharyngeal Specimen Collection Brush and Transport Media.

3. Clinical studies:

a. *Clinical Sensitivity:*

The NP Screen Test is a semi-quantitative test; therefore, clinical sensitivity is not applicable. Clinical performance was evaluated by calculating risks for Positive, Equivocal and Negative results; refer to section M.3.c.

b. *Clinical specificity:*

The NP Screen Test is a semi-quantitative test; therefore, clinical specificity is not applicable. Clinical performance was evaluated by calculating risks for Positive, Equivocal and Negative results refer to section M.3.c.

c. *Other clinical supportive data (when a. and b. are not applicable):*

Clinical Validation Study
Overview
Patients with signs or symptoms of NPC are often referred by family physicians to an

ear, nose, and throat (ENT) specialist for clinical examination and assessment of the nasopharynx using an endoscope. Depending on the findings of the endoscopy exam and other clinical information, the patient may be advised to have a biopsy. A clinical study was performed to determine the risk of nasopharyngeal carcinoma associated with different combinations of endoscopy findings and NP Screen results.

Study Design

The study included adult patients of Chinese descent with signs and symptoms of NPC. All patients who fulfilled the inclusion criteria and provided written consent in accordance with the IRB approved protocol were enrolled in the study. The collection site was located in Toronto, Canada. Upon enrollment, each patient received detailed clinical and endoscopy examinations at an ENT clinic, according to standard clinical practice. Following endoscopy, the ENT surgeon collected a nasopharyngeal specimen from each patient using the NP Screen Trans-Oral Collection Brush and collection procedure. The specimen was shipped to Primex Clinical Laboratory for NP Screen testing.

The endoscopy findings for each patient were categorized, based on commonly described endoscopic features of NPC, by degree of suspicion for NPC, as follows: High Suspicion, Intermediate Suspicion, Low Suspicion, or No Suspicion.

Expected Values

A total of 1146 patients were enrolled in the study. Of those, eight (0.7%) had invalid NP Screen results and were excluded from the analysis. There were 1,138 patients enrolled in the study with evaluable results. The percent of patients with Positive, Equivocal, and Negative NP Screen results, stratified by endoscopy at baseline, are presented in **Error! Reference source not found.**.

Table 5: Expected NP Screen Results

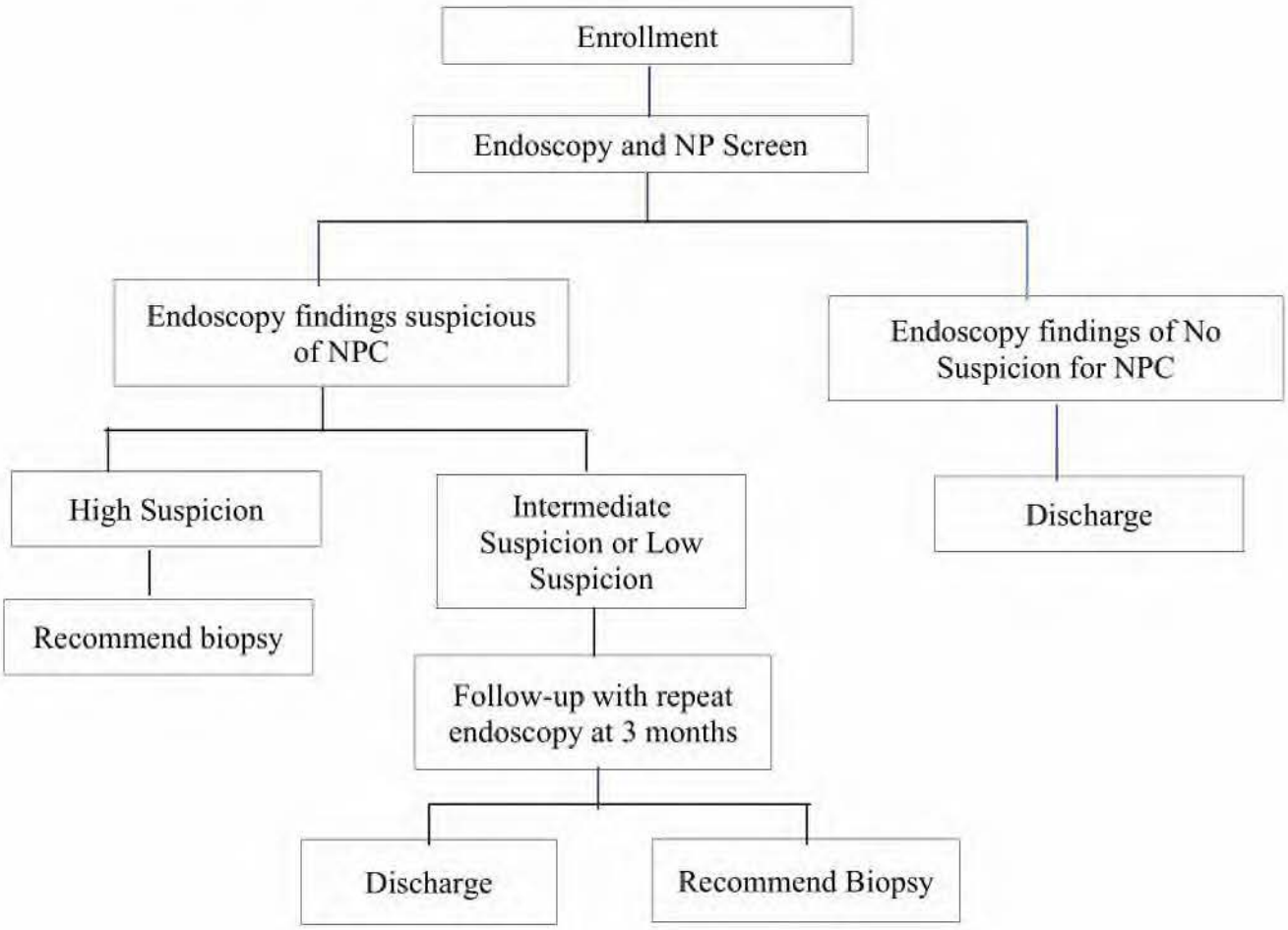
Endoscopy (Degree of Suspicion for NPC)	N	NP Screen Results		
		%Positive	%Equivocal	%Negative
High Suspicion	49	67.3% (33/49)	12.2% (6/49)	20.4% (10/49)
Intermediate Suspicion	54	18.5% (10/54)	7.4% (4/54)	74.1% (40/54)
Low Suspicion	363	2.5% (9/363)	3.3% (12/363)	94.2% (342/363)
No Suspicion	672	0.9% (6/672)	3.9% (26/672)	95.2% (640/672)
Combined	1,138	5.1% (58/1,138)	4.2% (48/1,138)	90.7% (1,032/1,138)

Clinical Performance

Patients with abnormal endoscopy findings of High Suspicion were recommended for biopsy. Patients whose endoscopy findings showed No Suspicion for NPC were recommended for discharge from the clinical study. Patients with abnormal endoscopy findings of Intermediate or Low Suspicion were recommended for follow-up with repeat endoscopy at 3 months. At the 3-month follow-up visit, based on the findings of the repeat endoscopy and other clinical information, the patient was discharged, or biopsy was recommended.

The clinical study design is summarized in Figure 1.

Figure 1: Clinical study design



Clinical Status

The clinical status for each patient was determined as follows:

1. For patients with High Suspicion endoscopy findings at baseline, biopsy is recommended, and clinical status is determined by results of the biopsy.

2. For the patients with Intermediate or Low Suspicion endoscopy findings at baseline, clinical status was determined at the 3-month follow-up visit. If biopsy was recommended for the patient at the 3-month follow-up visit (because of endoscopy findings) then clinical status for the patient was determined by results of the biopsy. If biopsy was not recommended for the patient based on the endoscopy findings at 3 months, then clinical status for the patient is considered as negative for NPC.
3. For the patients with endoscopy findings of No Suspicion at baseline, clinical status for the patient is considered as negative for NPC.

Data Analysis

Performance of the NP Screen assay with three results (Positive, Equivocal, Negative) is described by risks for each result along with 95% confidence intervals.

Risks

The pre-test risk and post-test risks of NPC for patients with Positive, Equivocal, and Negative NP Screen results were calculated for each category of baseline endoscopy findings, as presented in Table 6.

Table 6. Risks of NPC for Different Combinations of Endoscopy and NP Screen Results

Endoscopy (Degree of Suspicion)	N	Pre-Test Risk of NPC (Prevalence)	Positive NP Screen Result		Equivocal NP Screen Result		Negative NP Screen Result	
			Risk of NPC	95% CI	Risk of NPC	95% CI	Risk of NPC	95% CI
High Suspicion	49	79.6% (39/49)	100% (33/33)	(91.4%; 100%)	83.3% (5/6)	(47.7%; 98.4%)	10% (1/10)	(0.7%; 37.8%)
Intermediate Suspicion	54	16.7% (9/54)	90.0% (9/10)	(62.1%; 99.4%)	0.0% (0/4)	(0.0%; 45.5%)	0.0% (0/40)	(0.0%; 7.7%)
Low Suspicion	363	1.7% (6/363)	66.7% (6/9)	(39.4%; 88.0%)	0.0% (0/12)	(0.0%; 18.9%)	0.0% (0/342)	(0.0%; 1.0%)
No Suspicion	672	0.149% (1/672)	16.7% (1/6)	(1.6%; 33.6%)	0.0% (0/26)	(0.0%; 4.0%)	0.0% (0/640)	(0.0%; 0.146%)
Combined	1138	4.8% (55/1,138)	84.5% (49/58)	(74.0%; 91.7%)	10.4% (5/48)	(3.6%; 21.1%)	0.10% (1/1,032)	(0.01%; 0.91%)

Risks of 0.0% in the table mean small positive risks because patients with endoscopy findings not suspicious for NPC are considered as negative for NPC in the data analysis.

Conclusions for patients with High Suspicion endoscopy findings:

Data for 49 patients with High Suspicion endoscopy findings demonstrated that:

- Patients with NP Screen Positive results have NPC risk of 100% and the risk is statistically significantly higher than the pre-test risk of 79.6%.
- Patients with NP Screen Negative results have NPC risk of 10% and the risk is statistically significantly lower than the pre-test risk of 79.6%.

Conclusions for subjects with Intermediate Suspicion endoscopy findings:

Data for 54 subjects with Intermediate Suspicion endoscopy findings demonstrated:

- Patients with NP Screen Positive results have NPC risk of 90.0% and the risk is statistically significantly higher than the pre-test risk of 16.7%.
- Patients with NP Screen Negative results have NPC risk of 0.0% and the risk is statistically significantly lower than the pre-test risk of 16.7%.

Conclusions for subjects with Low Suspicion endoscopy findings:

Data for 363 subjects with Low Suspicion endoscopy findings demonstrated that:

- Patients with NP Screen Positive results have NPC risk of 66.7% and the risk is statistically significantly higher than the pre-test risk of 1.7%.
- Patients with NP Screen Negative results have NPC risk of 0.0% and the risk is statistically significantly lower than the pre-test risk of 1.7%.

Conclusions for subjects with endoscopy findings of No Suspicion:

Data for 672 subjects with endoscopy findings of No Suspicion demonstrated that:

- Patients with NP Screen Positive results have NPC risk of 16.7% and the risk is statistically significantly higher than the pre-test risk of 0.149%.
- Patients with NP Screen Negative results have NPC risk of 0.0% and the risk is statistically significantly lower than the pre-test risk of 0.149%.

4. Clinical cut-off**:**

   The NP Screen test has two cutoffs: one cutoff is for Negative results and the second cutoff is for Positive results.

5. Expected values/Reference range:

   For Expected values, see Table 5 above. Reference range is not applicable.

M. Instrument Name:

Not applicable.

N. System Descriptions:

1. Modes of Operation:

   Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?

   Yes _____ or No ___x____

   Does the applicant's device transmit data to a computer, webserver, or mobile device using wireless transmission?

   Yes _____ or No ___x_____

2. Software:

   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

   Yes ___x_____ or No _____

3. Specimen Identification:

   Specimen Identification labels are provided in the NP Screen Trans-Oral Nasopharyngeal Specimen Collection Kit.

4. Specimen Sampling and Handling:

   A nasopharyngeal specimen is collected by the clinician using the Trans-Oral Nasopharyngeal Brush and placed into the vial of Transport Medium. The specimen is shipped at ambient temperature to the laboratory.

   Information on specimen collection is provided in the package insert of the NP Screen Trans-Oral Nasopharyngeal Specimen Collection Kit.

5. Calibration:

   Not applicable.

6. Quality Control:

   Refer to section L.1.c for a description of the assay and sample controls.

O. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

Not applicable.

P. Proposed Labeling:

The labeling supports the decision to grant the De Novo request for this device.

Q. Identified Risks to Health and Mitigation Measures

Identified Risks to Health	Identified Mitigations
False test results	Use of certain specimen collection and transport devices. Certain labeling information. Certain design verification and validation.
Failure to correctly interpret the test results	Certain labeling information.

R. Benefit/Risk Analysis

Summary of the Assessment of Benefit

The benefit of the test, when used as a supplement to nasal endoscopy, along with other clinical information, would be aiding a clinician to assess the likelihood that EBV-associated nasopharyngeal carcinoma (NPC) is present in appropriate patients, namely adults of Chinese descent with signs and symptoms of NPC. The high prevalence of NPC in this population justifies authorizing use of this device. The clinical benefit of assessing the likelihood of EBV associated NPC would be the potential for initiation of further investigation and potentially intervention sooner than current medical practice to avoid the sequelae of untreated NPC, such as progression to more invasive disease requiring more aggressive treatment. Potentially, this device could result in reduced morbidity and improved survival in patients with undiagnosed NPC. The device is non-invasive and had favorable clinical performance characteristics in the clinical study. For patients with endoscopy findings in whom the recommendation to biopsy immediately would otherwise be uncertain, waiting 3 months for repeat evaluation is recommended as current standard of practice. The NP assay could be used in this population at the time of the first endoscopy to guide physicians to initiate further investigation and intervention.

Summary of the Assessment of Risk

The risks associated with the device, when used as intended, are those related to the risk of false test results and failure to correctly interpret the test results.

The risk of a false positive test result includes improper patient management, including biopsy, imaging, and/or treatment for nasopharyngeal cancer. A false positive will result in further assessment and biopsy of the site. Biopsies include the relatively rare risks of excessive bleeding and infection.

The risks of false negative tests include improper patient management, including missing an NPC diagnosis by a clinician choosing not to pursue further investigation and subsequently under-treating a patient with NPC in whom radiation with or without chemotherapy would otherwise be indicated. Untreated NPC can progress to more invasive disease requiring more aggressive treatment associated with increased morbidity and mortality.

Summary of the Assessment of Benefit-Risk

The clinical benefits outweigh the probable risks for the proposed assay, considering the mitigations of the risks provided in the special controls as well as general controls. The special controls, including verification and validation documentation, a detailed explanation of the interpretation of results and acceptance criteria for evaluating the validity of results, and the limiting statements in device labeling will help to ensure that errors will be uncommon and will facilitate accurate assay implementation and interpretation of results.

Patient Perspectives

This submission did not include specific information on patient perspectives for this device.

S. Conclusion

The De Novo request for the NP screen device is granted and the device is classified under the following and subject to the special controls identified in the letter granting the De Novo request:

Product code: OJY
Device Type: Device to detect or measure nucleic acid from viruses associated with head and neck cancers
Class: II (special controls)
Regulation: 21 CFR 866.3236