EVALUATION OF AUTOMATIC CLASS III DESIGNATION FOR SeCore™ CDx HLA SEQUENCING SYSTEM

DECISION SUMMARY

A. DEN Number:

BR 220737

B. Purpose for Submission:

De Novo request for evaluation of automatic class III designation for the SeCore CDx HLA Sequencing System

C. Measurands:

DNA sequences of the HLA-A gene

D. Type of Test:

Human Leukocyte Antigen (HLA) Typing Companion Diagnostic Test

E. Applicant:

One Lambda, Inc.

F. Proprietary and Established Names:

SeCore™ CDx HLA Sequencing System

G. Regulatory Information:

1. Regulation section:

21 CFR 866.5960

2. Classification:

Class II

3. Product code:

QUK

4. Panel:

Immunology

□ **I concur with the summary review.**

□ **I concur with the summary review and include a separate review to add further analysis.**

□ **I do not concur with the summary review and include a separate review.**

Office's Signatory Authority**:**

Date of FDA Notice of Granting the Classification Request:

Review Memos From the following reviewers were used in developing the Decision Summary:

Discipline	**Reviewer Names**
Analytical Studies and Clinical Studies	Meihong Liu Jamie Brewer (Consult reviewer from CDER)
Software	Kimberly Bigler
Statistician	Linye Song

H. Indications for use:

1. Indications for use

The SeCore CDx HLA Sequencing System is intended for the detection of human leukocyte antigen A-locus (HLA-A) alleles using genomic DNA isolated from whole blood samples. The device is intended to be used as a companion diagnostic (CDx) to aid in the selection of HLA-A*02:01 positive patients with unresectable or metastatic uveal melanoma who may benefit from treatment with KIMMTRAK® (tebentafusp-tebn) when used in accordance with approved therapeutic labeling.

2. Special conditions for use statement(s)

For prescription use only

For *in vitro* diagnostic (IVD) use only

3. Special instrument requirements

Applied Biosystems 3500 Dx / 3500xLDx Genetic Analyzer CS2 and Veriti™ Dx 96-Well Thermal Cycler Model 9912.

I. Device Description:

The SeCore CDx HLA Sequencing System is a Sanger sequence-based method for molecular typing of HLA-A Locus alleles. Sequencing-based typing is a high-resolution method for the identification of HLA polymorphisms. The process involves selective amplification of target regions by Polymerase Chain Reaction (PCR), agarose gel electrophoresis, and sequencing. The PCR is performed for locus-specific amplification of genomic DNA purified from whole blood specimens, generating ~1100 and 990 bp HLA-A locus products that are confirmed by

2.0% agarose gel electrophoresis. The resultant DNA products are loaded onto the Applied Biosystems 3500 Dx / 3500xLDx Genetic Analyzer CS2 for Sanger Sequencing by capillary electrophoresis which produces sample files. The sample files are then analyzed with the uTYPE™ CDx HLA Sequence Analysis Software.

The components of the SeCore CDx HLA Sequencing System and their functions are listed below:

1. Pre-PCR reagents including a PCR Amplification Mix with locus specific amplification primers and FastStart™ Taq DNA Polymerase enzyme.
2. Post-PCR reagents for Sanger Sequencing.
3. SeCore™ CDx HLA GSSP Kit that includes the Group Specific Sequencing Primer (GSSP) mixtures used for resolving ambiguities in initial sequencing data.
4. uTYPE™ CDx HLA Sequence Analysis Software to report detected HLA alleles and any ambiguities.
5. Instruments:
    - Veriti™ Dx 96-Well Thermal Cycler Model 9912 for PCR amplification.
    - Applied Biosystems 3500 Dx Series Genetic Analyzer CS2 with 3500 Dx Series Software 2011 v1.0 including 3500 Dx (8-capillary) and 3500xL Dx (24-capillary) for performing Sanger Sequencing of the PCR products.

Ambiguity resolution: In certain rare instances, the SeCore CDx HLA Sequencing System cannot fully resolve ambiguous alleles. The software provides the user with alternative approaches to HLA allele reporting and ambiguity resolution, such as reporting the G-code if ambiguous alleles are part of the same G-code or reporting an allele pair with ≥99% probability calculated based on allele frequencies.

J. Comparison with the Previously Cleared SeCore HLA Sequencing System:

The SeCore CDx HLA Sequencing System is technically identical to the previously cleared SeCore HLA Sequencing system (BK110038) except for the intended use and indications.

The SeCore HLA Sequencing System is intended for the identification and definition of Class I and II Human Leukocyte Antigens (HLA) and is for use in HLA typing. The SeCore HLA Sequencing System provides human histocompatibility information of HLA Class I (A, B, and C) and Class II (DPB1, DQB1 and DR) loci using genomic DNA isolated from whole blood specimens. The accompanying uTYPE Dx v1.0 HLA Sequence Analysis Software is intended to interpret and match sequencing data generated on the Applied Biosystems 3500 Dx /3500 xL Dx Genetic Analyzer CS2 to known HLA type sequences.

The SeCore HLA Sequencing System is an unclassified device with Product Code MZI.

The differences between the SeCore HLA Sequencing System and the SeCore CDx HLA Sequencing System are described in the Table 1 below.

Table 1. Comparison of the SeCore HLA Sequencing System with the SeCore CDx HLA Sequencing System

	SeCore HLA Sequencing System	SeCore CDx HLA Sequencing System
Software Technology	Windows XP or 7.0 operating system	Windows 10 operating system
Software Main Components	uTYPE Dx HLA Analysis Software Version 1.0	uTYPE CDx HLA Sequence Analysis Software Version 1.2
Where Used and Target population	Used for matching of donors and recipients in transfusion and transplantation.	To test patients with unresectable or metastatic uveal melanoma to determine eligibility to receive Tebentafusp-tebn (KIMMTRAK®).

K. Standard/Guidance Documents referenced:

ISO 13485:2016 Medical devices - Quality management systems - Requirements for regulatory purposes

ISO 14971:2019 Medical devices - Application of risk management to medical devices

EN 62366-1:2015 Medical devices - Application of usability engineering to medical devices

ISO 63204:2006 Medical device software - Software life -cycle processes

EN ISO 15223-1: 2021 Medical devices - Symbols to be used with information to be supplied by the manufacturer - General requirements

EN ISO 18113-1:2011 In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Terms, definitions, and general requirements

EN ISO 18113-2:2011 In vitro diagnostic medical devices -Information supplied by the manufacturer (labelling) - In vitro diagnostic reagents for professional use

EN 13612:2002 Performance evaluation of in vitro diagnostic medical devices

EN ISO 23640:2015 In vitro diagnostic medical devices -Evaluation of stability of in vitro diagnostic reagents

EN 13647:2002 Elimination or reduction of risk of infection related to in vitro diagnostic reagents

EN 13975:2003 Sampling procedures used for acceptance testing of in vitro diagnostic medical devices - Statistical aspects

L. Test Principle:

The SeCore CDx HLA Sequencing System directly identifies the DNA sequence of the target HLA genes. PCR is used with SeCore primers to perform locus-specific DNA amplification. Sanger sequencing is then used to determine the nucleotide sequence of the amplified product. Resulting data files are analyzed with uTYPE CDx HLA Sequence Analysis Software, which compares sample sequences to reference sequences in the IMGT HLA database for HLA allele assignment.

M. Performance Characteristics

The following were used to determine the performance characteristics of the SeCore CDx HLA Sequencing System:

a. Performance studies from the previously cleared SeCore HLA sequencing system (BK110038).
b. Additional analytical accuracy and precision studies on the SeCore CDx HLA Sequencing System.

1. Analytical Accuracy Studies

a) SeCore HLA Sequencing System Accuracy Study

The accuracy of the SeCore HLA Sequencing System for detection of HLA-A alleles was evaluated in the related 510(k) submission BK110038. The study used 71 UCLA well-characterized reference samples. Overall percent agreement of HLA-A allele detection with the reference results was 100% of point estimate, and 98.3% one sided Lower Bound (LB) of 95% confidence interval.

b) Additional Accuracy Study Focusing on the Target Allele

To evaluate the SeCore CDx HLA sequencing system's accuracy performance for detecting the target HLA-A*02:01 allele, 72 well-characterized UCLA reference samples and 33 clinical samples from Metastatic Uveal Melanoma (mUM) patients were tested on one lot of the SeCore CDx HLA sequencing kit. The assay was run on a Genetic Analyzer 3500xl Dx and Veriti Dx thermal cycler. The sequencing data was analyzed using the uTYPE CDx Software Version 1.2 and IMGT Version 3.44.0.0.

The HLA-A*02:01 status of the clinical samples was determined using the [redacted] on the [redacted] instrument. This CE-marked [redacted] assay is not FDA cleared; however, One Lambda provided a summary of the validation studies performed to support use of this [redacted] assay as a comparator method.

The accuracy was determined by Positive Percent Agreement (PPA), Negative Percent Agreement (NPA) and Overall Percent Agreement (OPA) with the established UCLA panel reference typing results or to the (b) (4) typing results.

Results: The study correctly reported HLA-A*02:01 associated with G-Code (HLA-A*02:01:01G) for all 40 HLA-A*02:01 positive samples, including 35 heterozygous and 5 homozygous samples. The remaining 65 samples were correctly identified with the absence of the target allele, HLA-A*02:01.

Testing results are summarized in the table below:

	Sample Types		
	Patient samples	**Reference Samples**	**Total**
HLA-A*02:01:01 G Detected	22	18	40
HLA-A*02:01 Not Detected	11	54	65
Total	33	72	105
PPA	40/40 = 100%		
NPA (LB 95% CI)	65/65 = 100% (95.5%)		
OPA (LB 95% CI)	105/105 = 100% (97.2%)		

Conclusion: The accuracy testing results for the SeCore CDx HLA Sequencing System met all acceptance criteria: PPA should be greater than 0.95 with LB of one-sided 95% CI using 59 or more HLA-A*02:01 positive samples, or 100%-point estimate using less than 59 HLA-A*02:01 positive samples. NPA should be greater than 0.95 with LB of the one-sided 95% CI using 59 or more A*02:01 negative samples, or 100%-point estimate using less than 59 HLA-A*02:01 negative samples. OPA should be greater than 0.95 with LB of one-sided 95% confidence interval (CI).

c) Additional Accuracy Study for Expanded Exon Coverage

To evaluate the accuracy performance of the SeCore CDx HLA Sequencing System with the expanded exon coverage (exon 1 - 5), a total of 73 well characterized HLA-A samples were tested and results for all 73 samples were concordant with the established reference typing for HLA-A alleles.

2. Reproducibility and Repeatability Studies

a) SeCore HLA Sequencing System Precision Studies (Reproducibility and Repeatability)

A precision study was performed to evaluate possible sources of variation that may affect test results, such as site to site, day to day, operator to operator, instrument to instrument variations, and the assay's repeatability. One lot of each SeCore HLA sequencing kit and related GSSP kits was tested with four previously characterized DNA samples in triplicate by two operators at each of the three external sites per day over six non-consecutive days. Testing was performed with one 3500xL Dx Genetic Analyzer CS2 instrument per site. The total number of genotyping events for the 3 external sites combined was 432 (4 samples x 3 replicates x 2 operators x 3 sites x 6 days) for each of six HLA loci (A, B, C, DRB1, DQB1 and DPB1). For DRB locus, 10 samples were tested including 4 samples for DRB1, 3 samples for DRB3, 2 samples for DRB4 and 1 sample for DRB5, resulting a total of 1080 events (10 samples x3 replicates x 6 runs x 2 operators x 3 sites).

100% concordance was observed with the known genotypes for each locus for all samples. The ambiguous results for each sample are reproducible and the same ambiguous results are obtained per site, operator, run, and replicate for each sample. Signal intensity and Noise-to-Signal (N/S) background also met the expected values.

In conclusion, the reproducibility and repeatability performance met the acceptance criteria: concordance to known HLA genotyping results, Sequencing Kit Signal Intensity ≥ 300 Relative Fluorescence Units (RFU), GSSP Signal Intensity ≥ 100 RFU and N/S Background ≤ 8%.

b) Additional Reproducibility and Repeatability Studies

The study was performed to demonstrate that additional exon coverage of the SeCore CDx HLA Sequencing System for HLA-A Locus kit has no impact on the assay's reproducibility performance. One lot of SeCore CDx HLA-A locus sequencing kit was tested using four well-characterized UCLA samples in quadruplicate by two operators per day over four non-consecutive days, results in a total 128 typing results.

A complete (100%, 128/128) overall concordance with established reference results was obtained. The results demonstrated that SeCore CDx HLA-A locus sequencing kit with expanded exon coverage maintains expected device reproducibility performance

characteristics.

3. SeCore HLA Sequencing System Lot to Lot Reproducibility Studies

The lot-to-lot reproducibility was evaluated for the SeCore HLA sequencing kit and the instrument consumables. Two studies were conducted: Study 1 tested three sequencing kit lots with one instrument consumable lot and Study 2 tested three instrument consumables lots and one sequencing kit lot. Representative sequencing kits and corresponding GSSP kits were tested. For each study, the kits were run with three previously characterized DNA samples in five replicates per day over five non-consecutive days using one 3500xL Dx Genetic Analyzer CS2 instrument. The total number of genotyping events for each study was 225 (3 samples x 5 replicates x 5 days x 3 lots). 100% concordance was obtained for all testing. Lot to lot reproducibility performance met the reproducibility acceptance criteria.

4. SeCore HLA Sequencing System Sensitivity Studies: Limit of Detection (LoD)

A range of genomic DNA input concentrations that meet the assay performance were determined in the validation study. The study tested representative tests using (b) (4) UCLA reference DNA samples at (b) (4) different concentrations: (b) (4) ng/µL.

Testing for all samples at all DNA dilutions except (b) (4) ng/µL met acceptance criteria: Signal Intensity ≥ 300 RFU and N/S background ≤ 8%, and 100% concordant of typing results with known results.

Based on testing results, the optimal DNA concentration for the SeCore HLA Sequencing System was set as 15-30 ng/µL.

5. SeCore HLA Sequencing System Sample Preparation Study

Sample preparation methods were assessed to establish specifications of the assay input sample quality. The effects of Citrate and EDTA anticoagulants used during the sample collection were also evaluated. The study used three different genomic DNA isolation methods for DNA extraction from eighteen whole blood samples collected in ACD or EDTA anticoagulated tubes. The resultant DNA extracts were used in testing with representative sequencing kits .

All test results met the acceptance criteria: Signal Intensity ≥ 300 RFU and N/S background ≤ 8% and no discrepancies in typing results between replicates.

In conclusion, no statistically significant differences were found between the three DNA isolation methods based on the Signal Intensity, background data and typing results. DNA quality at 1.7-1.9 OD260/280 ratio is recommended for using with the SeCore® HLA Sequencing System. Blood samples must be collected in ACD or EDTA anticoagulated tubes.

6. SeCore HLA Sequencing System Analytical Specificity (Interfering Substance Studies)

The effect of potential interfering substances (interferents) on the SeCore HLA Sequencing System was evaluated. The study included interferents from commonly used anticoagulants appropriate for molecular testing, chemicals commonly used in DNA extraction, and common endogenous substances that may inhibit or reduce assay function by affecting PCR or sequencing reactions. Interferents were directly added to the purified DNA. (b) (4) previously characterized DNA samples were tested in (b) (4) with one lot of representative

SeCore HLA sequencing kits , and related GSSP kits .

The study determined the lowest concentration of an interferent where failure occurred and the highest concentration without assay inhibition. The interfering substances tested in the study and their inhibitory concentrations obtained are described in the table below:

Substance	Highest concentration without inhibition
SDS (w/v)	0.0050%
100% EtOH	200 mmol/L
Phenol (v/v)	0.0125%
Sucrose	100,000 µmol/L
EDTA	100 µmol/L
ACD (w/v)	0.10%
500x Cholesterol	50x
Bilirubin, conj.	10.7 µmol/L
Hemoglobin	0.0156 g/L
Hemolyzed Blood (w/v)	0.001%

7. SeCore HLA Sequencing System Comparison Studies

The comparison studies tested a total of 299 samples at three external sites to evaluate the equivalence between the SeCore HLA Sequencing System with uTYPE Dx v1.0 HLA Sequence Analysis Software and the predicate device, SSP UniTray with UniMatch Plus interpretation software.

Of the 299 samples tested, 11 discordant typing results were obtained either due to possible new alleles (8/11) or differences between the technologies (3/11).

The concordance rates were 100% for detection of HLA-A Locus and range between 97.3% and 100% for other Class I loci (B and C) and Class II loci (DRB1, DRB3/4/5, DQB1, and DPB1). The one-sided 95% lower confidence limits for the concordance rates of all loci exceed 95% after resolving the initial discordant typing results.

8. SeCore HLA Sequencing kits shelf life

The SeCore HLA Sequencing kits were evaluated for shelf-life stability, shipping, consumable stability and on-board stability. All previously established product storage, shipping, and shelf-life claims remain unchanged for the SeCore CDx HLA Sequencing System. The system's Shelf-life Claims are described in the table below:

Component Name	Operating Temperature	Storage Temperature	Shelf Life	Shipping Conditions
SeCore CDx HLA Sequencing Kit	Room Temperature	-30 C to -10 C	24 Months	Dry Ice
SeCore CDx HLA GSSP Kit	Room Temperature	-30 C to -10 C	Mix = 30 Months BDT = 24 Months PPT Buffer = 24 Months	Dry Ice

9. Other design verification studies for the SeCore HLA Sequencing System

Other design verification studies included: Reagent Guard banding, Amplification and Sequencing Primer concentration, Group Specific Sequencing Primer concentration,

Thermocycling parameters, Ethanol purification time and centrifugation speed and Sequencer parameters. All verification studies passed the established specifications.

N. Clinical Performance:

Clinical validity of the SeCore CDx HLA Sequencing System was demonstrated through the safety and efficacy data of IMCgp100 treatment versus investigator's choice in advanced Uveal Melanoma from the clinical trial, Study IMCgp100-202 (NCT03070392). This study evaluated the corresponding therapeutic product KIMMTRAK (tebentafusp-tebn) in patients with HLA-A*02:01. Study subjects were screened for HLA-A*02:01 status using the SeCore HLA sequencing system cleared under BK110038 .

A total of 378 HLA-A*02:01 positive patients ≥ 18 years of age with metastatic uveal melanoma were enrolled and randomized (2:1) to receive KIMMTRAK (N=252) or investigator's choice (N=126) of either pembrolizumab, ipilimumab, or dacarbazine. The KIMMTRAK was administered weekly by intravenous infusion at 20 mcg on day 1, 30 mcg on day 8, 68 mcg on day 15 and every subsequent week until disease progression or unacceptable toxicity. The main efficacy outcome measure was overall survival.

The study demonstrated statistically significant and clinically meaningful improvement in overall survival in patients who were randomized to receive KIMMTRAK compared to patients randomized to receive investigator's choice therapy. The KIMMTRAK treatment arm for 252 patients resulted in 87 deaths (34.5%) and 21.7 months (95% CI: 18.6, 28.6) of median survival duration, while the investigator's choice arm for 126 patients resulted in 63 deaths (50%) and 16 months (95% CI: 9.7, 18.4) of median survival duration. The most common treatment emergent adverse events (TEAEs ≥ 30%) were cytokine release syndrome, rash, pyrexia, pruritus, fatigue, nausea, chills, abdominal pain, edema, hypotension, dry skin, headache and vomiting. Further information about the KIMMTRAK clinical studies can be found in the drug's labeling.

For the SeCore HLA Sequencing System used to test patients in the clinical trial, different models of the genetic analyzer instrumentation ((b) (4) vs AB 3500xL/Dx) and uTYPE HLA Sequencing Analysis software version were used. Overall, the differences in instrumentation and software when compared to the SeCore CDx HLA Sequencing System are minor, and data outputs are equivalent between the two instruments. The controlling mechanism for the base calling and genotyping algorithms is the same between the two software versions. Therefore, FDA determined that bridging studies were not required.

O. Proposed Labeling:

Proposed labeling for the SeCore CDx HLA Sequencing System satisfies the requirements under 21 CFR part 809.10 and specifies the therapeutic product for which the device will be used. The proposed labeling also satisfies the requirements in 21 CFR 801.109.

P. Software:

The uTYPE CDx HLA Sequence Analysis Software v1.2 was reviewed according to the FDA Guidance document, "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices," issued May 11, 2005. One Lambda, Inc provided information on software updates and changes as compared to the software cleared in BK110038. The main change is that the uTYPE CDx HLA Sequence Analysis Software v1.2

operates on Windows 10. The sponsor performed validation and verification testing on this software and provided hazard analysis information. The software documentation provided in support of the SeCore CDx HLA Sequencing System is acceptable.

Table 2. uType CDx HLA Sequencing Analysis Software Summary of Documentation

Level of Concern: **Moderate**			
	Present	**Absent**	**Adequate (Yes/No/ Assessment Incomplete)**
Software description:	x		Yes
Device Hazard Analysis:	x		Yes
Software Requirements Specifications:	x		Yes
Architecture Design Chart:	x		Yes
Design Specifications:	x		Yes
Traceability Analysis/Matrix:	x		Yes
Software Development Environment:	x		Yes
Verification & Validation Testing:	x		Yes
Revision level history:	x		Yes
Unresolved anomalies:	x		Yes
Cybersecurity/Interoperability	x		Yes

Q. Electromagnetic Compatibility and Electrical, Mechanical and Thermal Safety

The EMC and Wireless Coexistence of 3500 Dx/3500 xL Dx Genetic Analyzer CS2 were evaluated in BK110038. The instruments meet the FDA recognized consensus standard IEC 60601-1-1:2007, EMC for Medical electrical equipment-part 1-2: General requirements for basic safety and essential performance-Collateral standard: Electromagnetic compatibility-requirements and tests and Agency Guidance for Wireless coexistence. The instrument also meets the electrical safety standards IEC- 61010-1 Safety requirements for electrical equipment for measurement, control, and laboratory use.

R. Potential Risks and Mitigations:

The identified risks and mitigation measures associated with the device type are summarized in Table 3.

Table 3. Human Leukocyte Antigen Typing Companion Diagnostic Test Risks and Mitigation Measures

Identified Risk	**Mitigation Measures**
Inaccurate test results (false positive or false negative results) can result in adverse health consequences	General controls and special controls (1), (2), (3), (4)
Failure of software to correctly interpret test results can result in adverse health consequences	General controls and special controls (2)(viii)

S. Special Controls

The special controls for this device are:

(1) The intended use of the device must specify the target HLA allele(s) or antigen(s), the patient population(s), and the corresponding therapeutic product(s).

(2) Design verification and validation must include:

(i) Detailed documentation of an analytical accuracy study that uses well-characterized samples including clinical samples from intended use population(s) focusing on the target allele(s) needed for patient selection;

(ii) Detailed documentation of precision studies (repeatability, reproducibility) that evaluate possible sources of variation that may affect test results;

(iii) Detailed documentation of a study determining range of input sample concentrations that meet performance specifications;

(iv) Detailed description of the ambiguity resolution method, if applicable;

(v) For a sequencing-based assay, documentation of coverage and predefined coverage threshold of target genomic regions, pertinent variant types, and sequence contexts;

(vi) For multiplex assays, documentation of a risk assessment and design specifications that are in place to prevent incorrect reactivity assignment;

(vii) Description of a plan on how to ensure the performance of the device does not change when new HLA alleles are identified, and/or when reactivity assignments are changed; and

(viii) Detailed description of device software including standalone software, or software and bioinformatics analysis pipeline, if applicable, incorporated in the instruments, and documentation of software including the level of concern and associated risks, software requirement specifications, software design specifications (e.g., algorithms, alarms and device limitations), hazard analysis, traceability matrix, verification and validation testing, unresolved anomalies, hardware requirements, and effective cybersecurity management.

(3) Clinical validity data demonstrating the following, as applicable:

(i) Which patients identified by the HLA CDx test are most likely to benefit from the corresponding therapeutic product;

(ii) Which patients identified by the HLA CDx test are likely to be at increased risk for serious adverse reactions as a result of treatment with the corresponding therapeutic product.

Data may include summary reports from clinical trials, comparison studies using clinical samples, or through an alternative approach determined to be appropriate by FDA.

(4) If the HLA test used in the clinical trials is different from the HLA CDx test in the premarket notification submission, the submission must include results of a bridging study, or an alternative approach determined to be appropriate by FDA.

T. Benefit/Risk Assessment:

Summary of the Assessment of Benefit

Metastatic uveal melanoma is a life-threatening disease with a dismal prognosis and there are no effective treatments that improve survival. KIMMTRAK is a bispecific gp100 peptide-HLA-directed CD3 T cell engager for HLA-A*02:01-positive adult patients with

unresectable or metastatic uveal melanoma. The probable benefits of the SeCore CDx HLA Sequencing System were demonstrated through screening patients with metastatic uveal melanoma for HLA-A*02:01 in Study IMCgp100-202.

Study IMCgp100-202 was a randomized, open-label, multicenter clinical trial of 252 adult patients with metastatic uveal melanoma and HLA-A*02:01 allele positive who were assigned to receive KIMMTRAK. The clinical trial results show that for HLA-A*02:01-positive adult patients with unresectable or metastatic uveal melanoma, treatment with KIMMTRAK yielded a statistically significant and clinically meaningful improvement in overall survival. Given the available information, the data supports the conclusion that the SeCore CDx HLA Sequencing System has probable benefit in selecting HLA-A*02:01 allele positive patients with unresectable and metastatic uveal melanoma for treatment with KIMMTRAK.

Summary of the Assessment of Risks
There is potential risk associated with the use of this device, mainly due to 1) inaccurate test results (false positive or false negative results) that can result in adverse health consequences and 2) failure of software to correctly interpret test results that can result in adverse health consequences.

The risks associated with patients who are determined to be false positive by the CDx may be exposed to the drug treatment that is not beneficial and may lead to adverse events or delayed access to other available treatments. The risks associated with patients who are determined to be a false negative for A*02:01 by the HLA CDx may prevent the patients from accessing a beneficial therapeutic regimen. The risks of erroneous results are partially mitigated by the analytical performance of the device. The risk analysis review reveals no extraordinary hazards. Assuming a false positive result and subsequent exposure to the drug, the patient may experience adverse reactions associated with the drug. Based on data from the clinical trial, the most common adverse reactions (≥30%) were cytokine release syndrome, rash, pyrexia, pruritus, fatigue, nausea, chills, abdominal pain, edema, hypotension, dry skin, headache, and vomiting. The most common laboratory abnormalities (≥50%) were decreased lymphocyte count, increased creatinine, increased glucose, increased aspartate aminotransferase, increased alanine aminotransferase, decreased hemoglobin, and decreased phosphate.

The likelihood of false results was assessed by an analytical accuracy study that performed specifically to evaluate the concordance between the SeCore CDx HLA Sequencing System and the known results from well-characterized UCLA reference samples (72) and a validated (b) (4) assay used to characterize the patient samples (33). Out of 105 samples tested, the PPA was 100% (40/40) and the NPA was 100% (65/65). The analytical performance of the device mitigates the risks associated with the device.

Summary of the Assessment of Benefit-Risk
In summary, the probable benefits of the SeCore CDx HLA Sequencing System outweigh the probable risks considering the listed special controls and general controls.

U. Conclusion:

The De Novo request for SeCore CDx HLA Sequencing System is granted, and the device is

classified under the following:

Identification: A human leukocyte antigen (HLA) typing companion diagnostic (CDx) test is a prescription genotyping or phenotyping in vitro diagnostic product intended for use as an aid in identifying patients who have specific HLA allele(s) or express specific HLA antigen(s) and may benefit from treatment with a corresponding therapeutic product or are likely to be at increased risk for serious adverse reactions as a result of treatment with a corresponding therapeutic product.

Product Code: QUK

Device Type: Human Leukocyte Antigen Typing Companion Diagnostic Test

Class: II (Special Controls)

Regulation: 21 CFR 866.5960