DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

Immudex Aps
Liselotte Brix
Chief Operating Officer
Fruebjergvej 3
Copenhagen, DK 2100

March 2, 2017

Re: K153538
Trade/Device Name: Dextramer CMV Kit
Regulation Number: 21 CFR 864.5220
Regulation Name: Automated differential cell counter
Regulatory Class: II
Product Code: GKZ
Dated: February 22, 2017
Received: February 24, 2017

Dear Dr. Brix:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely,

Kelly Oliner -S

FOR
Leonthena R. Carrington, MS, MBA, MT (ASCP)
Director
Division of Immunology and Hematology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K153538

Device Name
Dextramer® CMV Kit

Indications for Use *(Describe)*

Dextramer® CMV Kit is a semi-quantitative assay intended for the identification and enumeration of cytomegalovirus (CMV)-specific CD8+ T cells in anticoagulated (Na Heparin) whole blood specimens by flow cytometry.

Dextramer® CMV Kit is indicated for assessment of CMV-specific immune status and risk of CMV reactivation in adult human stem cell transplant patients following immunosuppression and used in conjunction with other laboratory and clinical findings.

The kit cannot be used to measure CMV infection or disease.

The kit is limited to individuals with the following HLA types: A*0101, A*0201, B*0702, B*0801, B*3501.

Special instrument requirements:

FACSCanto II flow cytometer (Becton Dickinson).

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

D. 510(k) Summary

1. Applicant:

Immudex ApS
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DK-2100 København Ø
DENMARK

2. Contact Person:

Liselotte Brix
Phone: +45 39179772 / +45 40910121
E-mail: lb@immudex.com

3. Summary Preparation Date:

February 28, 2017

4. Device Name and Classification:

Trade Name (proprietary name): Dextramer® CMV Kit

Common Name (usual name): None

Classification: Class II

Product code: GKZ, Counter, differential cell

Panel: Hematology

Regulation section: 21 CFR § 864.5220, Automated differential cell counter

5. Substantial Equivalence Information:

Predicate name(s) and predicate 510(k) number(s):

Predicate Device Name(s)	Manufacturer	510(k) number(s)
iTAg MHC Tetramer CMV Kit	Beckman Coulter	K051122

Comparison with Predicate:

	Device	**Predicate**
Name	Dextramer® CMV Kit	iTAg MHC Tetramer CMV Kit
Intended Use	Identification and enumeration of cytomegalovirus (CMV)-specific CD8+ T cells in anticoagulated venous whole blood in adult human stem cell transplant patients by flow cytometry.	Same
Kit components & Accessory Reagents	Anti-CD8/FITC Anti-CD4/PE Anti-CD3/PerCP Dextramer CMV Set of 5 individual MHC Dextramers labeled with PE.	Anti-CD8/FITC Anti-CD4/PE Anti-CD3/PC5 CMV Tetramer Set of 5 individual MHC Tetramers labeled with PE.
	FACS Lysing Solution TruCount	iTAg Lyse Reagent Flow-Count™ Fluorospheres
Instrument	Flow cytometer	Same
Sample type	Whole blood	Same
Anti-coagulant	Heparin	EDTA
Cell type detected	CMV-specific CD8 + T cells Human T lymphocytes (CD3+), suppressor/cytotoxic (CD3+CD8+) T-lymphocyte subsets, and helper/inducer (CD3+CD4+) T-lymphocyte subsets	Same Same
Detection method	Multimers of MHC molecules displaying CMV-specific peptide Antibodies bound to CD3, CD4 and CD8	Same Same
MHC Multimer backbone	Dextran	Streptavidin
HLA types (peptide sequence)	HLA-A*0101 (VTEHDTLLY) HLA-A*0201 (NLVPMVATV) HLA-B*0702 (TPRVTGGGAM)	Same Same Same

	HLA-B*0801 (ELRRKMMYM) HLA-B*3501 (IPSINVHHY) Negative control	Same Same Similar
Controls	Negative control above Control cells	Same IMMUNO-TROL Control Cells

6. Device Description:

The Dextramer® CMV Kit comprises 5 CMV Dextramers, Negative control as well as 3 antibodies recognizing CD3, CD4, and CD8:

Dextramer reagents

HLA-A*0101 / VTEHDTLLY / PE	25 tests/0.25 ml	Cat. No. CA2131-PE
HLA-A*0201 / NLVPMVATV / PE	50 tests/0.50 ml	Cat. No. CB2132-PE
HLA-B*0702 / TPRVTGGGAM / PE	25 tests/0.25 ml	Cat. No. CH2136-PE
HLA-B*0801 / ELRRKMMYM / PE	25 tests/0.25 ml	Cat. No. CI2137-PE
HLA-B*3501 / IPSINVHHY / PE	25 tests/0.25 ml	Cat. No. CK2138-PE
Negative control / PE	150 tests/1.50 ml	Cat. No. CI3233-PE

Antibodies

Anti-CD8/FITC	2 ml	Cat. No. A-CD8-FITC
Anti-CD3/PerCP	2 ml	Cat. No. A-CD3-PerCP
Anti-CD4/PE	2 ml	Cat. No. A-CD4-PE

The Dextramer® CMV Kit accurately enumerates CMV-specific T cells in blood samples. This involves a two-step procedure followed by analysis by flow cytometry:

- Step 1: Determination of the percentage of CMV-specific $CD3^+CD8^+$ T cells in the sample (Tube A)

- Step 2: Determination of the absolute number of $CD3^+CD8^+$ T-cells in the sample (Tube C)

The absolute number of CMV-specific $CD3^+CD8^+$ T cells/μl blood is then determined.

7. Intended use(s):

Dextramer® CMV Kit is a semi-quantitative assay intended for the identification and enumeration of cytomegalovirus (CMV)-specific CD8+ T cells in anticoagulated (Na Heparin) whole blood specimens by flow cytometry.

Dextramer® CMV Kit is indicated for assessment of CMV-specific immune status and risk of CMV reactivation in adult human stem cell transplant patients following immunosuppression and used in conjunction with other laboratory and clinical findings.

The kit cannot be used to measure CMV infection or disease.

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Special instrument requirements:

FACSCanto II flow cytometer (Becton Dickinson).

8. Indication(s) for use:

Dextramer® CMV Kit is a semi-quantitative assay intended for the identification and enumeration of cytomegalovirus (CMV)-specific CD8+ T cells in anticoagulated (Na Heparin) whole blood specimens by flow cytometry.

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9. Performance Characteristics:

Non-clinical studies

Analytical sensitivity
The functional assay sensitivity is 1 cells/μl as determined by the lowest concentration of cells (cells/μl) that can be determined with a CV% below 20%.

Analytical specificity
100% (35/35) routine blood specimens from CMV seronegative stem cell transplant recipients showed 0.00 – 0.06 cells/μl and thus below the functional assay sensitivity of 1 cell/μl.

Inter-lab reproducibility
The inter-lab reproducibility CV ranged between 6% and 18%.

Intra-lab reproducibility
The intra-lab reproducibility CV ranged between 5% and 14%.

Linearity – Recovery
The Dextramer CMV assay showed linearity in the range of 1-107 CMV-specific T cells/μl with a slope ranging from 0.98-1.08. Recovery was 73-134%.

Interference
There was no significant interference from the tested cell populations equivalent to 2x normal level for monocytes, equivalent to 3x normal level for granulocytes, equivalent to 3x normal level for platelets, and equivalent to 2x normal level for red blood cells.

Cross-reaction
No significant cross-reaction with allele mismatching CMV Dextramer reagents. All results from analysis of 4 blood samples with CMV-specific T cells with HLA mis-matched CMV Dextramer were within 0.00 – 0.11 cells/μl and thus below the functional assay sensitivity of 1 cell/μl.

Comparison with predicate
Analysis of blood specimens from stem cell transplant recipients representing 5 alleles for a total of 117 MHC multimer measurements using iTAg MHC Tetramer CMV Kit and Dextramer CMV Kit showed substantial equivalence based on

Deming regression for enumeration of the subset of CD8+ T-cells and CMV-specific T-cells.

	Slope	95% CI	Intercept	95% CI	r
CD8+ T-cells	0.984	0.92 to 1.05	-0.4406	-8.47 to 7.59	0.905
CMV-specific T-cells	1.010	0.89 to 1.13	0.39	0.09 to 0.69	0.952

Clinical studies

A prospective study with 120 allogeneic SCT patients followed for up to one year for recurrence of CMV infection and determination of numbers of CMV-specific CD8+ T cells using the CMV Dextramer Kit. Dextramer analysis were performed pre-transplant at day 30, 100 and 360 and included the alleles HLA-A*0101, A*0201, B*0702, B*0801 and B*3501.

68 patients were CMV seropositive (recipient and/or donor) prior to transplantation of which 34 patients developed antigenimia.

2x2 tables are provided for each time point posttransplant showing correlation of CMV-specific T-cell and occurance of CMV antigenimia and used for calculation of the risk of CMV infection/antigenimia after Day 100

Risk of developing CMV antigenemia after Day 100

Risk is defined as risk of patients with less than 7 cells/ul of developing CMV infection post Day 100 compared to patients with more than 7 cells/ul.

Day 100	Development of antigenemia (post Day 100)		
# CMV+ T cells	Yes	No	Total
<7 cells/ul	9	1	10
≥7 cells/ul	5	14	19
Total	14	15	29
Risk	3.4 (95% CI: 1.57 – 7.46)		

Dextramer results were evaluated at Day 30, 100, and Day 365 post-transplant. Only day 100 shows significant association between CMV-specific CD8+ T cells status (<7 cells/μL or ≥ 7 cells/μL) and development of antigenemia. Results summarized in the table above show that the relative risk in developing antigenemia is 3.4 (95% CI: 1.57 – 7.46) for patients with < 7 cells/μL CMV-specific CD8+ T cells determined by the Dextramer CMV kit, as compared to patients with ≥ 7 cells/μL CMV-specific CD8+ T cells.

10. Conclusion:

The Dextramer® CMV Kit has similar intended use and indications as the predicates iTAg MHC Tetramer CMV Kit.

The performance of the Dextramer CMV Kit is substantially equivalent to the performances of iTAg MHC Tetramer CMV Kit.

Clinical data support the use of Dextramer® CMV Kit for assessment of CMV-specific immune status and risk of CMV reactivation in adult human stem cell transplant patients following immunosuppression and for use in conjunction with other laboratory and clinical findings.