

JUN 21 1999

510(k) Summary

K991454

Submitter: DAKO Corporation
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Contact: Gretchen M. Murray, Ph.D.

Date Summary Prepared: April 19, 1999

Device Name: DAKO® IgG1/FITC, Clone DAK-GO1, Code No. X0927; IgG1/RPE, Clone DAK-GO1 Code No. X0928; IgG1/RPE-CY5, Clone DAK-GO1, Code No. X0955

Device Classification: Class II according to 21 CFR 864.5220, on the basis that monoclonal antibodies are accessories for automated differential cell counters.

Panel: The device classification is under the Hematology and Pathology Devices panel, Division of Clinical Laboratory Devices.

Predicate Device: Gentrak Genclone mouse IgG₁, 679.1MC

Device Monoclonal Mouse IgG₁, DAK-GO1 FITC, RPE or RPE-CY5 conjugated are directed against *Aspergillus niger* glucose oxidase, an enzyme that is neither present nor inducible in mammalian tissues. Purified monoclonal mouse IgG1 is produced in tissue culture, dialyzed and conjugated with Fluorescein (FITC), R-phycoerythrin (RPE), or R-phycoerythrin (RPE) covalently coupled to cyanin 5 (Cy5). FITC CONJUGATED: One ml (1.0 ml) containing the conjugated antibody is supplied in 0.05M Tris-HCl buffer, pH 7.2, 15mM NaN₃, stabilized with 1% carrier protein. RPE and RPE-Cy5 CONJUGATED: One ml (1.0 ml) containing the conjugated antibody is supplied in 0.05M Tris-HCl buffer, pH 7.2, 15mM NaN₃, 0.1M NaCl stabilized with 1% carrier protein

Intended Use: For *In Vitro* Diagnostic Use

Monoclonal Mouse IgG₁, DAK-GO1 FITC, RPE or RPE-CY5 conjugated have been developed for use in flow cytometry for the peripheral blood. These reagents are intended to be used as negative control reagents for FITC, RPE or RPE-CY5 conjugated monoclonal antibodies of the IgG₁ heavy chain isotype in preparations of normal whole peripheral blood in routine immunophenotyping of lymphocytes.

Comparison of
Technological
Characteristics

Reproducibility of ten replicates from peripheral blood of three donors were run on two flow cytometers from different manufacturers. Normal peripheral blood samples were used for measuring lymphocytes for levels of non-specificity with Mouse IgG1, DAK-GO1 negative control reagents. Values are expressed as a percent of the total lymphocyte count.

FACScan	Mean % IgG ₁ /FITC+	±1 SD	%CV	n
Donor 1	0.80	0.25	0.31	10
Donor 2	0.86	0.35	0.40	10
Donor 3	0.61	0.23	0.37	10

Profile II	Mean % IgG ₁ /FITC+	±1 SD	%CV	n
Donor 1	1.30	0.62	0.49	10
Donor 2	1.06	0.32	0.30	10
Donor 3	1.14	0.13	0.12	10

FACScan	Mean % IgG ₁ /RPE+	±1 SD	%CV	n
Donor 1	0.70	0.27	0.38	10
Donor 2	0.67	0.30	0.45	10
Donor 3	0.76	0.27	0.36	10

Profile II	Mean % IgG ₁ /RPE+	±1 SD	%CV	n
Donor 1	0.36	0.12	0.35	10
Donor 2	0.33	0.17	0.52	10
Donor 3	0.38	0.07	0.18	10

The reproducibility results indicate that there is little variability among replicate samples for the measurement of non-specificity of percent positive lymphocytes. There is some variability between flow cytometers as indicated by the differences in percentages of lymphocytes detected. No reproducibility testing was performed for IgG₁/RPE-CY5. However, since the reagent is the same IgG₁ antibody as the FITC conjugate and the RPE conjugate except for being conjugated with a different fluorochrome, it is expected that IgG₁/RPE-Cy5, Code No. X0955 has the same consistent reproducibility as IgG₁/FITC, Code No. X0927 and IgG₁/RPE, Code No. X0928 when tested on lymphocytes.

Specificity of Monoclonal Mouse IgG₁, DAK-GO1 FITC, RPE and RPE-CY5 conjugated has been verified by tests performed on five apparently healthy adult donors of various races at DAKO Corporation. Cell populations tested were RBC's, granulocytes, monocytes, lymphocytes and platelets. The results indicate that there is no specific antibody binding of Monoclonal Mouse IgG₁, DAK-GO1 FITC and RPE conjugated with any of the cell populations. However, the RPE-CY5 conjugate did have a significant amount of binding with monocytes (3.22%). This nonspecific binding can be excluded from the lymphocyte analysis region with proper gating on the lymphocytes.

DAKO Mouse IgG₁/FITC, DAK-GO1 Specificity

	%Positive Red Blood Cells	%Positive Granulocytes	% Positive Monocytes	% Positive Lymphocytes	% Positive Platelets
Average (n=5) (range)	0.02 (0.0-0.1)	0.74 (0.1-1.9)	0.76 (0.2-1.5)	0.22 (0.0-0.8)	0.04 (0.0-0.1)

DAKO Mouse IgG₁/RPE, DAK-GO1 Specificity

	%Positive Red Blood Cells	% Positive Granulocytes	% Positive Monocytes	% Positive Lymphocytes	% Positive Platelets
Average (n=5) (range)	0.00 (0.0-0.0)	0.08 (0.0-0.01)	0.84 (0.4-2.0)	0.04 (0.0-0.1)	0.22 (0.0-0.7)

DAKO Mouse IgG₁/RPE-CY5, DAK-GO1 Specificity

	%Positive Red Blood Cells	% Positive Granulocytes	% Positive Monocytes	% Positive Lymphocytes	% Positive Platelets
Average (n=5) (range)	0.02 (0.0-0.1)	0.16 (0.0-0.3)	3.22 (0.0-11.9)	0.12 (0.0-0.3)	0.10 (0.0-0.4)

Correlations of Mouse IgG₁/FITC, DAK-GO1 and Mouse IgG₁/RPE, DAK-GO1 to predicate reagents, Mouse IgG₁/FITC, 679.1MC and Mouse IgG₁/RPE, 679.1MC were determined by testing duplicate samples with each reagent on peripheral blood lymphocytes on normal, apparently healthy individuals at one laboratory. Linear regression analysis of the data gave the following equations and Pearson correlations.

$$Y(\text{DAKO IgG1/FITC+ Lymphocytes}) = .28 + 1.39X(\text{Centrak IgG1/FITC + Lymphocytes})$$

$$R^2 = .4581$$

$$n = 36$$

$$Y(\text{DAKO IgG1/RPE+ Lymphocytes}) = .05 + .87X(\text{Centrak IgG1/RPE + Lymphocytes})$$

$$R^2 = .4429$$

$$n = 36$$

Normal levels of negative events were measured for each reagent at three geographically separate laboratories. The sample size(s) was 150 apparently healthy individuals. Normal means and ranges for each reagent were x, y, and z respectively. The regression analysis indicated that there was not a 1:1 linear correlation of the Mouse IgG₁/FITC, DAK-GO1 reagent and Mouse IgG₁/FITC, 679.1MC nor of Mouse IgG₁/RPE, DAK-GO1 reagent and Mouse IgG₁/RPE, 679.1MC. As expected with negative control reagents, the values are highly variable and less than one. This produced R-values that are more indicative of a random sample rather than a linear model. Linear regression analysis of a data set measuring negative events would be expected to show no correlation.

Linearity testing using human cell lines was *not* performed. There would be no specificity or sensitivity detected as the antibody is not directed against a human antigen.

Substantial Equivalence Comparison of DAKO's
 Mouse IgG₁, DAK-GO1 to Gentrak Genclone Mouse IgG₁, 679.1MC

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<u>Attribute</u>	<u>DAKO</u>	<u>Gentrak Genclone</u>
Clone:	Mouse IgG ₁ , DAK-GO1	Mouse IgG ₁ , 679.1MC
Epitope	Glucose oxidase from <i>Aspergillus niger</i>	Succinyl histamine bovine serum albumin (SH-BSA)
Intended Use	Negative control reagents for FITC, RPE or RPE-CY5 conjugated monoclonal antibodies of the IgG ₁ heavy chain isotype in preparations of normal whole peripheral blood by flow cytometric methods.	Negative control reagents for FITC, or RPE conjugated monoclonal antibodies of the IgG ₁ heavy chain isotype in preparations of normal whole peripheral blood by flow cytometric methods.
Clinical Utility	Use with monoclonal antibody test reagents of the IgG ₁ immunoglobulin isotype in flow cytometric procedures performed on normal donors.	Use with monoclonal antibody test reagents of the IgG ₁ immunoglobulin isotype in flow cytometric procedures performed on normal donors.
Stability	Mouse IgG ₁ /FITC - 3 years: Mouse IgG ₁ /RPE - 2 years: Mouse IgG ₁ /RPE-CY5 - 2 years: from time of manufacture.	2 years from time of manufacture.
Specificity	No specific reaction to lymphocytes, monocytes, granulocytes, platelets or red blood cells.	No specific reaction to lymphocytes, monocytes, granulocytes or red blood cells.
Storage	2-8°C, in the dark	2-8°C

**Testing Results for DAKO Mouse IgG₁/FITC/RPE/CY5, DAK-GO1 and
Gentrak Mouse IgG₁/FITC/RPE, 679.1MC**

	DAK-GO1/ FITC	679.1MC/ FITC	DAK-GO1/ RPE	679.1MC/ RPE	DAK-GO1/ RPE-CY5
Percent Positive Mouse IgG₁ Lymphocytes Mean (n = 153 for DAKO) (n = 36 for Gentrak)	0.59%	0.16%	0.24%	0.13%	1.59%
95.0% Range Mouse IgG₁ Positive Lymphocytes (n = 153 for DAKO) (n = 36 for Gentrak)	0-5.34%	0-0.3%	0-1.28%	0-0.4%	0.06-3.06%
% CV (n = 153 for DAKO) (n = 36 for Gentrak)	150.89%	146.67%	93.81%	84.93%	88.98%
Percent Positive Mouse IgG₁ Lymphocytes (by laboratory site) Site 1(n=53) Site 2(n=50) Site 3(n=50 for DAKO) (n=36 for Gentrak)	0.79% 0.47% 0.49%	0.16%	0.35% 0.20% 0.16%	0.13%	3.6% 0.53% 0.64%
95.0% Range (by laboratory site) Site 1(n=53) Site 2(n=50) Site 3(n=50 for DAKO) (n=36 for Gentrak)	0.06-5.34% 0-1.65% 0.1-1.5%	0-0.3%	0.08-1.28% 0-0.65% 0-0.5%	0-0.4%	0.34-3.06% 0.06-1.87% 0.1-2.6%
% CV (by laboratory site) Site 1(n=53) Site 2(n=50) Site 3(n=50 for DAKO) (n=36 for Gentrak)	174.15% 86.50% 90.01%	146.67%	79.80% 94.74% 80.85%	84.93%	74.59% 85.13% 173.63%
Mean Channel Fluorescence (by laboratory site) Mean Site 1(n=53) Site 2(n=50) Site 3(n=50 for DAKO) (n=36 for Gentrak)	30.52 172.79 1.57	3.07	81.23 169.00 1.99	2.19	82.15 398.90 1.56
95.0% Range (by laboratory site) Site 1(n=53) Site 2(n=50) Site 3(n=50 for DAKO) (n=36 for Gentrak)	16.23 - 116.63 0 - 642.69 0.87 - 3.22	0 - 16.15	20.13 - 307.12 0 - 888.83 0 - 7.146	0 - 12.48	28.23 - 205.5 49.7 - 2111.49 0.72 - 3.70
% CV (by laboratory site) Site 1(n=53) Site 2(n=50) Site 3(n=50 for DAKO) (n=36 for Gentrak)	71.94% 119.30% 46.46%	151.14%	114.43% 150.28% 102.09%	153.47%	79.82% 154.56% 54.25%

**Testing Results for DAKO Mouse IgG₁/FITC, DAK-GO1 versus
Gentrak Mouse IgG₁/FITC, 679.1MC**

	DAK-GO1/ FITC	679.1MC/ FITC
Percent Positive Mouse IgG₁ Lymphocytes Mean (n = 36)	0.50%	0.16%
95.0% Range Mouse IgG ₁ Positive Lymphocytes (n = 36)	0.1-1.4%	0-0.3%
% CV (n = 36)	95.62%	146.67%
Mean Channel Fluorescence Mean (n = 36)	1.51	3.07
95.0% Range (by laboratory site) (n = 36)	0.87-3.12	0 - 16.15
% CV (by laboratory site) (n = 36)	41.88%	151.14%

**Testing Results for DAKO Mouse IgG₁/RPE, DAK-GO1 versus
Gentrak Mouse IgG₁/RPE, 679.1MC**

	DAK-GO1/ RPE	679.1MC/ RPE
Percent Positive Mouse IgG₁ Lymphocytes Mean (n = 36)	0.16%	0.13%
95.0% Range Mouse IgG ₁ Positive Lymphocytes (n = 36)	0-0.5%	0-0.4%
% CV (n = 36)	88.13%	84.93%
Mean Channel Fluorescence Mean (n = 36)	1.77	2.19
95.0% Range (by laboratory site) (n = 36)	0-6.19	0-12.48
% CV (by laboratory site) (n = 36)	98.97%	153.47%



DEPARTMENT OF HEALTH & HUMAN SERVICES

JUN 21 1999

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Gretchen M. Murray, Ph.D.
Regulatory Affairs Manager
DAKO Corporation
6392 Via Real
Carpinteria, California 93013

Re: K991454
Trade Name: Monoclonal Mouse IgG₁ Clone DAK-GO1, FITC, RPE or RPE-CY5
Conjugated
Regulatory Class: II
Product Code: GKZ
Dated: April 22, 1999
Received: April 26, 1999

Dear Dr. Murray:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we 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). 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.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

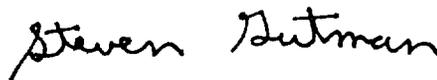
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Under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88), this device may require a CLIA complexity categorization. To determine if it does, you should contact the Centers for Disease Control and Prevention (CDC) at (770) 488-7655.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification"(21 CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597, or at its internet address "<http://www.fda.gov/cdrh/dsma/dsmamain.html>".

Sincerely yours,

A handwritten signature in black ink that reads "Steven Gutman". The signature is written in a cursive style with a large initial 'S'.

Steven I. Gutman, M.D, M.B.A.
Director
Division of Clinical
Laboratory Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

510(k) Number (if known): K991454

Device Name: Monoclonal Mouse IgG₁ Clone DAK-GO1, FITC Conjugated
Monoclonal Mouse IgG₁ Clone DAK-GO1, RPE Conjugated
Monoclonal Mouse IgG₁ Clone DAK-GO1, RPE-CY5 Conjugated

Indications For Use:

Mouse IgG₁, clone DAK-GO1 Negative Control Reagents are fluorescent conjugated (fluorescein isothiocyanate isomer 1 (FITC), R-Phycoerythrin (RPE), or R-Phycoerythrin-Cyanin 5 (RPE-CY5)) monoclonal antibodies that have been developed for use as negative control reagents for FITC, RPE or RPE-CY5 conjugated monoclonal antibodies of the IgG₁ heavy chain isotype in preparations of normal whole peripheral blood by flow cytometric methods. Negative control reagents are one component of the suggested controls for monoclonal antibody (MAb) combinations for routine immunophenotyping of lymphocytes in peripheral blood.

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)



(Division Sign-Off)

Division of Clinical Laboratory Devices

510(k) Number K991454

Prescription Use
(Per 21 CFR 801.109)

OR

Over-The-Counter Use
(Per 21 CFR 801.110)

IVD Use
(Per 21 CFR 801.119)

(Optional Format 1-2-96)