



August 23, 2018

Biokit, S.A.  
Joan Guixer  
QA & RA Director  
Can Male S/N  
Llica d'Amunt, 08186  
Barcelona, Spain

Re: K181333

Trade/Device Name: ADVIA Centaur Herpes-1 IgG  
Regulation Number: 21 CFR 866.3305  
Regulation Name: Herpes simplex virus serological assays  
Regulatory Class: Class II  
Product Code: MXJ  
Dated: May 17, 2018  
Received: May 25, 2018

Dear Joan Guixer:

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. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm> identifies combination product submissions. 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 Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see <https://www.fda.gov/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm>); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 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 comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (<https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/>) and CDRH Learn (<http://www.fda.gov/Training/CDRHLearn>). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (<http://www.fda.gov/DICE>) for more information or contact DICE by email ([DICE@fda.hhs.gov](mailto:DICE@fda.hhs.gov)) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

**Steven R. Gitterman -S** for

Uwe Scherf, Ph.D.  
Director  
Division of Microbiology Devices  
Office of In Vitro Diagnostics  
and Radiological Health  
Center for Devices and Radiological Health

Enclosure

## Indications for Use

510(k) Number (if known)  
k181333

Device Name  
ADVIA Centaur Herpes-1 IgG

### Indications for Use (Describe)

The ADVIA Centaur® Herpes-1 IgG (HSV1) assay is for in vitro diagnostic use in the qualitative determination of IgG antibodies to herpes simplex virus type 1 (HSV-1) in human serum and plasma (EDTA and lithium heparin) using the ADVIA Centaur systems. The test is indicated for testing sexually active adults or expectant mothers for aiding in the presumptive diagnosis of HSV infection. The predictive value of a positive or negative result depends on the prevalence of HSV-1 infection in the population and the pre-test likelihood of HSV-1 infection.

The test is not FDA cleared for screening blood or plasma donors. The performance of this assay has not been established for immunocompromised patients, pediatric patients or matrices other than human serum and plasma (EDTA and lithium heparin).

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.

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## 510(K) SUMMARY

This 510(k) Summary of Safety and Effectiveness is being submitted in accordance with the requirements of the Safe Medical Device Act of 1990 and 21 CFR 807.92.

<b>1. Submitter's Information</b>	Biokit, S.A. Can Malé S/N Lliçà d'Amunt 08186 Barcelona (Spain)	
<b>2. Contact Person</b>	Joan Guixer, QA & RA Director Phone: +34 93 860 90 00 / +34 657 88 33 47 Email: jguixer@biokit.com	
<b>3. Preparation Date</b>	May 17 <sup>th</sup> , 2018	
<b>4. Device Trade Name</b>	ADVIA Centaur Herpes-1 IgG	
<b>5. Regulatory Information</b>	Regulation Number	21 CFR 866.3305
	Regulation Description	Herpes simplex virus serological assays.
	Classification	Class II Special Controls
	Product Code	MXJ
	Classification Panel	Microbiology
<b>6. Predicate Device</b>	K000238 (Focus HerpeSelect 1 and 2 Immunoblot IgG)	

<b>7. Indications for Use / Intended Use</b>	The ADVIA Centaur Herpes-1 IgG (HSV1) assay is for <i>in vitro</i> diagnostic use in the qualitative determination of IgG antibodies to herpes simplex virus type 1 (HSV-1) in human serum and plasma (EDTA and lithium heparin) using the ADVIA Centaur systems. This assay is intended for use as an aid in the determination of serological status to HSV-1 and in the diagnosis of herpes simplex virus infection.
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<b>8. Device Description</b>	The ADVIA Centaur Herpes-1 IgG (HSV1) assay is a fully automated, two-step sandwich immunoassay using indirect chemiluminometric technology. The specimen is incubated with the Solid Phase, which contains HSV-1-specific recombinant-gG1 antigen. Antigen-antibody complexes will form if anti-HSV-1 antibody is present in the specimen. The Lite Reagent contains monoclonal anti-human IgG labeled with acridinium ester, and is used to detect HSV-1 IgG in the specimen.
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COMPARISON PREDICATE		
Item	Predicate	New Device
<b>Trade Names</b>	Focus HerpeSelect 1 and 2 Immunoblot IgG	ADVIA Centaur Herpes-1 IgG
<b>510K n°</b>	K000238	Pending
<b>Manufacturer</b>	Focus Diagnostic Cypress, CA 90630 -USA	Siemens Heathcare Diagnostics Inc. 511 Benedict Avenue, Tarrytown, NY 10591- USA
<i>Similarities</i>		
<b>Intended use</b>	Focus Diagnostics HerpeSelect 1 and 2 Immunoblot IgG test is	The ADVIA Centaur Herpes-1 IgG (HSV1) assay is for <i>in vitro</i>

	intended for qualitatively detecting the presence or absence of human IgG class antibodies to HSV-1 and HSV-2 in human sera. The test is indicated for testing sexually active adults or expectant mothers for aiding in the presumptive diagnosis of HSV-1 and HSV-2 infection. The predictive value of a positive or negative result depends on the population's prevalence and the pretest likelihood of HSV- 1 and HSV-2 infection. The performance of this assay has not been established for use in a pediatric population, for neonatal screening, for testing of immunocompromised patients, for use by a point of care facility or for use with automated equipment	diagnostic use in the qualitative determination of IgG antibodies to herpes simplex virus type 1 (HSV-1) in human serum and plasma (EDTA and lithium heparin) using the ADVIA Centaur systems. This assay is intended for use as an aid in the determination of serological status to HSV-1 and in the diagnosis of herpes simplex virus infection.
<b>Measurand</b>	To detect the presence or absence of human IgG class antibodies to HSV-1 and HSV-2	To detect IgG antibodies to herpes simplex virus type 1 (HSV-1).
<b>Regulation Section</b>	21 CFR 866.3305	Same
<b>Product Code</b>	LGC	MXJ
<b>Classification</b>	Class II Special Controls	Same
<b>Assay Type</b>	Qualitative	Same
<b><i>Differences</i></b>		
<b>Technology</b>	Nitrocellulose immunoblot	Chemiluminescent immunoassay
<b>Sample type</b>	Human serum	Human serum and plasma (EDTA and lithium heparin)

## 9. Performance Summary

### Precision

A precision study was performed according to CLSI EP05-A3 using the Negative and Positive Controls as well as 6 samples prepared at different levels in the assay range. Each material was tested in duplicate, twice a day for 20 days, for a total of 80 replicates per level.

The ADVIA Centaur HSV1 assay is designed to have the following repeatability and within-lab precision requirements:

ADVIA Centaur HSV1 Level (Index)	Design Requirement	
	Repeatability % CV	Within-Lab % CV
< 0.5	NA <sup>a</sup>	NA
0.51–0.79	≤ 10.0%	≤ 15.0%
0.80–1.20	≤ 6.0%	≤ 8.0%
1.21–3.00	≤ 5.0%	≤ 7.0%
3.01–6.00	≤ 5.0%	≤ 7.0%
> 6.00	≤ 5.0%	≤ 10.0%

<sup>a</sup> NA = not applicable

The results for this study are presented below.

#### Precision results for the HSV-1 Assay

Specimen Type	N	Mean (Index)	Repeatability		Within-Lab	
			SD	CV (%)	SD	CV(%)
Negative Control (Plasma)	80	0.26	0.01	NA <sup>a</sup>	0.03	NA <sup>a</sup>
Positive Control (Plasma)	80	2.98	0.10	3.2	0.18	6.1
Serum 1	80	0.25	0.03	NA <sup>a</sup>	0.04	NA <sup>a</sup>
Serum 2	80	0.57	0.03	4.8	0.03	5.9
Serum 3	80	0.97	0.03	3.1	0.04	4.5
Serum 4	80	1.61	0.05	3.1	0.09	5.3
Serum 5	80	4.08	0.20	4.9	0.26	6.4
Serum 6	80	13.37	0.53	4.0	1.04	7.7

NA<sup>a</sup> = Not applicable

### Sample matrix

This study was performed on one ADVIA Centaur XP instrument, using 68 sets of matched samples of different matrixes (serum, serum separator tube (SST), EDTA plasma and lithium heparin plasma) from commercial sources

The samples were analyzed in duplicate in randomized order using one reagent lot.

- Comparing Serum Separator Tube (y) vs Serum (x): (Deming regression)  $y = -0.01 + 0.99 x$ ,  $r=0.996$ , sample range for both matrixes 0.10-19.15 Index Value and 0.10-19.59 Index Value respectively. Note – correlation coefficient is calculated using linear regression.
- Comparing EDTA Plasma(y) vs Serum (x): (Deming regression)  $y = -0.02 + 0.96 x$ ,  $r=0.998$ , sample range for both matrixes 0.10-19.14 Index Value and 0.11-19.19 Index Value respectively. Note – correlation coefficient is calculated using linear regression.
- Comparing Lithium Heparin Plasma(y) vs Serum (x): (Deming regression)  $y = -0.02 + 0.96 x$ ,  $r=0.998$ , sample range for both matrixes 0.10-19.15 Index Value and 0.10-18.73 Index Value respectively. Note – correlation coefficient is calculated using linear regression.

The results supports that Serum Separator Tube is equivalent matrix to Serum, EDTA Plasma is equivalent matrix to Serum and Lithium Heparin Plasma is an equivalent matrix to Serum.

### Panels

The commercial sample panels, Seracare Diagnostics and ToRCH-mixed Zeptometrix, and CDC panel were analysed.

The Seracare Diagnostics panel included 25 characterized HSV samples. All of the samples were evaluated with the ADVIA Centaur Herpes-1 IgG assay on ADVIA Centaur XP instrument and 92% total agreement was observed with reference assay 1.

The ToRCH-mixed Zeptometrix panel included 24 characterized HSV samples. All of the samples were evaluated with the ADVIA Centaur Herpes-1 IgG assay on ADVIA Centaur XP instrument and 96% total agreement was observed with reference assay 1.

The CDC panel included 100 blind characterized HSV samples. All of the samples were evaluated with the ADVIA Centaur Herpes-1 IgG assay on ADVIA Centaur XP instrument and 100% total agreement was observed in concordance with the results provided by the CDC.



### Interferences

Potential interference in the ADVIA Centaur HSV1 assay from the compounds listed below is designed to be  $\leq 10\%$ . Interfering substances at the levels indicated were tested as described in CLSI Document EP7-A2.

The testing was done in three levels of samples in the assay range (high negative, low positive and positive samples) with at least one reagent lot on ADVIA Centaur XP instrument.

Testing confirmed no interference (Demonstrate  $\leq 10\%$  change in results) for the ADVIA Centaur Herpes-1 IgG up to the following concentrations:

Serum specimens that are...	Demonstrate $\leq 10\%$ change in results up to...
Biotin	3500 ng/mL
Hemoglobin	500 mg/dL
Bilirubin complex	40 mg/dL
Bilirubin free	40 mg/dL
Hypoproteinemia	3 g/dL
Hyperproteinemia	12 g/dL
Lipemia	1000 mg/dL
Cholesterol	400 mg/dL

### Cross-reactivity

The ADVIA Centaur HSV1 assay was evaluated for potential cross-reactivity with other viral antibodies, disease-state specimens, and other populations. The HSV-1 IgG status of each specimen was verified using the Comparative Assay. Repeat equivocal specimens on the Comparative Assay were sent to a reference laboratory for Western Blot testing. Total percent agreement for the following clinical categories was 95.8% (413/431). The following results were obtained:

#### Cross Reactivity Study Performance Results

Clinical Category	Number tested	ADVIA Centaur HSV1	Comparative Assay
		Reactive	Positive
Antibody to hepatitis B surface antigen (Anti-HBs)	10	8	8
Anti-gliadin	10	6	6
Anti-nuclear antibody (ANA)	10	5	5

Clinical Category	Number tested	ADVIA Centaur HSV1	Comparative Assay
		Reactive	Positive
<i>Candida albicans</i>	10	10	9
<i>Chlamydia trachomatis</i>	10	6	7 <sup>a</sup>
Cytomegalovirus (CMV IgG)	10	6	7 <sup>b</sup>
Elevated IgG	10	8	8
Elevated IgM	10	9	10 <sup>a/c</sup>
Epstein-Barr virus (EBV VCA IgG)	10	9	9
<i>Escherichia coli</i>	10	9	9
Flu vaccine recipients	10	3	3
<i>Gardnerella vaginalis</i>	10	7	7
Hepatitis C virus (HCV)	25	19	21
Hepatitis B surface antigen (HBsAg)	10	9	9
Herpes simplex virus type 2 (HSV-2)	74	35	33 <sup>a</sup>
Heterophile antibodies	10	1	1
Human anti-mouse antibody (HAMA)	31	24	25 <sup>a</sup>
Human herpes virus 6 (HHV-6)	10	6	5
Human herpes virus 8 (HHV-8)	10	9	9
Human immunodeficiency virus (HIV)	10	10	10
Human Papillomavirus (HPV)	10	6	6 <sup>a</sup>
Multiple myeloma	10	10	10
<i>Neisseria gonorrhoeae</i>	25	17	16
Parvovirus B19	10	4	4
Rheumatoid Factor (RF)	10	6	6
Rubella IgG	10	7	7
Syphilis	10	9	9 <sup>a</sup>
Systemic lupus erythematosus (SLE)	26	17	17
Toxoplasma IgG	10	10	10
Varicella zoster virus (VZV)	10	5	6 <sup>a</sup>
<b>Total Specimens</b>	<b>431</b>	<b>290</b>	<b>292</b>

<sup>a</sup> One sample was confirmed positive by Western Blot

<sup>b</sup> One sample was confirmed positive by Comparative Assay

<sup>c</sup> Two samples were confirmed positive by Comparative Assay

### Clinical study

A multisite clinical study to compare the reference with ADVIA Centaur Herpes-1 IgG was performed. Sensitivity and specificity were determined by comparing the performance of the ADVIA Centaur HSV1 assay to a commercially available anti-HSV-1 IgG immunoblot method (Comparative Assay) and a validated Western Blot reference confirmatory test (University of Washington, Seattle). A total of 864 specimens ( $\geq 18$  years of age), including specimens from 274 pregnant women, were collected within the United States and tested at 3 independent external laboratories. Samples were analyzed in singlicate.

Of these specimens, 520 were reactive, and 344 were nonreactive with the ADVIA Centaur HSV1 assay. The overall agreement was 97.0% (838/864) with a 95% confidence interval (CI) of 95.6%–97.9%.

Of the 864 specimens tested by the Comparative Assay, 22 were equivocal and further tested by the Western Blot test. After Western Blot testing, 19 of the specimens were resolved to be negative and 3 remained equivocal.

The results obtained for the intended use population are presented below

Intended use population		Comparative Assay. Equivocal results have been resolved by Western Blot (WB)			
		Positive	Negative	Equivocal	Total
ADVIA Centaur HSV1	Reactive	507	13	0	520
	Nonreactive	10	331	3	344
	<b>Total</b>	<b>517</b>	<b>344</b>	<b>3</b>	<b>864</b>

The sensitivity of the ADVIA Centaur HSV1 assay was 97.5% (507/520), with a 95% confidence interval (CI) of 95.8%–98.5%.

The specificity of the ADVIA Centaur HSV1 assay was 96.2% (331/344), with a 95% confidence interval (CI) of 93.6%–97.8%.

Sensitivity and specificity were determined for the pregnant population by comparing the performance of the ADVIA Centaur HSV1 assay to the Comparative Assay and Western Blot confirmatory method. The results of the pregnant women samples are presented below:

**Pregnant women Study Contingency (WB resolution) table**

Pregnant women		Comparative Assay Equivocal results have been resolved by Western Blot (WB)			
		Positive	Negative	Equivocal	Total
ADVIA Centaur HSV1	Reactive	155	2	0	157
	Nonreactive	2	115	0	117
	<b>Total</b>	<b>157</b>	<b>117</b>	<b>0</b>	<b>274</b>

The sensitivity of the ADVIA Centaur HSV1 assay was 98.7% (155/157) with a 95% confidence interval of 95.5%–99.7%.

The specificity of the ADVIA Centaur HSV1 assay was 98.3% (115/117) with a 95% confidence interval of 94.0%–99.5%.

## **10. Stability**

The onboard stability of the ADVIA Centaur Herpes-1 IgG reagents is 60 days with a calibration interval of 28 days. The onboard stability of the ADVIA Centaur Herpes-1 IgG Calibrators is 8 hours. The opened vial stability of the ADVIA Centaur Herpes-1 IgG Calibrators is 65 days. Unopened reagents and calibrators are stable until the date printed on the box label when stored at 2-8°C.

## **11. Conclusion**

The analytical and clinical study results demonstrate that the ADVIA Centaur Herpes-1 IgG are substantially equivalent to the predicate device, Focus HerpeSelect 1 and 2 Immunoblot IgG (FDA cleared under K000238), and that the assay is safe and effective for its labeled intended use.