

Recommendation to Waive Pre-Approval Inspection Memo - Seraclone Blood Grouping Reagent Anti-S (Monoclonal)

Date: July 29, 2008
From: Marion Michaelis, Reviewer, OCBQ/DMPQ/MRB II, HFM-676
To: Administrative Bundled File, Biotest AG (LIC #1702):

Products for use on the Tango Automated Blood Group Analyzer

(STN)	Biological Products	Cell Line(s)	Strip Proprietary Name
BL 125097/10	Blood Grouping Reagent, Anti-D (Monoclonal)(IgM) (Formulated for Automated Testing)	BS226	Component of Erytype S Rh+K
	Blood Grouping Reagent, Anti-D (Monoclonal)(IgM) (Formulated for Automated Testing)	BS232	Component of Erytype S Rh+K
BL 125206/0	Blood Grouping Reagent, Anti-C (Monoclonal) (Formulated for Automated Testing)	MS24/P3x25513G8	Component of Erytype S Rh+K
BL 125202/0	Blood Grouping Reagent, Anti-E (Monoclonal) (Formulated for Automated Testing)	MS260/MS12	Component of Erytype S Rh+K
BL 125205/0	Blood Grouping Reagent, Anti-c (Monoclonal)	MS33	Component of Erytype S Rh+K

(STN)	Biological Products	Cell Line(s)	Strip Proprietary Name
	(Formulated for Automated Testing)		
BL 125203/0	Blood Grouping Reagent, Anti-e (Monoclonal) (Formulated for Automated Testing)	MS16/MS21/ MS63	Component of Erytype S Rh+K
BL 125204/0	Blood Grouping Reagent, Anti-K (Monoclonal) (Formulated for Automated Testing)	MS56	Component of Erytype S Rh+K

NOTE- Erytype S are strip wells (eight wells per strip) containing: Anti-D, Anti-D, Anti-C, Anti-c, Anti-E, Anti-e and Anti-K+ Neg Cont

BL 125208/0	Reagent Red Blood Cells For Use in Automated Systems	Cell Line(s)
	Erytypecell A 1 and B	N/A
	Biotestcell Pool; Biotestcell 1, 2; Biotestcell 3	N/A
	Biotestcell I8; Biotestcell I11	N/A
BL 125218/0	Blood Grouping Reagent Anti-D (Monoclonal) (IgG Blend)	BS221/H4111B7
Seraclone- Liquid BGR for manual tube testing:		
BL 125217/0	Blood Grouping Reagent, Anti-Jk b	MS8

BL 125208/0	Reagent Red Blood Cells For Use in Automated Systems	Cell Line(s)
	(Monoclonal)	
BL 125231/0	Blood Grouping Reagent, Anti-Jk a (Monoclonal)	MS15
BL 125219/0	Blood Grouping Reagent, Anti-A (Murine Monoclonal)	A003
BL 125220/0	Blood Grouping Reagent, Anti-B (Murine Monoclonal)	B005
BL 125221/0	Blood Grouping Reagent, Anti-A,B (Murine Monoclonal)	BS63 and BS85
BL 125224/0	Blood Grouping Reagent, Anti-M (Murine Monoclonal)	BS57
BL 125225/0	Blood Grouping Reagent, Anti-N (Murine Monoclonal)	BS41
BL 125230/0	Blood Grouping Reagent, Anti-K (Monoclonal)	MS56
BL 125232/0	Blood Grouping Reagent, Anti-k (Murine Monoclonal)	Lk1
BL 125233/0	Blood Grouping Reagent, Anti-Le a (Murine Monoclonal)	LEA2
BL 125213/0	Blood Grouping Reagent, Anti- P 1 (Murine Monoclonal)	650

Other Reagents for Manual Tubes Testing

(STN)	Anti-Human Globulin	Cell Line(s)
BL 125242/0	Anti-Human Globulin (Rabbit/Murine Monoclonal)	BRIC-8
BL 125215/0	Anti-Human Globulin	N/A
BL125098/8	Anti-Human Globulin (Formulated for Automated Testing)	N/A
(STN)	Reagent Red Blood Cells	Cell Line(s)
BL 125207/0	Biotestcell A 1 and B	N/A
	Biotestcell A 2	N/A
	Biotestcell Pool; Biotestcell 1, 2; Biotestcell 3	N/A
	Biotestcell I8; Biotestcell I11	N/A

Applicant: Biotest AG, Dreieich, Germany location.

Products: See above bundled file listing.

Through: Chiang Syin, Ph.D., Branch Chief, OCBQ/DMPQ/MRB II, HFM-676

Concurrent Clearance Routing

John A. Eltermann, Jr., R.Ph., M.S.

Date CONCUR

Director, Division of Manufacturing and Product
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DO NOT
CONCUR

Elizabeth Callaghan

Date CONCUR

Acting Director, Division of Hematology, HFM-370

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DO NOT
CONCUR

Summary

We recommend waiver of the pre-approval inspection, BLAs and BLS for Biotest AG, for manufacturing multiple new Blood Grouping Reagents, Anti-Human Globulin, and Reagent Red Blood Cells (specified above).

Brief History

Biotest AG, U.S. License 1702, Dreieich, Germany, submitted a bundle consisting of 30 new BLAs and 2 BLSs in September 2006 (see above). Biotest is currently licensed to manufacture several Erytype S Blood Grouping Reagents are for use on the TANGO Automated Blood Bank System. The purpose of this submission is to obtain approval for additional monoclonal antibodies as components of Erytype S plates, to update the CMC with information related to sublotting and testing of bulk antibodies, and to obtain approval for a complete line of liquid reagents for use in manual immunohematology tube tests.

This bundle is a companion submission to 4 BLAs for Blood Grouping Reagents (Monoclonal)(For Further Manufacturing Use)(FFMU) submitted by DIAGAST, U.S. License 1744; and 10 BLSs and 2 BLAs for Blood Grouping Reagents (Monoclonal)(For Further Manufacturing Use)(FFMU)and Anti-Human Globulin (Murine Monoclonal)(For Further Manufacturing Use)(FFMU) submitted by Millipore (Celliance) U.S. License 1721. The BLAs/BLSs were submitted by DIAGAST and Millipore in September 2006.

Description of Change:

- BLAs for manufacturing new Blood Grouping Reagents, Anti-Human Globulin, and Reagent Red Blood Cells (specified above) and associated process and manufacturing changes to previously licensed BGR's.

Basis for the Waiver:

This waiver is based on criteria outlined in Center wide SOPP 8410 "Determining When Pre-Licensing/Pre-Approval Inspections are Necessary." As stated in that SOPP, it is CBER's policy that a pre-license or pre-approval inspection will generally be necessary for an application if any of the following criteria in bold are met:

- The facility does not hold an active US license.

Biotest AG, Dreieich, Germany does hold U.S. license No. 1702.

- The FDA has not inspected the facility in the last two years.

This facility (Dreieich, Germany) in the last two years was inspected by:

1. The first inspection was conducted by Team Biologics (Jacqueline Diaz Albertini) during the time period of 19-28 September 2006 and was a GMP inspection done as part of the Team Biologics work-plan for FY 2006.
 2. The second inspection was conducted by CBER (Susan Yu and Joanne Pryzbylik) during the week of June 28 through July 6, 2004 and was a Pre-Licensing Inspection (PLI) for the manufacture of Blood Grouping Reagents (BGR) and Anti-Human Globulin (AHG) for use on the TANGO, an automated blood bank analyzer.
- **The previous inspection(s) revealed significant GMP violations in areas related to the processes in the submission (similar processes) or systemic problems, such as QC/QA oversight.**
 1. The inspection in September 2006 was classified VAI. The GMP inspection was done as part of the Team Biologics work-plan for FY 2006.
 2. The inspection in June-July 2004 was classified VAI. The PLI inspection was conducted for the manufacture of Blood Grouping Reagents (BGR) and Anti-Human Globulin (AHG) for use on the TANGO, an automated blood bank analyzer.
 - **The establishment is performing significant manufacturing step(s) in new (unlicensed) areas using different equipment (representing a process change). This would include areas that are currently dedicated areas that have not been approved as multi-product facilities/buildings/areas.**

All areas used for the manufacturing are licensed areas.

- **The manufacturing process is sufficiently different (new production methods), specialized equipment or facilities) from that of other approved products produced by the establishment.**

The production process is similar to other immunohematology reagents and systems for blood grouping, phenotyping, and antibody screening products produced at the facility.

Waiver Recommendation:

Based on the information provided in the BLA and related correspondence supporting the overall compliance status of the license holder, the review committee recommends waiving the pre-approval inspection for the facility changes associated with these supplements.

07/29/08

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Marion Michaelis, HFM-676
Reviewer, DMPQ