# Recommendation to Waive Pre-Approval Inspection - Seraclone Anti-s (Monoclonal)

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Biologics Evaluation and Research
Division of Manufacturing and Product Quality

**MEMORANDUM: Recommendation to Waive Pre-Approval Inspection**
**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) (Formulated for | MS33 | Component of Erytype S |

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

| (STN) | Biological Products | Cell Line(s) |
|---|---|---|
| BL 125222/0 | Blood Grouping Reagent, Anti-D (Monoclonal) (IgM) | BS226 |
| BL 125223/0 | Blood Grouping Reagent, Anti-D (Monoclonal Blend) | BS232/BS221/H4111B7 |
| BL 125226/0 | Blood Grouping Reagent, Anti-C (Monoclonal) | MS24 |

| (STN) | Biological Products | Cell Line(s) |
|---|---|---|
| BL 125227/0 | Blood Grouping Reagent, Anti-c (Monoclonal) | MS33 |
| BL 125228/0 | Blood Grouping Reagent, Anti-E (Monoclonal) | MS12/MS260 |
| BL 125229/0 | Blood Grouping Reagent, Anti-e (Monoclonal) | MS16/MS21/MS63 |
| BL 125212/0 | Blood Grouping Reagent, Anti-Fy a (Monoclonal) | GD-FYA-02 |
| BL 125214/0 | Blood Grouping Reagent, Anti-s (Monoclonal) | P3YAN3 |
| BL 125216/0 | Blood Grouping Reagent, Anti-S (Monoclonal) | MS94 |
| BL 125217/0 | Blood Grouping Reagent, Anti-Jk b (Monoclonal) | MS8 |
| 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 | **N/A** |

| | (STN) | Anti-Human Globulin | Cell Line(s) |
|---|---|---|---|
| | | Automated Testing) | |
| | **(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 Quality, HFM-670
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research DO NOT CONCUR

Elizabeth Callaghan Date CONCUR
Acting Director, Division of Hematology, HFM-370
Office of Blood Research and Review
Center for Biologics Evaluation and Research 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_
Marion Michaelis, HFM-676 Date
Reviewer, DMPQ