DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
1401 Rockville Pike
Rockville, MD 20852-1448

Date: July 10, 2008

To: Files of STNs 125212/0 and 125214/0

From: Teresita C. Mercado, Consumer Safety Officer, Devices Review Branch

Subject: Review memo and recommendation: Biotest AG's Blood Grouping Reagents Anti-Fy[a] (Monoclonal) and Anti-s (Monoclonal)

Through: Sheryl A. Kochman, Chief, Devices Review Branch

Background:

Biotest AG, located in Dreieich, Germany submitted these applications for the manufacture of Seraclone® Blood Grouping Reagents (BGR) Anti-Fy[a] (Monoclonal) and Anti-s (Monoclonal), which are intended for typing blood specimens using manual tube agglutination methods. The Anti-Fy[a] (Monoclonal) (IgG) (For Further Manufacturing Use) [FFMU] and Anti-s (Monoclonal) (IgG) (FFMU) materials are supplied by Diagast under a shared manufacturing agreement with Biotest AG. The license applications for these FFMU products have been submitted to the FDA and are being reviewed as companion submissions to the final container products.

CBER received the original submission dated September 22, 2006 on September 29, 2006. Regulatory documents in the submission include Form FDA 356h, draft labeling, chemistry, manufacturing and controls, establishment information and stability data. CBER issued a Complete Response (CR) letter on July 27, 2007. Biotest responded to this CR letter in a letter dated November 30, 2007. CBER issued a second CR letter on January 31, 2008 and a third CR letter on May 16, 2008. CBER received the responses to these CR letters on March 17, 2008 and June 23, 2008 respectively. The May 16, 2008 CR letter includes labeling questions only. This memorandum is a review of the response to the May 16, 2008 CR letter. Since this response is the last amendment to the application, this memorandum also includes this reviewer's regulatory action recommendation.

Chronology of Events:

September 29, 2006 – Original submission dated September 22, 2006 received in CBER
July 27, 2007 – Complete Response letter issued
December 3, 2007 – November 30, 2007 response to CR letter received in CBER
January 31, 2008 – CBER issued a 2nd CR letter
March 17, 2008 – CBER received response to the 2nd CR letter
May 16, 2008 – CBER issued a 3rd CR letter
June 23, 2008 – CBER received response to the 3rd CR letter

Review:

Labeling

1. Please submit corrected labels to include your full name (Biotest Medical Diagnostics GmbH) and new license number on the vial, container and package insert labels.

   Biotest's Response
   Biotest included their full name and new license number on the vial, container and package insert labels. Because of the limited space on the vial label, Biotest is requesting that the business address be omitted from the vial label.

2. Seraclone Anti-Fy^{a} Package Insert

   a. Under "Summary," it states "Seraclone Anti-Fy^{a} may cause hemolytic disease…" Please delete "Seraclone."

      Biotest's Response
      Biotest deleted "Seraclone" from the *Summary* Section.

   b. Under "Reagent"

      i. It states, "It is derived from red blood cell culture…" Please delete "red blood cell".

         Biotest's Response
         Biotest deleted only the words "red blood" since the standard wording for this is "cell culture".

      ii. With respect to Diagast, please delete "FFMU" and insert their current license number.

         Biotest's Response
         Biotest made the requested changes.

   c. Material required but not provided Section. You state that use of an optical aid for reading and grading agglutination results is not allowed. You also reference the Technical Manual, 15th edition in your package insert bibliography. The standard of practice in the US as recommended by the American Association of Blood Banks Technical Manual requires the use of an agglutination viewer to aid in the grading of hemagglutination reactions. This standard operating procedure is accepted for use by CBER as referenced by 21 CFR 606.100(d)(1). If an optical aid cannot be used to grade reactions, please add this contraindication (prominently bolded) to this section to alert the user.

      Biotest's Response
      Biotest added "optical aid (optional) to the *List of materials required but not provided*. Under the *Interpretation of results* section, Biotest added the following

statement, “An agglutination reader may facilitate the reading of tube tests (as recommended by the ABB Technical manual, 15th edition).

Reviewer’s Comment
AABB mentions the use of an optical aid or agglutination viewer so I recommend that Biotest use one of these terms instead of “agglutination reader”. “Agglutination reader” is suggestive of an automated device that reads agglutination reactions.

d. Summary Section. Please use capital letters for the biologics product proper name, i.e., Blood Grouping Reagents.

Biotest’s Response
Biotest used capital letters for the biologics proper name.

3. Seraclone Anti- s (Monoclonal) Package Insert

a. Please make the same corrections as described in b, c, and d above.

Biotest’s Response
Biotest made the requested changes.

Additional Changes to the Labeling
In addition to the changes requested by CBER, Biotest made the following labeling changes:

- Replace “Biotest Monoclonal Anti-Fy^a with “Biotest Monoclonal Anti-Fy^a Blood Grouping Reagents” in the *Quality Control Section* of the Package Insert.
- In the *Limitations Section* of the Package Insert, the statement “Samples with cold agglutinins may be processed using standard warming techniques” was replaced with “False positive results or reactions suspected to be due to cold agglutinins should be resolved according to in-house procedures.”
- Under the *Specific Performance Characteristics Section* of the Package Insert, the full name of Biotest was added.
- A hyphen was added to the lot number on the vial and package labels to distinguish the 7- digit lot number form the 2 digits that signify the sublotting number.
- For shipping purposes, a two dimensional barcode was added to the package label.

Review:

All the review issues have been resolved. I recommend the approval of STNs 125212/0 and 125214/0.