



Our STNs: BL 125212/0 and 125214/0

January 31, 2008

Biotest AG  
Attention: Mr. William Weiss  
Biotest Diagnostics Corporation  
66 Ford Road, Suite 220  
Denville, NJ 07834

Dear Mr. Weiss:

We have completed the review of your submissions dated November 30, 2007 to your biologics license applications (BLA) for the licensure of Blood Grouping Reagents Anti-Fy<sup>a</sup> (Monoclonal) and Anti-s (Monoclonal) submitted under section 351 of the Public Health Service Act. We also make reference to a telecon on January 18, 2008 between Ms. Pamela Vaughn (Alquest) and Ms. Najma Khan (CBER).

We would like to correct a typographical error in our letter of July 27, 2007 in which we requested additional information. In that letter, we stated that the date of your submissions was September 22, 2007. We would like to recognize that your submissions were actually dated September 22, 2006. We apologize for any confusion this may have caused.

We have identified the following issues with your responses:

1. Forms FDA 2567 indicate that Seraclone<sup>®</sup> Anti-Fy<sup>a</sup> and Anti-s are of [REDACTED] monoclonal origin. Both the container and the package insert indicate that these two reagents are of human monoclonal origin. Please clarify, make the necessary corrections, and resubmit the corrected documents.
2. You listed Biotest Coombscell-E in the package inserts as an example of the IgG coated red blood cells that can be used to verify negative reactions in an antiglobulin test. Please note that Biotest Coombscell-E is not a cleared product and should not be mentioned in the package insert. Please replace the reference to the Biotest Coombscell-E with a generic reference to IgG coated red blood cells and submit the revised package insert or submit a 510(k) for the product.
3. Also regarding the package inserts, please note:
  - a) The "Materials" section is in the wrong location in the insert; it should be before "Test Procedure" as required by 21 CFR 809.10.
  - b) Please clarify if use of an optical aid for reading agglutination results is allowed and, if so, please list it/them as optional materials.

- c) The package insert does not have the “Stability of the Reaction” section as required by 21CFR 809.10(b)(8)(iv). The “Stability of the Reaction” section should be located between “Test Procedure” and “Quality Control.”
4. Please revise the lot release protocol templates to:
- a. Make the reagent lot number more prominent.
  - b. In the “CC” column, place replace the STN with your US license number
  - c. Include the bioburden acceptance criterion and document the results, e.g., no growth.
  - d. Include preservative and concentration.
  - e. Include test cell concentration and suspending medium.
  - f. Include reagent diluent.
  - g. Include the test incubation temperature.
5. If additional results of the stability studies are available at the time you reply to this letter, please include them.

In addition, based on information provided to CBER in the January 18, 2008 telecon, it is our understanding that you do not have samples and lot release protocols ready for submission to CBER. We cannot approve these applications until samples and lot release protocols have been received.

Also, while the reagents that are the subject of these applications are not for use on the Tango, they are bundled with numerous other submissions that are tied to the Tango. We have not received a new 510(k) to allow for the use of those additional reagents on the Tango. We cannot approve these applications until the 510(k) for the Tango is submitted, reviewed, and cleared.

We reserve final comment on the proposed labeling until the applications are otherwise acceptable. We may have comments when we see the proposed final labeling.

Should additional information relating to the safety and effectiveness of these biological IVD products become available prior to our receipt of the final printed labeling, revision of that labeling may be required.

You may request a meeting or teleconference with us to discuss the steps necessary for approval. For PDUFA products please submit your meeting request as described in the FDA Guidance for Industry: Formal Meetings With Sponsors and Applicants for PDUFA Products February, 2000 (<http://www.fda.gov/cber/gdlns/mtpdufa.pdf>). For Non PDUFA products, please contact the regulatory project manager. For details, please also follow the instructions described in CBER’s SOPP 8101.1: Scheduling and Conduct of Regulatory Review Meetings with Sponsors and Applicants, available at (<http://www.fda.gov/cber/regsopp/81011.htm>).

Within 10 days after the date of this letter, you should take one of the following actions: (1) amend the applications; (2) notify us of your intent to file amendments; or (3) withdraw the applications.

We stopped the review clock with the issuance of this letter. We will reset and start the review clock only when we receive your complete response, which includes related 510(k) submissions and samples and lot release protocols.

If you have any questions, please contact Sheryl A. Kochman, at (301) 827-6123.

Sincerely yours,

/s/

For Elizabeth Callaghan  
Acting Director  
Division of Blood Applications  
Office of Blood  
Research and Review  
Center for Biologics Evaluation  
and Research