

Memorandum: Meeting with Biotest - Seraclone Blood Grouping Reagent Anti- Fya (Monoclonal)

Memorandum

Date: August 28, 2007

From: Teresita C. Mercado/OBRR/DBA, HFM-390

To: Files

Subject: Meeting with Biotest

Meeting Date: August 28, 2007

Time: 9:50 AM – 10:30 AM

Location: Woodmont Office Center, Conf 2

Meeting Requestor / Sponsor: Biotest AG

FDA Participants:

Sheryl Kochman, Chief, Devices Review Branch, OBRR

G. R. Gentile, Director Regulatory, OD

Joanne Pryzbylik, Consumer Safety Officer, Devices Review Branch, OBRR

Weishi (Vivian) Yuan, Statistician, OBE

Najma Khan Consumer, Safety Officer, Devices Review Branch, OBRR

Teresita Mercado, Consumer Safety Officer, Devices Review Branch, OBRR

Biotest AG Participants:

Rolf Vornhagen, Managing Director, Technical Division

Dr. Silke Milbradt, Product Manager

Ute Greiner, QA Manager

Biotest US Participants:

Candace Williams, Vice President Transfusion Diagnostics

Joy Thompsen, Manger Transfusion Technical Services

Biotest US Participants:

-----, Principal Consultant

-----, Senior Principal Consultant

Meeting Objectives:

To discuss Biotest's additional performance study proposal.

Background: Biotest submitted the following information and questions prior to the meeting.

Biotest would like to propose collecting the recommended additional product performance data by *in-house* testing of both patient samples and some purchased (rare) specimens. This in-house data would be collected either by 1) testing purchased samples at the Biotest New Jersey office (BDC), using the TANGO and manual methods, where indicated; or 2) by BDC personnel testing patient and purchased samples at a local hospital that has offered to permit BDC to utilize their TANGO system and lab space to perform the testing.

During the “in-house” testing, Biotest would collect additional data related to:

- adding a third “site” for rare antisera testing with different sample demographics than the original 2 sites (see Question 19 of the July 27, 2007 CR Letter, STNs BL125216/0 and 125217/0, and other CR letters)
- use of other anti-coagulants and serum (Question 38e of the July 27, 2007 CR Letter, STNs BL125216/0 and 125217/0, and other CR letters)
- sample age (Question 40d of CR July 27, 2007 Letter, STN BL125215/0 and 125242/0)
- sample storage conditions (Question 21 of CR July 27, 2007 Letter, STN BL125215/0 and 125242/0)
- variations on sample collection and storage, and donor/patient age (Question 15 of July 27, 2007 CR Letter , STNs BL125215/0and 125242/0)
- interfering substances (hemolysis, lipids, jaundiced/icteric) (Question 33 of July 30, 2007 CR Letter, STNs BL125207/0 and 125208/0)

Biotest will develop a statistically sound test plan for each of these performance tests. If in-house testing is acceptable to FDA, this can commence within a few weeks, as soon as the protocols are written and approved by Biotest. If Biotest must utilize clinical trial sites, it will take several months to obtain institutional approval and to schedule the studies, delaying the Complete Response until early 2008, at best.

Biotest proposes not to collect additional data on the Anti-D (Monoclonal) (IgG Blend) for use on Solidscreen II for the following reasons. The reported rate of agreement of 93.5 % was determined using Olympus PK data as the reference method (See Question 9 of July 31, 2007 CR Letter, STN BL125218/0). It happened that the PK test reagents were not a suitable reference method for the Anti-D Blend testing, in that the PK reagents are known to not detect all Cat. VI, weak Ds. When the 31 discordant Anti-D Blend TANGO results were compared to the resolution data collected by manual methods (the alternate approved reference method), the results were 100% concordant. This brings the rate of agreement for the Anti-D Blend to >99%, as recommended by FDA. Therefore, additional testing is not indicated, and will not be included in the protocol for proposed additional studies.

Discussion:

Questions for the FDA and FDA's Responses (in bolded text)

1. Is it acceptable to perform the additional "clinical" testing "in-house", as described by either of the above *in-house* options?

Normally, FDA requires performance data from three different field trial sites. However, since the bulk of the studies the Agency is asking for are related to sample conditions and only one study is related to reagent performance as compared to a comparator, all of the studies can be done in-house by either method proposed by Biotest, i.e. testing purchased samples at the Biotest New Jersey office (BDC), using the TANGO and manual methods, where indicated; or testing by BDC personnel testing patient and purchased samples at a local hospital that has offered to permit BDC to utilize their TANGO system and lab space to perform the testing.

For the studies on anticoagulant and serum, sample age, sample storage, variations on sample collection and storage, donor/patient age and interfering substances (hemolysis, lipids, jaundiced/icteric), the Agency will accept data from one lot of product. For citrated samples, Biotest need only to test CPD anticoagulated samples. They should also test heparinized and clot samples. FDA expects at 95% confidence level, a rate of agreement of 95% (lower confidence limit) for these studies.

For additional testing of rare antisera FDA would like to see data from at least two lots of each product from two different bulks.

Biotest could use the Rest of the World lots for the study as long as these lots are manufactured and formulated in the same manner as the US products. Since Biotest has to submit three conformance lots of each product, they could use some of these products (labeled as IUO) for the additional performance testing. Some of the product could be labeled for lot release and the rest unlabeled until approval. The unlabeled vials could be labeled with the final approved label and could then be sold in the US.

2. Is it necessary to test three lots of each Biotest product, or would it be sufficient to test less (one or two lots)?

Biotest should test at least two lots manufactured from two different bulk s

3. If more than one lot is needed per product, can they be produced from the same lot of BGR or AHG bulk reagent?

No, the lots should be manufactured from different bulks.

4. Does FDA agree with our rationale for not testing additional samples with the Anti-D (Monoclonal) (IgG Blend), or is it necessary to perform more testing of these antisera (STN BL125218/0)?

It is not necessary to perform additional testing of the Anti-D (Monoclonal) (IgG Blend).

Other Discussion Items:

- FDA requested that Biotest submit the drafts of the lot release protocols as soon as possible rather than waiting to include them in their response to the CR letters.
- FDA asked Biotest to submit the conformance lots for each of the products. FDA will accept one full and two pilot lots for each product.

Prepared: TMercado, 08/28/07

Revised: SKochman, 08/28/07