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Diagnostics, Inc.

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Docket Management Branch
(HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

I am writing to voice our official comments regarding the "Guidance for Industry, Revised Recommendations f Donor and Product Management Based on Screening Tests for Syphilis" Docket No. 2003D-0236, June 25 2003"

Fujirebio Diagnostics is the manufacturer of the syphilis screening reagents used in the FDA licensed Olympus P TP assay system PK-TP. This assay system detects treponemal specific antibodies.

Fujirebio Diagnostics would like to thank the FDA for the opportunity to comment on two aspects of the propos FDA guidance, "Revised Recommendations for Donor and Product Management Based on Screening Tests f Syphilis."

The first set of comments refers to paragraphs 4 and 5 of the background section which state: "After this new ass (referring to the PK-TP) was adopted for screening blood and blood components, significant increases in don reactive rates were encountered with a corresponding increase in donor deferral rates. The reason for this increa in reactive screening test results with treponemal-based assays was that, with few exceptions, detectable antibodi to T. pallidum persist for a lifetime, as explained above."

We believe that these quoted statements need to be clarified to reflect the difference between screening a confirmatory testing. To our knowledge, the best and largest source of data to address the comparison betwe non-treponemal and treponemal-based assays is a study conducted by the American Red Cross over a two year fi month period (May 1993-September 1995) shortly after the implementation of the PK-TP screening assay. The data indicate that although the rate of screen reactive, confirmatory positive results was greater when the PK-T test replaced the use of non-treponemal screening assays, the rate of screening test reactive donations actual **decreased** with the introduction of the PK-TP assay. [1] The study authors report (see Table 1 of their publicatio an RPR positive screening rate of 0.26% compared to a PK-TP positive screening rate of 0.21% or 0.12 depending upon whether the initially introduced PK-TP assay or its subsequent modification was used. Based this very large dataset, it does not appear correct to state that there was "a significant increase in donor reacti rates" or "an increase in reactive screening test results" when PK-TP testing was implemented.

On the other hand, the rate of confirmatory positive results did initially increase when the PK-TP assay w introduced. We agree that the reason for this is that the PK-TP assay detected antibodies to T. pallidum th persisted for a lifetime and were not detected by RPR testing. Table 1 of the ARC study indicates that the rate PK-TP confirmed positives as a percentage of screened donations was 0.07% (with the modified assay) compared to 0.02% with RPR screening. Interestingly, when repeat donors who were detected with the PK-T assay were removed from the donor population, the ongoing PK-TP confirmed positive rate dropped to 0.03% donations from repeat donors, which is not very different from the 0.02% reported with RPR. Because don deferral occurs only for those donors that are both screening and confirmatory test positive, the FDA is correct

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stating that donor deferral rates initially increased after introduction of the PK-TP assay. However, we do believe that this initial increase detected 8-10 years ago (which subsequently returned to very near the R baseline) is relevant to the donor and product management issues that are discussed in the current propo guidance document.

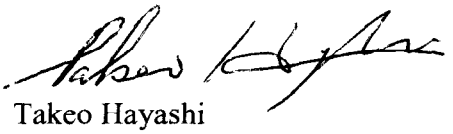
We believe that it is the intent of the background section of the guidance to convey the fact that treponemal spec assays detect more donors with T. pallidum antibody than do non-treponemal assays. Although the curr guidance makes this point, we are concerned (in light of the data presented above) that it does so in a way t might lead some readers to misinterpret PK-TP test performance. We suggest that FDA can more accurat convey their message by rewording the two sentences quoted in the first part of our letter as follows:

"After this new assay (referring to the PK-TP) was adopted for screening blood and blood components, an incre in screening reactive, confirmed positive results was found. The major reason for this was that detecta antibodies to T. pallidum persist for a lifetime, as explained above."

Our second comment on the proposed guidance refers to confirmatory testing. We note that the FDA refers confirmatory testing throughout the proposed document as an "FTA or other confirmatory test". We recognize t historically the FTA was the test commonly used to confirm reactivity on a syphilis screening assay. Howe there are now several T. pallidum specific tests that can be used for this purpose. We therefore suggest that after guidance document mentions the multiple confirmatory tests that can be used (e.g. FTA, EIA, MHATP, TP.I and Treponemal Western Blot), the terminology "confirmatory test" should replace the phrase "FTA or ot confirmatory test" throughout the document.

Thank you for your careful review and consideration of our comments.

Sincerely,



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Reference

1. Aberle-Grasse J, Orton SL, Notari E et al. Predictive value of past and current screening tests for syphili blood donors; changing from a rapid plasma reagin test to an automated specific treponemal test for screeni Transfusion 1999; 39:206-211