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SUMMARY

This For Cause inspection of IVD Research, Inc. was initiated under CDRH, OIVD-directed inspection FACTS assignment # 955366. The inspectional request originated from HFZ-440 in a memo dated July 16, 2008. The assignment was specific to covering the firm's operations as an exporter of unapproved in-vitro diagnostic devices and to determine if the firm is distributing unapproved in-vitro diagnostic devices in domestic commerce, especially to (b) (4). The inspection was conducted in accordance with Compliance Program 7382.845-Inspection of Medical Device Manufacturers and covered PAC 82845G, 81011 and 82012. Profile classes CCR and SIP were covered. The firm does not manufacture tracked or sterile devices. Dengue, Leptospira, and Chagas devices were covered during this inspection.

The previous inspection was conducted from 12/15/04 – 12/17/04 and covered CAPA and Production and Process Controls. An 8-item FDA-483 was issued for quality system deficiencies such as lack of process validation, change control and deficient storage procedures. The firm's management promised to correct all observations. The inspection was classified VAI.

IVD Research, Inc. manufactures cleared and non-cleared in-vitro diagnostic (IVD) devices and conducts research for development of new IVDs. Non-cleared 510(k) IVD devices are being distributed in domestic commerce. This was verified by CDRH and the firm (see Exhibit 8). The firm also sells bulk shipments of (b) (4) kits such as Dengue and Leptospira to (b) (4). located in (b) (4). (b) (4) receives the components in bulk and assembles the device into finished kits. (b) (4) maintains on-file the instructions for use (DFU) for IVDs they purchase from IVD Research (e.g. Dengue and Leptospira) and reformats the labeling under their name. The devices are kitted by (b) (4) and sold under the (b) (4)

name according to Ms. Roode. An IVD Research DFU is not provided with each bulk shipment, (See CR 250489 for Dengue IgG).

This current inspection revealed IVD Research, Inc. is distributing unapproved Dengue, Leptospira and Chagas in-vitro diagnostic devices in bulk and kitted nationwide to distributors, manufacturers and other customers such as hospitals in domestic commerce.

Significant Quality System Regulation deficiencies were noted during the inspection resulting in a 16-item FDA-483. Deviations included the firm has no design and development plans, design changes were not documented and validated, process validations were not performed and stability studies do not support an 18-month expiration date for IVD products. The firm's management promised to correct all observations and to respond in writing to the Los Angeles District within (b) (4) days.

Documentary samples (DOC 250488 of Leptospira Total and DOC 250489 of Dengue IgG) were collected to document the sale and distribution of unapproved IVD devices within the United States. The center directed assignment is enclosed as **Attachment 4.** There were no refusals.

ADMINISTRATIVE DATA

Inspected firm:	IVD Research, Inc.
Location:	5909 Sea Lion Place, Suite D Carlsbad, CA 92010
Phone:	760-929-7744
FAX:	(760)431-7759
Mailing address:	5909 Sea Lion Place, Suite D Carlsbad, CA 92010
Dates of inspection:	9/9/2008, 9/10/2008, 9/11/2008, 9/12/2008, 9/17/2008, 9/18/2008, 9/22/2008, 9/24/2008, 9/25/2008, 9/30/2008, 10/9/2008
Days in the facility:	11
Participants:	Deborah A. Greco, Investigator

On 9/9/08, I presented my credentials and issued a FDA-482, Notice of Inspection to David N. Lambillotte, President and owner. Mr. Lambillotte said he was the most responsible person at the firm. On 10/9/08, I issued a FDA-482 to Ms.. Kathy Hildebrand, Director of Operations due to time away from the firm. Ms. Hildebrand said Mr. Lambillotte was not present and in his absence, she is the next most responsible person at the firm.

The firm's hours of operation are (b) (4). They have (b) (4) full-time employees. Mr. Lambillotte provided a copy of the firm's FDA device registration and listing, **Exhibit 1.** Upon my review of the device listing, I noted not all of the firm's devices were listed such as Leptospira IgG. Mr. Hall said he was in the process of updating the firm's registration on the FDA website.

All future FDA correspondence should be addressed to:
David N. Lambillotte, President
5909 Sea Lion Place, Suite D
Carlsbad, CA 92010

HISTORY

There has been no change in the firm's history of business since the last inspection dated December 2004. Mr. Lambillotte is the President and his wife, Ann Marie Lambillotte is the Vice President of IVD Research, Inc. Mr. Lambillotte provided a copy of the firm's organizational chart, **Exhibit 2.**

Mr. Lambillotte said the firm continues to manufacture and distribute IVDs for human use under the name of IVD Research, Inc. Mr. Lambillotte said the firm is also a manufacturer of IVDs for animal use which are sold under the name of SafePath. Mr. Lambillotte said he is the sole owner of SafePath.

Mr. Lambillotte also provided a copy of the firm's floor plan, **Exhibit 3.**

INTERSTATE COMMERCE

Mr. Lambillotte said the firm continues to sell about (b) (4)% of their IVD kits internationally. Mr. Lambillotte said (b) (4)% of the raw materials used in the firm's products are received in interstate commerce.

I reviewed the firm's Certificates of Exportability, **Exhibit 4A**. The certificates expire 10/18/08 and 9/21/08. I asked if the firm had renewed their certificates. Ms. Roode said she sent in the renewal but did not maintain a copy. On 10/9/08, I asked if the firm received their new Certificates of Exportability. Ms. Roode said she had just received them, **Exhibit 4B.**

I requested a copy of the firm's customer list for human IVDs. On 9/9/08, Ms. Roode provided to me the firm's current customer list, **Exhibit 5A.** She said the customers on the list receive human IVD devices. She said the list does not include IVDs sold to USDA firms or for Research Use Only (RUO). Ms. Roode also provided to me an additional customer list. She highlighted in yellow, the firm's in the United States (U.S.) they sold IVD kits to within the last two years (2006-2008), **Exhibit 5B.** Ms. Roode provided to me a third list. This is a list of customers she said also purchase bulk products (b) (4) such as positive and negative controls, buffers and stop solutions, **Exhibit 5C.**

On 9/18/08, Ms. Roode provided to me the firm's U.S. distributor list, **Exhibit 6.** I asked if (b) (4) (b) (4), which she identified on their customer list, was a distributor for the firm. Ms. Roode said they were. I asked why they had been left off the distributor list. She said she wasn't sure. Later in the discussion, Ms. Roode said (b) (4) was also a distributor of the firm. I asked why they were not on the firm's distributor list. She again said she wasn't sure. I requested a current list of the firm's U.S. distributors.

On 9/22/08, Ms. Roode provided to me a new distributor list which she said was the most current list, **Exhibit 7A.** I requested this list to include the address locations for U.S. distributor. Ms. Roodes provided to me a new list which included the address locations of the U.S. distributors, **Exhibit 7B.** Ms. Roode said none of the distributors on the lists were for the distribution and sale of USDA or RUO devices.

During the inspection, I requested an Invoice for the last sale of Chagas. Ms. Roode provided me with an Invoice, dated 6/11/08 which stated "RUO9". Ms. Roode also provided to me the tracking sheet which stated "Research Use". I again asked if any of the firm's devices were for RUO. Ms. Roode said there is one firm on the lists provided that does receive RUO devices. The firm is (b) (4) located in (b) (4). She said they have a "RUO" designation in their purchase orders that will indicate if they are requesting to purchase a product for RUO. She said they are one of the firm's distributors, **Exhibit 78.**

Ms. Roode said the firm ships their products using carriers such as (b) (4), (b) (4), (b) (4) and also hand carries products to local customers such as (b) (4)

Ms. Roode provided me with the most recent invoices and the associated shipping (tracking) documents for U.S. companies that have purchased non-cleared IVDs (bulk or kitted). I also requested the associated labeling sent with each device, **Exhibit 70,** (Item number 3 of the assignment). Ms. Roode said some of the IVDs were last sold to a specific company prior to 2007. As such, she said the firm did not keep shipping documents and/or labeling at that time.

Ms. Roode said, Invoice number 5972 (see Exhibit 70) shows the purchase of a Strongyloides kit which had been hand delivered by Mr. Lambillotte to a company located in (b) (4). Ms. Hildebrand said Mr. Lambillotte was hired as a consultant to teach (b) (4) in the use of and/or to manufacturer these kits. She said there is no tracking or shipping information as Mr. Lambillotte brought the kit with him on his flight. She said the kit components were not labeled. As such, no labeling could be provided for this IVD. He received a (b) (4) consulting fee for this service.

Ms. Roode said Invoice number 4892 (see Exhibit 70) was actually a Schistosoma kit sold to the (b) (4) (b) (4). She said the Invoice says it is a Strongyloides kit which is an error.

Ms. Roode said with Invoice number 5865 (see Exhibit 70) there is a notation that says Lepto M (cal.) DFU needs revision. I asked Ms. Roode what this meant. She said the firm needed to update the DFU on file with (b) (4). She said IVD Research will provide one DFU to their distributors for them to keep on file. The distributor in turn will use that information and reformat the labeling (DFU) with their letter head. The date (b) (4) last received an IVD Research DFU is unknown per Ms. Roode.

I requested a copy of the DFU on file at (b) (4) which required updating. Ms. Roode provided this DFU enclosed with Invoice 5865, Exhibit 70. The DFU is dated 9/2007. Ms. Roode also said the distributor (b) (4) (b) (4) will translate the DFU into another language if it is to be sold for export. Ms. Roode said distributors such as (b) (4) will receive labeled, bulk components (b) (4) which the distributor in-turn will place into kitted devices under their name.

I also collected all agreements the firm has on file with their U.S distributors, **Exhibit 71**, (Item number 3 of the assignment).

JURISDICTION

Ms. Roode said the firm manufactures Class I, Class II and Class III, ELISA wells (strips) IVDs for sale and distribution. She said the firm also manufactures and sells IVD solutions such as buffers, wash solutions and stop solutions which can be sold separately based on customer orders.

Ms. Roode said the firm has the following 510ks:
Giardia (K020583)
Crytpo/Giardia (K024113)
C. Difficile Toxin A + B (K032897)
Cryptosporidium (K031059)

I requested a list of IVDs the firm manufactures and requested the firm designate if they are Class I, II or III; the 510k or PMA number; and if they are sold in the U.S. and/or for export only. Ms. Roode provided this list, **Exhibit 8,** (Item number 1 of the assignment).

The IVDs identified in Exhibit 8 for which labeling was not provided either have 510k Clearance or are exempt per Ms. Roode. Ms. Roode also provided me with a copy of the firm's product brochure **(Exhibit 37)**. She also provided me with the firm's outer boxes for fully kitted (b) (4) IVDs **(Exhibit 38).**

Ms. Roode provided me with labeling for the firm's products which have not been cleared (see 510k listing, Exhibit 8) including those sold for RUO, **Exhibits 9 – 36.** Exhibits16, 18, 20, 27 and 30 are IVDs with Calibrators. Exhibit 23 is the Chagas DFU with the RUO designation and associated labels. The RUO labeling contains product specifications and references patient use, (Item number 4 of the assignment).

I asked Ms. Roode for a listing of all sales to (b) (4); (b) (4); the (b) (4) (b) (4); and (b) (4). Ms. Roode provided me with all invoices associated with the sale of IVD products to (b) (4) at my request (note: the most current sale, Invoice 5865, is located in Exhibit 70). Additional Invoices, labeling and tracking documents for domestic shipments were also included with some of these records, **Exhibit 72.**

The firm's SafePath products are for animal use only and were not covered during this inspection. Mr. Lambillottee said the firm's SafePath products are regulated by the USDA.

The firm markets or promotes their products at industry meetings and on the company website which is www.ivdresearch.com.

RESPONSIBILITY AND PERSONS INTERVIEWED

Mr. Lambillotte, President and owner: Mr. Lambillotte said he has owned IVD Research since 1996. He said he has ultimate responsibility for the firm's operations. Mr. Lambillotte said he is not as involved with the day-to-day operations as he was during the last inspection. He said he is at the firm on a daily basis and primarily handles new sales and budgets. He said he also oversees laboratory operations, answers questions and occasionally helps in the manufacture of products. Mr. Lambillotte said he recently hired Kathy Hildebrand and Shelby Hall to conduct validations and other duties for compliance with the quality system regulations. Mr. Lambillotte said he has the authority to stop all operations, has hiring and firing authority and makes all decisions regarding capitol expenditures at the firm.

Kathy Hildebrand, Director of Operations: Ms. Hildebrand said she was hired in July 2008 as the Director of Operations. She said prior to working at IVD Research, Inc. she worked for (b) (4) (b) (4) as the Director of Operations. She said (b) (4). Ms. Hildebrand said she oversaw all manufacturing and quality control operations at that firm. In her position with IVD Research, she said she was hired to oversee the firm's day-to-day operations. She said she is responsible for complaints, CAPA, developing policies and procedures, shipping, receiving, quality assurance and quality control. Ms. Hildebrand said she has hiring and firing authority over laboratory personnel and can make capitol expenditures up to (b) (4). She said she has (b) (4) direct reports which are production technicians. Ms. Hildebrand answered questions regarding the firm's daily operations, purchasing controls, manufacturing, validations, design controls and receiving. She said she reports directly to Mr. Lambillotte.

Crystal Roode, Regulatory Assistant QC Technician: Ms. Roode said she has worked for the firm for 4 years. She said she is responsible for document control, purchasing controls, QA/QC operations, receiving, shipping and conducts laboratory procedures such as quality control tests for final release. Ms. Roode is the firm's designated Management Representative. Ms. Roode said she has a degree in Biology from (b) (4) (b) (4). She has no prior work experience. Ms. Roode answered questions regarding the firm's daily operations, design controls, complaints, CAPA, purchasing controls, manufacturing, procedures, shipping and receiving. She said she reports directly to Ms. Hildebrand.

(b) (6) **Consultant:** (b) (6) said he is the firm's consultant. He said he was hired to conduct calibrations of equipment, equipment qualifications and process validations. (b) (6) said he has worked for the firm for 2 years. Prior to working at IVD Research, he worked for (b) (4) as a facilities manager. He said he conducted validations, calibrations and instrument qualifications at (b) (4) (b) (6) reports directly to Mr. Lambillotte.

(b) (4)

MANAGEMENT CONTROLS

I reviewed the Quality Manual, Quality Policy, Organizational Chart, Management Review and Internal Audit procedures. The firm has established an organizational structure and has documented the Management Representative. Ms. Hildebrand said the firm has begun to implement quality audits. She said they are conducted by (b) (6) . I reviewed the firm's internal audit schedule for 2008, which appeared in order. Management reviews are held (b) (4) . I reviewed the last management meeting agenda items held in (b) (4) and executive management was in attendance.

MANUFACTURING / DESIGN OPERATIONS

Design Operations

I reviewed the firm's design control procedures, **Exhibit 39.** The procedures require the completion of checklists as the Design History File (DHF). The procedures were developed and implemented in 2002. Some of the procedures were updated in 2008. Mr. Lambillottee said the firm developed these procedures in order to come into compliance with the quality system regulations. He said they completed the check lists to establish a DHF. However, he said he has no supporting documentation other than laboratory notebook pages which show a general description of how each IVD was originally manufactured, **Exhibits 40-46.** Mr. Lambillottee said the laboratory notebook pages are the first production of each device.

He said he keeps the laboratory notebooks in his office and they have not been made part of each DHF. I included the notebook pages requested (Leptospira, Chagas and Dengue) with each DHF exhibit to show the time frame of first production and subsequent design changes.

Mr. Lambillotte said he had no information related to how each device was developed (e.g. Leptospira, Chagas and Dengue); where the formulation came from and had no design specifications for these devices. Mr. Lambillotte said some of these devices were pre-device regulations (e.g. Dengue IgG) and as such these were not included in the design observations cited. The other devices were designed after June 1998 when design controls were in affect. Ms. Hildebrand said design changes to each device had also been made over the years such as labeling and dilution concentrations but the change had not been documented.

Ms. Hildebrand said the firm has no design and development plan for any of their devices. Ms. Roode and Ms. Hildebrand agreed a design and development plan was required for the following devices: Leptospira IgG, Leptospira IgG/IgM (total), Leptospira IgM, Dengue IgM and Dengue IgG/IgM (total), **FDA-483, Observation 1.**

I asked Ms. Hildebrand for the firm's device master record for Dengue, Chagas and Leptospira. Ms. Hildebrand said there is no device master record for any of the firm's devices.

Ms. Roode said there is no device master record (e.g. labeling specifications, packaging specifications and formulation specifications) for Leptospira IgG, Leptospira IgG/IgM (total), Leptospira IgM, Dengue IgM, Dengue IgG/IgM (total), **FDA-483, Observation 2.**

Mr. Lambillotte confirmed this information was correct. He said he developed the firm's devices from his knowledge of IVD processes over the years such as with Dengue, Chagas and Leptospira. He said the only information he has is what is maintained in his laboratory notebooks for these devices, (See Exhibits 40-46).

I asked for the dates of the first commercial distribution of Dengue, Chagas and Leptospira to U.S. companies by the firm, (Item #2 of the assignment). Ms. Roode provided Invoices for the first commercial sale of Dengue, Chagas and Leptospira within the U.S., (See Exhibit 40-46). Note: I included these Invoices as the first page of each DHF exhibit.

Ms. Roode said the only documentation the firm kept for the first commercial distribution of Dengue, Chagas and Leptospira is an invoice of the first sale of these devices. Ms. Roode said the firm did not maintain any tracking records to show how these devices were shipped in domestic commerce.

I stated and Ms. Hildebrand acknowledged the firm's procedures to control the design process of the firm's devices (e.g. Dengue, Chagas and Leptospira) were not complete and/or were not implemented. For example, the procedures do not require safety and risk analysis factors and system requirements such as software and equipment specifications, **FDA-483, Observation 3, #1.** The procedures also do not require the firm to document design validations such as written product specifications, protocols, expected outcomes and final results, **FDA-483, Observation 3, #2.**

I also observed the firm has not implemented their design control procedures for changes made to their IVDs. I reviewed the firm's DHF and device history records (DHR) and noted the firm made changes to Dengue, Leptospira and Chagas IVDs after they had been released to production. For instance, the firm changed the positive control for Leptospira IgM, Leptospira IgG and Leptospira IgG/IgM from what had been established in the DHFs for these devices.

Ms. Roode said the firm initially developed the Leptospira device using a (b) (4) serum (DHF) (e.g. see Exhibit 40, page 12), but the supply ran out so they switched to a (b) (4) serum (see DFUs), (e.g. see Exhibit 40, page 27 and 35). Ms. Roode said then the supply of (b) (4) serum ran out so they switched to (b) (4), (e.g. see Exhibit 41, page 14 and page 21). Ms. Hildebrand said none of these changes had been documented in the DHF and had not been validated, **FDA-483, Observation 3, #3 and #4.**

Ms. Hildebrand said the firm also made changes to the quality control requirements for the Leptospira IgM (See DHF for Leptospira IgM). Ms. Hildebrand stated the reason why this change was made, the date it was made and the supporting documentation was unknown as it had not been documented in the DHF and had not been validated, **FDA-483, Observation 3, #3.** The DFU for Leptospira IgM, dated 4/2003 (See DHF) stated an index value of less than (b) (4) for the negative control and an index value of greater than (b) (4) for the positive control. The DFU dated 5/2006 (See DHF) changed this value to (b) (4) to (b) (4) for the negative control and (b) (4) for the positive control.

The firm also did not document or validate changes to the firm's DFU for Chagas, Dengue and Leptospira. In addition, the firm's dilution for the manufacture of the Leptospira IgG strips was (b) (4) in the DFU, (Exhibit 41, page 8). Ms. Hildebrand said this dilution changed to a (b) (4) for the (b) (4) preparation. Mr. Lambillotte said the concentrations will vary depending on the antibody strength.

The firm also changed the Leptospira (b) (4) buffer for the positive control (DHF) to an (b) (4) (b) (4) Buffer (DHR), (see Exhibit 65, page 2). Ms. Hildebrand said the reason for this change and the date of the change had been made was unknown as it had not been documented in the DHF and had not been validated.

Ms. Hildebrand highlighted each change in pink (see DHFs, e.g. Exhibit 42, page 14) from what is currently being used for these IVD kits (See DHRs, Exhibits 65-69). The firm also added a (b) (4) to some of their kits, (See Exhibits 9-38, labeling). The date of this change was not documented.

I asked to see the firm's stability studies to support expiration dates as specified in Attachment 1-1, (SOP-036), **Exhibit 47.** Ms. Roode said no studies had been performed and the data contained in Attachment 1-1 is based on their experience with IVDs and industry standards, **Observation 3, #5.**

I asked if the firm ever conducted any shipping studies to ensure IVDs are received within the specified temperature range as stated in their DFUs. Ms. Hildebrand said no. She said they will ship the IVD on ice if needed but no studies have been conducted. I noted some shipments are sent (b) (4) and may travel several days to arrive at a company location (see Exhibit 69A, page 10).

Production and Process Controls

IVD Research is located in a business park and occupies (b) (4) square feet. The facility is separated into an office area, manufacturing and testing, and a warehouse. The warehouse contains raw material freezers and finished devices. The manufacturing area is an open room divided by employee work benches and large work tables. Some room temperature in-process materials are stored around the perimeter of the room.

The manufacturing area also contains the computer that stores the (b) (4) software and the master labels. The product labels are stored electronically and printed as needed. Mr. Lambillotte said they do not typically keep labeled IVD kits in inventory. He said the components are assembled into kits and labeled after receiving a request from a customer. He said the order sizes could vary from (b) (4) kits. He said they prepare a limited number of components in advance and maintain a small inventory for last minute kit orders.

Labeling

The firm uses a (b) (4) labeling system identified below:

(b) (4) labels are placed on bulk product containers such as reagents, buffers and other solutions shipped to customers.

(b) (4) labels are placed on IVD products sold in bulk called (b) (4). Ms. Roode said the individual kit component (solutions, buffers, plates) are not labeled. She said each component is placed, in bulk, into clear plastic bags and the outer bag is labeled as to its contents (e.g. Stop Solution, IVD Plates). An example of this packaging and labeling can be seen in Exhibit 68, page 19-21. Ms. Roode said an IVD Research DFU is not provided with each bulk shipment.

(b) (4) labels called (b) (4) are for fully assembled kits with IVD Research's labeling (letterhead and address) on all kit components and the outer box, (See Exhibit 38). Ms. Roode said an IVD Research DFU is provided with each kit.

IVD Research also ships plain white boxes with each order for labeling by the distributor as in the case of (b) (4). In this case, Ms. Roode said, (b) (4) will place their own label on the outer boxes for sale and distribution.

Ms. Roode said each bulk kit (b) (4) is shipped to a distributor who will assemble the kit and place their labeling (letterhead and address) on the outer box and kit containers. Ms. Roode said if the IVD is sold in bulk (b) (4), than IVD Research is an OEM manufacturer for the company it is sold to.

In some cases, as with (b) (4). the firm will ship labels with the distributor's name and address on the label. An example of these labels can be seen in Exhibit 72.

Process Validation

I asked Ms. Hildebrand for the firm's validation of the manufacturing processes for Dengue, Leptospira and Chagas. Ms. Hildebrand said the firm has not validated any IVD manufacturing processes including those for Dengue, Leptospira and Chagas, **FDA-483, Observation 4, #1,** (Observation #4 is a repeat observation from the 12/2004 inspection). Ms. Hildebrand was not able to provide any documentation to show a process had been validated as she said the firm has not validated any of their manufacturing processes. She said there are also no established procedures for conducting process validations.

I asked Mr. Hall for a list of the firm's equipment and dates of last calibrations, **Exhibit 48.** Mr. Hall provided this list and indicated which ones were in use and which are designated for USDA use. He said the majority of the equipment designated for human IVD manufacturing had never been calibrated. He said, the dates of calibration were not included on the list provided as they had not yet been conducted. Mr. Hall said he is in the process of having this completed.

Mr. Hall acknowledged there is no documentation of calibration dates, the individual performing each calibration and the next calibration date for measurement and test equipment has not been established. (Observation #16 is a repeat observation from the 12/2004 inspection). Mr. Hall said there are no calibration records for the (b) (4) equipment used to fill IVD plates, **(FDA- 483, Observation 16 #1);** the (b) (4) Plate Reader, **(FDA- 483, Observation 16 #2);** and weekly calibration of the firm's pH meter used in production is not being documented, **(FDA- 483, Observation 16 #3).**

Ms. Hildebrand said (b) (6) has also begun to qualify the firm's equipment but it is not yet complete. For instance, the firm purchased their new (b) (4) reader in May 2008. The firm has been using a (b) (4) reader prior to this date. (b) (6) said the (b) (4) reader was not qualified until 9/19/08. He said he completed the IQ, OQ, and PQ during this inspection and the PQ had been completed 9/19/08. I reviewed the qualification documentation and observed this was the date the IQ, OQ and PQ had been started and completed, **FDA- 483, Observation 4, #2.** I asked (b) (6) for a copy of the cover page of each to show the start date and completion dates of each qualification however, by the close of the inspection, (b) (6) did not provide this information.

Procedures

I also reviewed the firm's (b) (4) Filling Procedure using the (b) (4) equipment, (SOP-097, Rev 1, dated 1/2/08), **Exhibit 49.** This equipment is used to fill IVD plates at the firm. I observed one of the firm's technicians filling IVD plates for Fasiola (no other production was occurring at the firm during this inspection). The technician, (b) (6), rinsed the (b) (4) equipment with (b) (4) water prior to the start of the test. I asked if this is how he cleans and maintains the equipment and he said yes. He said no other cleaning procedure or methods are used at the firm.

The (b) (4) Filling procedure specifies a required cleaning procedure at the beginning and end of each day and during cleanup between batches of different IVDs. I asked if this procedure was being used at the firm and if it had been validated. Ms. Roode said no, **FDA- 483, Observation 4, #3**. Ms. Roode said the last time they used this procedure was in July 2008. She said the laboratory technicians should be filling out the Maintenance Log to show the cleaning had been performed. The last cleaning recorded was in July 2008, (See Exhibit 49), **FDA- 483, Observation 6, #2.**

Storage

I observed (b) (4) freezers in the firm's back storage area. These freezers are not labeled and there is a mix of different products stored in each freezer. The raw materials are stored in plastic bags. Ms. Roode said when the firm receives a product they will store them in these freezers until they have been "accepted". She said they consider these products to be "R & D" until they are either tested or accepted by way of a Certificate of Analysis (COA). Then the raw material receives an "Accept" sticker and is placed into the production freezer located in the laboratory. Ms. Roode said there is no written procedure for this process.

However, during the inspection, I observed several bags of antibodies and other IVD components to have Accept stickers and/or Quarantine stickers in the back storage area freezers. I observed several components to be expired and/or have no sticker at all with just a name on the product such as "Fasciola and Ascaria Bleeds, 11-30-06". I asked Ms. Hildebrand to photocopy this bag of product, **Exhibit 50.**

Another product (Toxocara) had a Quarantine sticker dated 6/28/04, **Exhibit 51**. Others were given a receiving number (RCV number) but had no "accept" sticker. Some are expired (e.g. Leptospira positive serum, RCV# 568-3 and RCV# 568-4, expiration date of 10/00) and/or have dates dating back to 1998 (e.g. Tococara RCV # 1400). Others have no dates at all on them, **Exhibit 52**. Ms. Roode said she is not able to tell me when some of these raw materials had actually been received, where they had been used and their age because she said the firm's receiving log does not go back that far.

I asked Mr. Lambillotte if he uses expired products in IVDs. He said he is able to use all components stored in the freezers as they never really expire. He said as long as they are frozen, they can be used. Later, during the inspection, Ms. Roode said the raw materials with expiration dates are used for R&D purposes only.

Ms. Hildebrand explained as raw materials are "received" from the warehouse freezers, they are given a RCV number prior to use in production. She said the firm does not "receive" a raw material, date it and number it upon receipt and storage in the warehouse freezers. She said the RCV number gets assigned once the firm decides to use that raw material in an IVD. Then it gets logged into their log book and can then be tracked through production. Ms. Hildebrand also said the firm does not have an inventory system for what is being stored in the warehouse freezers.

Ms. Roode also said the firm continues to send antigens to a farm located in (b) (4). She said the farm injects rabbits and goats with the antigen for antibody production. Once antibodies are generated, the firm purchases the antibodies for use in their IVDs. The farm is called (b) (4) located at (b) (4) (b) (4). Mr. Lambillotte said the farm is inspected by the U.S.D.A. Ms. Roode said the firm also purchases antibodies from (b) (4) such as Cryptosporidium and Giardia. Ms. Roode said (b) (4) is on the firm's approved supplier list.

Ms. Hildebrand agreed the firm has not established procedures for the control of raw materials received and stored such as bleeds (antibodies) used in the firm's IVDs to prevent mix-ups, damage, deterioration, contamination or other adverse effects pending use and to ensure that no obsolete, rejected or deteriorated product is used or distributed, **FDA-483, Observation 5,** (Observation #5 is a repeat observation from the 12/2004 inspection).

Ms. Roode said raw materials such as "bleeds" and positive and negative controls are frozen and thawed then re-frozen and re-thawed several times during the year for different production runs. I asked Ms. Roode's if the firm had established procedures and/or validated for the number of times a raw material such as an antigen and antibody can be frozen and thawed prior to use. She said no, **FDA-483, Observation 6, #1.**

I asked if the firm had process control procedures that describe any process controls necessary to ensure conformance to specifications. I was provided with the firm's Filling Solutions Procedure, SOP-020, Rev 2, dated 12/13/07 which requires the completion of production and process forms (b) (4) for bulk and production solutions, **Exhibit 53.** I asked if these forms were being used and made part of the DHR. Ms. Hildebrand said no, **FDA-483, Observation 6, #3.**

I noted the firm was not following their Material Inspection Procedure, SOP-033, Rev 2, dated 1/14/08 for the control of labels, **Exhibit 54**. Labels are not made part of the firm's DHR, **FDA-483, Observation 6, #4.**

Ms. Hildebrand also acknowledged the fact the firm is not following their Purchasing Control Procedure SOP-077 and Purchasing Procedure, SOP-003, which requires the purchase of product through approved vendors, **Exhibit 55 and 56, FDA-483, Observation 6, #5.**

DHRs

I reviewed 11 device history records as per QSIT, Table 1, Row B. I observed all 11 DHRs lacked formulations and processes steps. The firm is not recording or documenting the formulations for making IVD strips, (See exhibits 65-69B and 75-78).

Solution buffers are recorded on forms but not referenced or made part of the DHR. Ms. Roode said these forms are kept in a separate file and if the RCV number is not recorded in the laboratory notebooks then the firm is unable to trace back to the exact dilution buffer or solution used in that IVD.

In addition, 11 out of 11 DHRs reviewed showed the firm was using previously recorded information in their notebooks to manufacturer an IVD. The information lists part numbers for the analyst to make an IVD. I asked (b) (6) how he knows what dilutions to make and how he knows what the mixing times are. He said he just knows from past experience. He also said the Executive VP of R&D, Bret Sheffield will take an

antibody from the freezer and calculate the dilutions needed. This information is written on the back of a sticker and that is how he knows which dilution will work for the batch he is making.

The DHRs also confirmed a surrogate, (b) (4) surum is being used as the positive control for Leptospira IVDs. The DHFs state the positive control for Leptospira is a (b) (4) serum. The firm's DFU says the positive control is a (b) (4) serum (See Exhibits 40-46).

I asked Ms. Roode if the firm had procedures to ensure the device history records for each batch, lot, or unit are maintained to demonstrate that the device is manufactured in accordance with the device master record and the Quality Systems regulation. Ms. Roode said the firm only has general procedures which describe the general manufacturing practices such as cleaning the work space before starting a kit, final kit assembly procedure which defines the final job number for a product and a strip production procedure which gives general steps of completing paperwork in the production of an IVD plate.

I reviewed the firm's Strip Production procedure SOP-019, Rev 4 dated 12/13/07, **Exhibit 57**. The procedure does not provide product specific specifications. Ms. Roode said IVDs are manufactured using notes recorded from previously produced batches. She said there are no written specifications (DMR) and no work instructions (e.g. mixing and drying times) for manufacturing an IVD, **FDA-483, Observation 8.**

As part of this assignment, I collected examples of each device history record (DHR) for Dengue IgM, Dengue IgG, Dengue IgM/IgG (total); Chagas and Leptospira IgM, Leptospira IgG and Leptospira IgM/IgG (total), **Exhibits 65- 69.** (Note: the DHR for Leptospira IgG/IgM (total) and Dengue G are in CR numbers 250488 and 250489).

I asked for the associated labeling that went with each DHR collected (b) (4). I also requested and received an Invoice and tracking record for each DHR. These are included with Exhibits 65-69. The Invoices and tracking records show non-cleared IVDs sold and shipped to distributors and other customers within the U.S.

The DHR for Chagas, (Exhibit 67) has labeling which says for "Export only". The DHR for Dengue IgM (Exhibit 68, page 3 and 14-17) shows this kit was manufactured using a positive human serum as the positive control. Ms. Roode provided the Invoice for the purchase of this serum. It is labeled Lot# (b) (6) and is dated 7/14/06. She said the person was sick with Dengue and her blood was purchased and used as the control for this kit, (see Exhibit 68, pages 14 – 17). Note: the (b) (4) packaging in this DHR was provided as an example and is not a photocopy of lot number RD1069. However, Ms. Roode said this is the same labeling and packaging sent with all (b) (4) kits", see Exhibit 68, page 24.

I asked if this patient's blood had been tested for HIV and Hepatitis B as stated in the DFU, (e.g. see Exhibit 19A, page 5). Ms. Roode said it had not. She said this blood sample has been stored at the firm and used in IVDs since 2006, (see Exhibit 68, page 17).

The DHR for Dengue IgG/IgM, (Exhibit 69A, page 5) also shows a human serum used as a positive control. I asked for the receiving records to show where this positive control was purchased and any related testing. Ms.

Roode said those records can not be located as this control was purchased prior to the firm implementing procedures to keep this documentation. She provided a receiving log, which shows the positive control was received 11/13/01 from (b) (4) (Exhibit 69A, page 6).

Ms. Roode said there are no testing records or COA to show if this control had been tested for HIV or Hepatitis B as stated in the firm's DFU. This control was used to manufacture Dengue Total on 2/8/08 and 11/12/07, (see Exhibit 69A, page 7 and Exhibit 69B, page 4).

Exhibit 69B, page 4 is another example of a Dengue kit manufactured with this positive control. The IVDs were manufactured on 11/24/07 and have been sold in 2008, (see page 8 and 15).

Ms. Hildebrand agreed that the firm's device history records are incomplete such as missing dates and signatures of operators and reviewers, and processing steps have not been established and documented, **FDA-483, Observation 9.** Ms. Hildebrand stated she is in the process of developing formulation sheets for each IVD which will include ingredient information, amounts of each component to add, concentration and dilutions, mixing times, the technician's signature and date along with a reviewer's signature.

Ms. Hildebrand said the device history record does not include the primary identification label and labeling for each device, **FDA-483, Observation 10.** She said the finished product labels and labeling are not made part of the firm's device history records. She said (b) (4) labels are copied and placed in a file for reference with the Invoice number. However, the labels are not referenced in the laboratory notebooks and not made part of the DHR. She said (b) (4) labels are printed as needed.

Purchasing Controls

I reviewed the firm's Purchasing Control Procedure, SOP-077, Rev 2, dated 1/9/08 (**Exhibit 55**) and Purchasing Procedure, SOP-003, Rev 2, dated 1/29/04, **Exhibit 56.** The firm's Purchasing Control Procedures, SOP-077 and SOP 003 are not complete in that they do not specify quality requirements that must be met by suppliers, contractors and consultants, **FDA-483, Observation 15 #2.**

I requested a copy of the firm's approved vendor list, **Exhibit 73.** I reviewed 11 incoming inspection records in accordance with OSIT, Table 1, Row B for products used in production. I observed the firm received raw materials from (b) (4) and that this firm is not on the approved supplier list, **FDA-483, Observation 13, #3.** Ms. Hildebrand said these are products used for QC purposes only and have not been used in an IVD, **Exhibit 74.**

I reviewed a DHR for Strongylodies manufactured on 9/15/08. This IVD utilized a Strongylodies antigen received from the (b) (4) and a Strongylodies antibody received from the (b) (4). Both of these suppliers are not on the firm's approved vendor list. These products were used in a Strongylodies IVD sold and distributed to several customers. One Invoice and tracking record was collected to document the sale and distribution to (b) (4), **Exhibit 75.** Note: Strongylodies is not a 510k cleared device and is for export only on the firm's 510k listing, see Exhibit 8.

In addition, the paperwork for the Strongylodies IVD does not state whether the antibodies are from a (b) (4) (b) (4) bleed as stated in their DFU and if the negative control is a (b) (4) serum. There is no COA from the (b) (4) and Ms. Roode said this material was not tested prior to use for HIV and Hepatitis B as stated in the firm's DFU. This was verbally discussed with Ms. Hildebrand and Ms. Roode.

I observed (b) (4) is not on the firm's approved supplier list. The firm received Fasciola antibodies from this company on 2/6/06. No COA or testing data is attached, **FDA-483, Observation 13 #2, Exhibit 76.** Also included in Exhibit 76 is a Fasciola rabbit antigen received into production on 7/25/07. Ms. Hildebrand said there is no information on where this product was purchased. It was used as a positive control in one of the firm's IVDs, LN 556 and sold to a firm is (b) (4). (b) (4) IVDs remain in inventory. Note: Fasciola is not a 510k cleared device and is for export only on the firm's 510k listing, see Exhibit 8.

I observed (b) (4) is not on the firm's approved supplier list. The firm purchased a Toxocara antibody from them on 12/15/05. There is no COA and no testing data associated with this purchase. This antibody was used in the manufacture of a Toxocara IVD on 6/13/07, RD852. (b) (4) the kits were sold to the (b) (4) located in (b) (4), **FDA-483, Observation 13 #1, Exhibit 77.** Note: Toxocara is not a 510k cleared device and is for export only on the firm's 510k listing, see Exhibit 8.

The firm's consultant, (b) (6) is not on the firm's approved supplier list, **FDA-483, Observation 13 #4.**

Ms. Hildebrand acknowledged the firm has not established purchasing information that clearly includes/describes the specified requirements for purchased or otherwise received products and services. (Observation #14 is a repeat observation from the 12/2004 inspection). I stated the firm has not specified requirements for purchased products and services, **FDA-483, Observation 14 #1.** The firm has not established purchasing agreements with the (b) (4), (b) (4) and their consultant, (b) (6), **FDA-483, Observation 14 #2.**

I observed that adequate quality requirements that must be met by suppliers were not defined and documented. Ms. Hildebrand acknowledged that the firm has not established quality requirements that must be met by suppliers, **FDA-483, Observation 15 #1.**

I observed and Ms. Hildebrand acknowledged that not all suppliers are qualified before use in accordance with the firm's Purchasing Control procedure, **FDA-483, Observation 15 #3.**

Complaints/MDR/CAPA

I reviewed the firm's Product Complaint and Investigation procedure, SOP-009, Rev 1, dated 12/12/07, **Exhibit 58.** I noted that the procedure requires a formal statement from a complainant in order for it to be a complaint. Ms. Hildebrand said she would remove that statement as some people may not make that statement verbally but they may still be making a complaint. I also noted the firm's procedure requires complaints to be written and transmitted to the President within (b) (4) of receipt. The procedure also requires the complaint form be completed and assigned a number within (b) (4) hours of notification

I reviewed the firm's complaint log from 2004- present, **Exhibit 59.** Ms. Roode said the firm does not receive many complaints. For instance, the log shows (b) (4) complaints for 2008. I asked why 2006 complaints

were recorded out of order on the log. Ms. Hildebrand said the firm's has not been consistent in how these have been recorded.

I reviewed 11 complaints in accordance with QSIT, Table 1, Row B. My review showed the firm was not implementing their procedure to ensure that all complaints are processed in a uniform and timely manner. For instance, Customer complaint PCI# (b) (4) was received 6/30/08. The retain sample was tested on 7/18/08. The PCI form was not completed until 8/22/08, **Exhibit 60, FDA-483, Observation 11, #1a.** Customer complaint PCI# (b) (4) was received 11/21/07. The PCI form was not completed until 5/13/08 and the complaint was not investigated, **Exhibit 61, FDA-483, Observation 11, #1b.**

I also asked if complaints involving the possible failure of the device were investigated to determine if they failed to meet defined specifications. Ms. Roode said the firm usually will test the retain samples kept and to see if they meet the quality control parameters. However, if they do not receive back the complaint samples, sometimes the case is closed and no further action is taken. I noted several complaints had not been investigated because samples had not been returned. For instance, complaint PCI # (b) (4) was not investigated because the firm did not receive back the IVD referenced in the complaint, **Exhibit 62, FDA-483, Observation 12, #1.** Complaint PCI # (b) (4) was not investigated because the firm did not receive back clearer data, **Exhibit 61, FDA-483, Observation 12, #2** and complaint PCI # (b) (4) was not investigated because the kits were returned because "FDA discontinued sales in the USA", **Exhibit 63, FDA-483, Observation 12, #3.** I asked Ms. Roode why this statement had been made on the complaint form. She said because that is what the customer told them when the complaint was made. (Observation #12 is a repeat observation from the 12/2004 inspection).

I asked if the firm had a written MDR procedure and if they evaluated complaints for MDR reporting. Ms. Hildebrand said the firm has not established a written MDR procedure, **FDA-483, Observation 7.** She also said the firm would begin to evaluate complaints for MDR Reporting. Ms. Roode said the firm has never filed an MDR and I confirmed this via the FDA website.

I reviewed the firm's Corrective and Preventive Action Procedure, SOP-076, Rev 2, dated 1/9/08. I reviewed the firm's CAPA Index from 2006 to present, which recorded (b) (4) CAPAs in the last (b) (4) years. Ms. Hildebrand said the firm has begun to open CAPAs as required by their procedure.

MANUFACTURING CODES

The firm assigns a final lot number to all (b) (4) and (b) (4) (Fully assembled) kits. Ms. Roode said the firm is required to use an RD designation before the sequential number if the final lot is manufactured for Research Use Only and an LN designation if the final lot is for commercial distribution. However, she said they have not had good control over their numbering system and the firm's laboratory personnel was assigning RD numbers to all final lots produced. As such, Ms. Roode said there is no difference between an RD and LN number. She said all of the lots, regardless if there is an RD or LN lot number, were sold for commercial distribution. Ms. Roode said the only product sold for RUO was to (b) (4), (b) (4) and their invoice indicates this as such by the code RUO.

I reviewed the firm's Lot Number Assignment procedure, SOP-008, Rev 3, dated 12/13/07 and Final Kit Assembly SOP-021, Rev 3, dated 12/18/07, **Exhibit 64.** Ms. Roode said the procedures are not being followed in that RD numbers have been assigned to IVD batches released for distribution. She said the firm began to use the LN designation consistently during this inspection. Ms. Roode also explained the coding system for a final lot. She said a (b) (4) job number is recorded as exampled below:

(b) (4)

Ms. Roode said all (b) (4) jobs are being recorded on the (b) (4) job form, (See Exhibit 64).

REFUSALS

No refusals were encountered during the inspection.

DISCUSSIONS WITH MANAGEMENT

On 10/9/08, I issued a 16-item Inspectional Observation, FDA-483, to Ms. Kathy Hildebrand, Director of Operations. Also present was Ms. Crystal Roode.

Prior to the FDA-483 discussion, I explained the FDA-483 represented my observations of objectionable conditions made during the inspection and that these conditions might be determined, after review by the agency, to be violations of the Federal Food, Drug and Cosmetic Act which could result in the issuance of a warning letter or other regulatory actions. I discussed the Inspectional Observations with Ms. Hildebrand and Ms. Roode and provided an opportunity for discussion.

Mr. David Lambillotte, President was out of the office and not available this day. Ms. Hildebrand and Ms. Roode agreed with the observations and promised to correct each observation. Ms. Hildebrand said she would send a written response to the Los Angeles District Director within (b) (4) days.

OBJECTIONABLE CONDITIONS AND MANAGEMENT'S RESPONSE
(Note: Observations 4, 5, 12, 14, and 16 are repeat observations from the 12/2004 inspection)

Observations listed on form FDA 483

OBSERVATION 1

A design and development plan has not been established.

Specifically, there is no design plan for the following devices:

a. Leptospira IgG
b. Leptospira IgG/IgM (total)
c. Leptospira IgM
d. Dengue IgM
e. Dengue IgG/IgM (total)

Annotation: Promised to correct

Reference: 21 CFR 820.30(b)

Supporting Evidence and Relevance: The firm has no design and development plan for devices.
Exhibits 39-46

Discussion with Management: Ms. Hildebrand and Ms. Roode agreed with the observation and promised to correct.

OBSERVATION 2

The device master record does not include or refer to the location of specifications.

Specifically, there is no device master record (e.g. labeling specifications, packaging specifications, formulation specifications) for the following devices:

a. Leptospira IgG
b. Leptospira IgG/IgM (total)
c. Leptospira IgM
d. Dengue IgM
e. Dengue IgG/IgM (total)

Annotation: Promised to correct.

Reference: 21 CFR 820.181(a)

Supporting Evidence and Relevance: The firm has no device master record for devices.
Exhibits 39-46

Discussion with Management: Ms. Hildebrand and Ms. Roode agreed with the observation and promised to correct.

OBSERVATION 3

Procedures to control the design process of the device were not complete and implemented.

Specifically, the firm's design control procedures are not complete and/or have not been implemented. For example,

1. They do not require safety and risk analysis factors and system requirements such as software and equipment specifications.

2. They do not require fully documented design validations which include written product specifications, protocols, expected outcomes and final results.

3. Changes made to the quality control requirements for the Leptospira IgM and changes made for the positive control for the Leptospira from a (b) (4) to a (b) (4) serum were not documented and validated.

4. Changes made for the Letpospira from a (b) (4) serum to a (b) (4) (b) (4) have not been documented and validated.

5. The firm has not conducted stability studies to support expiration dates as specified in Attachment 1-1, (SOP-036).

Annotation: Promised to correct.

Reference: 21 CFR 820.30(a)

Supporting Evidence and Relevance: The firm is not implementing their design control procedures such as design changes and design transfer. The firm's design control procedures are also incomplete as they do not

require specific information to be implemented, maintained and recorded such as design validation, equipment requirements, written protocols and final results.
Exhibits 39 and 47

Discussion with Management: Ms. Hildebrand and Ms. Roode agreed with the observation and promised to correct.

OBSERVATION 4

A process whose results cannot be fully verified by subsequent inspection and test has not been validated and approved according to established procedures.

Specifically,

1. Manufacturing processes for Dengue, Leptospira and Chagas have not been validated.

2. The (b) (4) reader was not qualified until 9/19/08.

3. Cleaning as specified in the firm's procedure, SOP-097, Rev 1 for the (b) (4) equipment used to fill IVD plates has not been validated.

Annotation: Promised to correct.

Reference: 21 CFR 820.75(a)

Supporting Evidence and Relevance: The firm's manufacturing processes for Dengue, Leptospira and Chagas have not been validated. The firm's (b) (4) plate reader was not qualified until the inspection and competed on 9/19/08. This equipment is used during the manufacturing processes of IVDs at the firm. The firm's cleaning and maintenance procedure for the (b) (4) equipment was not validated. All plate IVDs are filled using this machine.
Exhibits 49 and 48

Discussion with Management: Ms. Hildebrand and Ms. Roode agreed with the observation and promised to correct.

OBSERVATION 5

Procedures for controlling the storage of product in storage areas and stock rooms were not established to prevent mix-ups, damage, other adverse effects.

Specifically, the firm has not established procedures for the control of raw materials received and stored such as bleeds (antibodies) used in the firm's IVDs to prevent mix-ups, damage, deterioration, contamination or other adverse effects pending use and to ensure that no obsolete, rejected or deteriorated product is used or distributed.

Annotation: Promised to correct

Reference: 21 CFR 820.150(a)

Supporting Evidence and Relevance: The firm has not established procedures for the control of raw materials received and stored such as bleeds (antibodies) used in the firm's IVDs to prevent mix-ups, damage, deterioration, contamination or other adverse effects pending use and to ensure that no obsolete, rejected or deteriorated product is used or distributed.
Exhibits 50 - 52

Discussion with Management: Ms. Hildebrand and Ms. Roode agreed with the observation and promised to correct.

OBSERVATION 6

Process control procedures that describe any process controls necessary to ensure conformance to specifications were not established and implemented.

Specifically,

1. The firm has not established procedures for the number of times a raw material such as an antigen and antibody can be frozen and thawed prior to use.

2. The firm is not cleaning the (b) (4) equipment and maintaining cleaning logs (b) (4) as specified in SOP -097, Rev 1. The last cleaning entry for this unit is dated July 2008. This equipment is used to fill all IVD kit strips (plates).

3. The firm is not following their Filling Solutions Procedure, SOP-020, Rev 2 which requires the completion of production and process forms (b) (4) for bulk and production solutions.

4. The firm is not following their Material Inspection Procedure, SOP-033, Rev 2 for the control of labels.

5. The firm is not following their Purchasing Procedures SOP-077 and SOP-003, which requires the purchase of product through approved vendors.

Annotation: Promised to correct.

Reference: 21 CFR 820.70(a)

Supporting Evidence and Relevance: The firm is not following their procedures to ensure conformance to specifications. The firm has not implemented procedures that describe any process controls necessary to ensure conformance to specifications such as the number of allowable freeze and thaw cycles for a raw material.
Exhibits 49, 53, 54, 55 and 56

Discussion with Management: Ms. Hildebrand and Ms. Roode agreed with the observation and promised to correct.

OBSERVATION 7

Written MDR procedures have not been developed.

Annotation: Promised to correct

Reference: 21 CFR 803.17

Supporting Evidence and Relevance: There is no MDR procedure and the firm is not evaluating complaints for MDR reporting.
Exhibits 58 - 63

Discussion with Management: Ms. Hildebrand and Ms. Roode agreed with the observation and promised to correct.

OBSERVATION 8

Procedures have not been defined to ensure that device history records for each batch, lot, or unit are maintained to demonstrate that the device is manufactured in accordance with the device master record and the Quality Systems regulation.

Specifically, the firm's procedure SOP-019, Rev 4 is not complete as it does not ensure each IVD device is manufactured according to established specifications. For instance, IVDs are manufactured using data recorded in laboratory notebooks from previously produced batches. There are no written specifications (DMR) and no work instructions (e.g. mixing and drying times).

Annotation: Promised to correct.

Reference: 21 CFR 820.184

Supporting Evidence and Relevance: The firm's procedure does not ensure each IVD device is manufactured according to established specifications. IVDs are manufactured using data recorded in laboratory notebooks from previously produced batches. There are no written specifications (DMR) and no work instructions (e.g. mixing and drying times).
Exhibits 57 and 65 - 69

Discussion with Management: Ms. Hildebrand and Ms. Roode agreed with the observation and promised to correct.

OBSERVATION 9

The device history record does not demonstrate the device is manufactured in accordance with the device master record.

Specifically, the firm's device history records are incomplete. For instance, a) dates and signatures of operators and reviewers are missing and b) processing steps have not been established and documented.

Annotation: Promised to correct.

Reference: 21 CFR 820.184

Supporting Evidence and Relevance: The firm's device history records are incomplete. For instance, a) dates and signatures of operators and reviewers are missing and b) processing steps have not been established and documented.
Exhibits 65 - 69

Discussion with Management: Ms. Hildebrand and Ms. Roode agreed with the observation and promised to correct.

OBSERVATION 10

The device history record does not include the primary identification label and labeling for each device.

Specifically, finished product labels and labeling are not made part of the firm's device history records.

Annotation: Promised to correct

Reference: 21 CFR 820.184(e)

Supporting Evidence and Relevance: The firm's finished product labels and labeling are not made part of the firm's device history records. The DHRs also do not specify where labeling can be located and are not referenced in or made part of the laboratory notebooks. (Note: I requested the labeling for each DHR collected and enclosed them as part of the DHR exhibits).
Exhibits 65 - 69

Discussion with Management: Ms. Hildebrand and Ms. Roode agreed with the observation and promised to correct.

OBSERVATION 11

Complaint handling procedures have not been implemented to ensure that all complaints are processed in a uniform and timely manner.

Specifically,

1. The firm is not implementing their Product Complaint and Investigation SOP-009, Rev 1 to ensure that all complaints are processed in a uniform and timely manner. For instance,

a. Customer complaint PCI# (b) (4) was received 6/30/08. The retain was tested on 7/18/08. The PCI form was not completed until 8/22/08.

b. Customer complaint PCI# (b) (4) was received 11/21/07. The PCI form was not completed until 5/13/08 and the complaint was not investigated.

Annotation: Promised to correct

Reference: 21 CFR 820.198(a)(1)

Supporting Evidence and Relevance: The firm is not following their complaint procedure.
Exhibits 58, 60 and 61

Discussion with Management: Ms. Hildebrand and Ms. Roode agreed with the observation and promised to correct.

OBSERVATION 12

Complaints involving the possible failure of a device to meet any of its specifications were not investigated where necessary.

Specifically,

1. Complaint PCI # (b) (4) was not investigated because the firm did not receive back the IVD referenced in the complaint.

2. Complaint PCI # (b) (4) was not investigated because the firm did not receive back clearer data.

3. Complaint PCI # (b) (4) was not investigated because the kits were returned because "FDA discontinued sales in the USA".

Annotation: Promised to correct

Reference: 21 CFR 820.198(c)

Supporting Evidence and Relevance: The firm is not investigating all complaints.

Exhibits 61 - 63

Discussion with Management: Ms. Hildebrand and Ms. Roode agreed with the observation and promised to correct.

OBSERVATION 13

Records of acceptable suppliers and consultants were not maintained.

Specifically,

1. The (b) (4) is not on the firm's approved supplier list.

2. (b) (4) is not on the firm's approved supplier list.

3. (b) (4) is not on the firm's approved supplier list.

4. The firm's consultant with the initials (b) (6) is not on the firm's approved supplier list.

Annotation: Promised to correct.

Reference: 21 CFR 820.50(a)(3)

Supporting Evidence and Relevance: The firm is using vendors for services and supplies which are not on the firm's approved supplier list.
Exhibits 73 - 77

Discussion with Management: Ms. Hildebrand and Ms. Roode agreed with the observation and promised to correct.

OBSERVATION 14

Purchasing information that clearly includes/describes the specified requirements for purchased or otherwise received products and services was not established.

Specifically,

1. The firm has not specified requirements for purchased products and services.

2. The firm has not established purchasing agreements with the (b) (4), (b) (4) and their consultant (b) (6).

Annotation: Promised to correct.

Reference: 21 CFR 820.50(b)

Supporting Evidence and Relevance: Purchasing information that clearly includes/describes the specified requirements for purchased or otherwise received products and services has not been established.
Exhibits 55 and 56, 73 - 77

Discussion with Management: Ms. Hildebrand and Ms. Roode agreed with the observation and promised to correct.

OBSERVATION 15

Adequate quality requirements that must be met by suppliers were not defined and documented.

Specifically,

1. The firm has not established quality requirements that must be met by suppliers.

2. The firm's Purchasing Control Procedures (e.g. SOP-077 and SOP 003) is not complete in that it does not specify quality requirements that must be met by suppliers, contractors and consultants.

3. Not all suppliers are qualified before use in accordance with the firm's Purchasing Control procedure (e.g. Consultant with the initials (b) (6), (b) (4) and (b) (4)).

Annotation: Promised to correct.

Reference: 21 CFR 820.50(a)

Supporting Evidence and Relevance: Quality requirements that must be met by suppliers have not been defined and documented.
Exhibits 55 and 56, 73 - 77

Discussion with Management: Ms. Hildebrand and Ms. Roode agreed with the observation and promised to correct.

OBSERVATION 16

There is no documentation of calibration dates, the individual performing each calibration, and the next calibration date for measurement and test equipment.

Specifically, there are no calibration records for the following equipment:

1. (b) (4) equipment used to fill IVD plates
2. (b) (4) Reader
3. Weekly calibration of the firm's pH meter used in production is not being documented

Annotation: Promised to correct.

Reference: 21 CFR 820.72(b)(2)

Supporting Evidence and Relevance: Calibration and equipment qualifications are not being performed. Exhibit 48

Discussion with Management: Ms. Hildebrand and Ms. Roode agreed with the observation and promised to correct.

ATTACHMENTS

1. FDA-482 issued to David N. Lambillotte, dated 09/09/08
2. FDA-482 issued to Kathy B. Hildebrand, dated 10/09/08
3. FDA-483 issued to Kathy B. Hildebrand, dated 10/09/08
4. Center Directed Assignment, dated July 16, 2008

EXHIBITS

1. IVD Research device registration and listing
2. IVD Research Organizational Chart
3. IVD Research floor plan

4A. Certificates of Exportability (expired)
4B. Certificates of Exportability (renewed certificates)
5A. IVD Research Customer List
5B. IVD Research Customer List – customers sold IVDs within the last two years
5C. IVD Research Customer List – customers sold Level I bulk solutions
6. IVD Research U.S. Distributor List
7A. Updated U.S. Distributor List
7B. Updated U.S. Distributor List with address locations
8. IVD Research 510k product list
9. Adenovirus Antigen Detection Kit – 4 sets of Labeling
10. Giardia/Cryptosporidium Combo Antigen Detection Kit – 4 sets of Labeling
11. E. coli O157 Antigen Detection Kit – 4 sets of Labeling
12. E. histolytica/dispar Antigen Detection Kit – 4 sets of Labeling
13. Rotavirus Antigen Detection Kit – 4 sets of Labeling
14. E. coli Verotoxin Detection Kit – 4 sets of Labeling
15. Dengue IgG Detection Kit – 4 sets of Labeling
16. Dengue IgG Detection Kit with a (b) (4) – 4 sets of Labeling
17. Dengue IgG/IgM Detection Kit – 4 sets of Labeling
18. Dengue IgG/IgM Detection Kit with a (b) (4) – 4 sets of Labeling
19. Dengue IgM Detection Kit – 4 sets of Labeling
20. Dengue IgM Detection Kit with a (b) (4) – 4 sets of Labeling
21. Ascaris Detection Kit – 4 sets of Labeling
22. Chagas Serology Detection Kit – 4 sets of Labeling
23. Chagas Serology Detection Kit for Research Use Only – 4 sets of Labeling
24. Campylobacter Fecal Antigen Detection Kit – 4 sets of Labeling
25. Fasciola Serum Detection Kit – 4 sets of Labeling
26. Leptospira IgG Detection Kit – 4 sets of Labeling
27. Leptospira IgG Detection Kit with a (b) (4) – 4 sets of Labeling
28. Leptospira IgG/IgM Detection Kit – 4 sets of Labeling
29. Leptospira IgM Detection Kit – 4 sets of Labeling
30. Leptospira IgM Detection Kit with a (b) (4) – 4 sets of Labeling
31. Strongyloides Serology Detection Kit – 4 sets of Labeling
32. Toxocara Serum Detection Kit – 4 sets of Labeling
33. Diphtheria Toxoid Serum Detection Kit – 4 sets of Labeling
34. Tetanus Toxoid Serum Detection Kit – 4 sets of Labeling
35. Legionella Urinary Antigen Detection Kit – 4 sets of Labeling
36. Visceral Leishmania Serology Detection Kit – 4 sets of Labeling
37. IVD Research Product Brochure - 4 sets of Labeling
38. IVD Research outer boxes for (b) (4) kits - 4 sets of Labeling

39. Design Control Procedures
40. First commercial release of Leptospira IgM, first production run and Leptospira IgM DHF
41. First commercial release of Leptospira IgG, first production run and Leptospira IgG DHF
42. First commercial release of Leptospira IgG/IgM, first production run and Leptospira IgG/IgM DHF
43. First commercial release of Dengue IgG/IgM, first production run and Dengue IgG/IgM DHF
44. First commercial release of Dengue IgM, first production run and Dengue IgM DHF
45. First commercial release of Dengue IgG, first production run and Dengue IgG DHF
46. First commercial release of Chagas, first production run, and Chagas DHF
47. Stability Program Procedure, SOP-036 and Attachment 1-1
48. Equipment List
49. Plate Filling with (b) (4) Procedure, SOP-097
50. Photocopy of Fasciola and Ascaria Bleeds
51. Photocopy of Toxocara antibodies
52. Photocopy of Leptospira and Toxocara with RCV #s
53. Filling Solutions Procedure, SOP-020
54. Material Inspection Procedure, SOP-033
55. Purchase Control Procedure, SOP-077
56. Purchasing Procedure, SOP-003
57. Strip Production Procedure, SOP-019
58. Product Complaint and Investigation Procedure, SOP-009
59. Complaint Log
60. PCI-(b) (4)
61. PCI-(b) (4)
62. PCI-(b) (4)
63. PCI-(b) (4)
64. Lot Number Assignment Procedure, SOP-008 and Final Kit Assembly Procedure, SOP-021
65. Device History Record for Leprospira IgG, labeling and shipping documentation to (b) (4)
66. Device History Record for Leprospira IgM, labeling and shipping documentation to (b) (4)
67. Device History Record for Chagas, labeling and shipping documentation to (b) (4)
68. Device History Record for Dengue IgM, (b) (4) kit packaging and shipping documentation to (b) (4)

69A. Device History Record for Dengue IgG/IgM (total), labeling and shipping documentation to (b) (4)

69B. Device History Record for Dengue IgG/IgM (total), labeling and shipping documentation to (b) (4) (b) (4) ;(b) (4) and (b) (4)

70. Invoices, labeling and tracking information for domestic companies receiving non-exempt IVDs with no 510k
71. IVD Research Agreements on file with distributors
72. List of all sales (b) (4), (b) (4), (b) (4) and (b) (4)
73. Approved Vendor List

74. Incoming Inspection Records - (b) (4)
75. Incoming Inspection Records – (b) (4) and (b) (4), Strongylodies DHR and shipping docs
76. Incoming Inspection Records – (b) (4) - Fasciola DHR, labeling and Invoice
77. Incoming Inspection Records – (b) (4) – Toxocara DHR, (b) (4) packaging & shipping information.
78. Chagas DHR, shipping information and RUO labeling

Deborah Greco, Investigator