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## Summary

A Clinical Investigator Inspection Assignment of a Premarket, Original Drug BIMO Inspection Assignment was conducted of the following clinical investigator (CI):

David R. Young, DVM, PhD
Young Veterinary Research Services
213 S. Roselawn Avenue
Turlock, CA 95380

This inspection was assigned by the Office of Food and Veterinary Medicine (OFVM) as Field Accomplishments and Compliance Tracking System (FACTS) Assignment #11599990 and was conducted in accordance with Compliance Program (CP) 7348.811 (Bioresearch Monitoring Clinical Investigators and Sponsor-Investigators). The OFVM assignment (**Attachment 1**) requested a clinical investigator inspection of Dr. David R. Young, DVM, PhD, for the (b) (4) study; a (b) (4) conducted under (b) (4). The study inspected is entitled:

(b) (4)

The following background information was included with the CVM assignment: Division of Bioresearch Monitoring Assignment (**Attachment 1**) and Study (b) (4) protocol.

Dr. Young was the clinical investigator (CI) for this protocol. The protocol will be referred to as the (b) (4) study for the remainder of this report.

Inspection included a review of training records, daily observations, case report forms, notes to file, and (b) (4) records. In general, Dr. Young's records indicate that he complied with the overall requirements for the (b) (4) protocol.

At the conclusion of this inspection on 3/8/2016, the Form FDA 483, Inspectional Observations, was not issued to Dr. Young and no discussion items were brought to Dr. Young's attention.

There were no refusals during this inspection and no samples collected. Any correspondence regarding this inspection should be direct to Dr. Young referenced in the "**Administrative Data**" section.

## Administrative Data

| | |
|---|---|
| Inspected firm: | David R. Young |
| Location: | 213 S. Roselawn Ave.<br>Turlock, CA 95380-9166 |
| Phone: | 209-632-1919 |
| FAX: | 209-632-1944 |
| Mailing address: | 7243 East Avenue<br>Turlock, CA 95380-9166 |
| FDA 482 Issued to: | David R. Young, DVM, Ph.D. |
| FDA 482 Issued to: | Corinne L. Young, CVT, L.A. TG, Laboratory Manager |
| FDA 483 Issued to: | None |
| FDA 484 Issued to: | None |
| Email address: | youngdvm@yvrs.com |
| Website address: | www.youngvetresearchservices.com |
| Dates of inspection: | 3/7/2016, 3/8/2016 |
| Days in the facility: | 2 |
| Participants: | Karen J. Bak, Investigator |

On 3/7/2016, I presented my FDA credentials and issued the FDA Form 482, Notice of Inspection (**Attachment**), to David R. Young, DVM, PhD, who identified himself as clinical investigator (CI) for the Study Number (b) (4) protocol. I was introduced to the following individuals:

Corinne L. Young, CVT, L.A. TG, Laboratory Manager
(b) (6), (b) (7)(C), Research Coordinator

Also on 3/7/2016, I issued a second FDA Form 482, Notice of Inspection (**Attachment**), to Corinne L. Young, CVT L.A. TG., Laboratory Manager at Dr. Young's second location (office and test article storage location).

At the conclusion of the inspection (3/8/2016), no Form FDA 483, Inspectional Observations, was issued to Dr. Young.

Any correspondence should be directed and addressed to:

Dr. David R. Young, DVM, PhD
7243 East Avenue
Turlock, CA 95380

## History

Dr. Young has been previously inspection by FDA under a different FEI and name: Young Veterinary Research Services (YVRS) under FEI: 3003004483. Dr. Young and YVRS continue to conduct research studies on animals and YVRS was incorporated in the State of California on 8/21/2015. The last comprehensive surveillance inspection/data audit of Dr. Young was conducted on 3/18/2016 and awaits official classification. At the time of the (b) (4) study, all dog subjects were housed at (b) (4)

YVRS' home office is located at 7243 East Avenue, Turlock, CA 95380. This location is also used for large animal studies. Study files and test articles are received, stored, and shipped back to the appropriate sponsor from this location.

## Individual Responsibility and Persons Interviewed

Prior to starting the inspection on 3/2/2016, I telephoned Dr. Young and notified him that I would begin this inspection on 3/7/2016. During the telephone conversation, I discussed the general nature of the inspection with Dr. Young and also informed him that I would need to meet with him at the beginning of the inspection and have all study records available for review, including: protocol, source documents, worksheets, monitoring correspondence, and case report forms (CRFs).

The following individuals provided the relevant information for this inspection:

David R. Young, DVM, PhD, is responsible for the management and oversight of the clinical trial and is the most responsible person. During the course of this clinical study, Dr. Young's was responsible for conducting physical exams, performing health checks, selecting study animals, and performing day-to-day activities associated with the clinical study.

Corrine Young, Laboratory Manager, was responsible for providing general information on the company, employees, and office practices during this inspection.

## Overall Operations

During the course of this inspection, (b) (4) Study (b) (4) ) was inspected as per the assignment memo. This inspection of Dr. Young's conduct covered the following elements for each protocol:

- Protocol
- Curriculum Vitae
- Test Article Control
- Record Retention
- Authority and Administration for Studies
- Review of source data
- Data Collection (b) (4) and treatment administration)
- Adverse Events

### *1. Curriculum Vitaes and Study Participant Record*

Curriculum Vitaes were collected for Dr. David Young (**Exhibit 1**), Corinne Young (Laboratory Manager) (**Exhibit** 2), and technicians (**Exhibit 3**). I was also provided a copy of Dr. Young's clinical trials for the last three years (**Exhibit 4**). Dr. Young, his laboratory manager, and technicians all signed the "Study Participant Record" (**Exhibit 5**).

### *2. Test Article Control*

The receipt, storage, dispensation, and final disposition of all study drug products were reviewed. Ms. Young stated that the test article drug for the (b) (4) trial was maintained at Dr. Young's home office located at 7243 East Avenue, Turlock, CA. I reviewed the drug accountability logs and investigation veterinary product return records and no test article control discrepancies were noted for the (b) (4) trial.

### *3. Other Study Records*

All other study-related information for the protocols, i.e., correspondence files, animal facility design, kennel layout, sign-in logs were maintained in the same binder. These regulatory binders were reviewed, complete and no discrepancies were noted.

***4. Records Custody and Retention***

Ms. Young stated that the source documentation for the protocol, case-reporting forms, and regulatory binder would be maintained and stored on-site at a designated building that is monitored with an alarm. Ms. Young further stated that the documentation is maintained for the required period, or longer, as instructed by the sponsor.

## Authority and Administration for Studies

As previously stated, Dr. Young was the CI for this study. The protocols used during the study were compared to the protocol submitted with the assignment and are the same. During the course of the clinical trial, there were two protocol amendments. The signed protocol amendments were reviewed and no discrepancies were noted.

Prior to the study, Dr. Young signed the form, "Statement of Investigator" on 10Marl4 (See **Exhibit 6**, page 2 of 2). He also signed the form, "Owner Consent Form – Contract Research Organizations" also on 10March14 **(Exhibit 7)**.

At the conclusion of the study, Dr. Young signed the form, "Investigator Compliance Statement" **(Exhibit 8)** and (b) (4) "Study Closeout Record" on 16Jul14 **(Exhibit 9)**.

The firm's organizational chart is attached as **Exhibit 10**.

Dr. Young stated that he was ultimately responsible for the conduct of the study and the overall control of the study and he was contacted by (b) (4) and has participated in past studies in association with (b) (4).

This inspection of this protocol, (b) (4) study ((b) (4) ), found that Dr. Young adhered to the protocol, maintained the required source documentation, and ensured that source data is accurate and complete.

## Facilities and Test Article Control

This data validation inspection was of study entitled (b) (4) The study dates took place 12Mar14 – 17Jun14. This time period includes the (b) (4) . No discrepancies were noted.

The firm has SOPs for the receipt, storage, and access authority to the test articles. Dr. Young showed where test articles are stored. The storage area is monitored with a portable thermometer to

monitor temperatures. The storage area is kept under lock and key. The firm's SOPs were reviewed and no discrepancies were noted.

## Animal Care and Accountability

The animal study site is located at 7423 East Avenue, Turlock, CA 95380. Review of the firm's SOPs and available records for animal care were reviewed including feed, water, and identification of animals. The weigh scale calibration records were reviewed and no discrepancies were noted.

## Study and Record Review

The original source data was not present at the site during the inspection. Dr. Young stated that the source data was provided to the sponsor and provided me with exact copies of the source data during this inspection. Exact copies of the source documentation of the following areas were reviewed:

- Training: Prior to the start of the (b) (4) study, a training session was provided by the monitor, US Clinical Research via teleconference. The training encompassed the study objectives, GCP and regulatory compliance, pre-enrollment activities, animal husbandry and health, (b) (4) and treatment site evaluations (**Exhibit 11**).

- The monitor visited the site on 22 Mar 14 and 24 Mar 14 to observe Day 0 activities, review study files, and (b) (4) (**Exhibit 12**).

- Daily observations were conducted during all aspects of the studies and no discrepancies were noted.

- Review of the case reports forms for (b) (4), treatment administration,

- Review of the firm's chain of custody records and correspondence was conducted and no discrepancies were noted.

- A review of the study subject's CRFs inclusion/exclusion was compared to the case report forms (source documentation) in the study binder was conducted and no discrepancies were noted.

At the conclusion of the study, Dr. Young submitted a signed "Investigator Compliance Statement", "Study Closeout Record," and "Data Transfer Certification" all dated 16Jul14. Dr. Young stated that during the course of the study, they did not observe any unusual issues associated with the study animals.

## Reports to Sponsor Monitor

There was no under-reporting of SAEs or AEs to the sponsor observed in the study records during this inspection.

## Adverse Events

During the course of the study, four adverse events reported to the sponsor. A summary of the four adverse events are as follows:

**Animal ID** (b) (4) On 24 Marl 14 was observed with a cut on the right hind leg by paw area, swollen and limping. Animal ID(b) (4) received a high dose of Baytril for 3 days and recovered **(Exhibit 13)**.

**Animal ID** (b) (4)**:** On 16 May 14 received bite wounds on the right-side front leg after a fight with dog (b) (4) under the cage. Animal ID(b) (4) received a high dose of Baytril for three days and recovered **(Exhibit 14)**.

**Animal ID** (b) (4) Dog was found dead on the morning of 27 April 2014. The dog was observed to be of normal behavior the day before. A necropsy revealed that the cause of death was hypertrophic cardiomyopathy. The sponsor was notified **(Exhibit 15)**.

**Animal ID** (b) (4) On 4 May 2014 during daily general health examinations, a slow growing mammary mass was detected. The sponsor was notified on 4 May 2014. Dr. Young received an email from (b) (4) on May 6, 2014 at 6:25 a.m. confirming that Animal ID(b) (4) was to be removed from the study and that same email referred to Protocol Section 13.6 where is states: "Animals removed from the study will be handled at the discretion of the Investigator" **(Exhibit 16 and Exhibit 17)**.

Animal ID(b) (4) was removed from the study per the request of the sponsor. Animal ID (b) (4) was returned to the general colony on 6 May 2014 and no longer part of the study. After the Animal ID (b) (4) was returned to the general colony, another examination was performed later in the day (May 6, 2014) to determine suitability for surgery. It was then determined that Animal ID(b) (4) was not a candidate for mammary mass removal and that the humane decision would be to euthanize the animal.

In all four cases, the sponsor was notified and these were reported on the CRF(b) (4) and CRF(b) (4): Listing of Adverse Events.

## Additional Information

During the inspection, Dr. Young stated that he signed the waiver for a copy of the Final Study Report. The monitor was the author of the Final Study Report. During the data audit, I compared the Final Study Report that was provided with this assignment to the source data (exact copies). I verified that the form titled, "(b) (4) " provided with this assignment was the exact copy of Dr. Young's records that was submitted to the sponsor.

It appears that the data in the Final Study Report was incorrectly entered and off by a row of numbers. I observed that on page 39 of 145 of the provided protocol and beginning with subject (b) (4), the (b) (4) reported Pre-Treatment numbers was not accurate with the data submitted by Dr. Young.

For example, in the Final Study Report, Animal ID (b) (4) reported (b) (4) however; Dr. Young's Source Data reported (b) (4) However, Animal ID (b) (4) reported "(b) (4) " in Dr. Young's Source Data.

| Treatment Group | Animal ID | Pre-Treatment (Final Study Report) | Pre-Treatment (Dr. Young's Source Data) |
|---|---|---|---|
| | | (b) (4) | |

(b) (4)

## Refusals

Dr. Young and his staff were cooperative, provided all requested documentation, and answered all questions when asked.

## General Discussion with Management

On 3/8/2016, a closeout meeting was held with the following individuals present: Dr. David R. Young, Clinical Investigator, Corinne Young, Laboratory Manager, and (b) (6), (b) (7)(C), Research Coordinator. The Form FDA 483, Inspectional Observations, was not issued to Dr. Young and no discussion items were presented.

## Exhibits

1. David R. Young, Clinical Investigator curriculum vitae (7 pages)
2. Corinne Young's curriculum vitae (2 pages)
3. Technician curriculum vitaes (15 pages)
4. Dr. Young's clinical trial history (5 pages)
5. Study Participant Record (2 pages)

6. Signed "Statement of Investigator" (2 pages)
7. Signed copy of "Owner Consent Form – Contract Research Organizations" (1 page)
8. Signed copy of "Investigator Compliance Statement" (1 page)
9. Signed copy of "Study Closeout Record" (1 page)
10. Young Veterinary Research Studies Organizational Chart (1 page)
11. Personnel Training Records (4 pages)
12. Monitor Site Visit Record (1 page)
13. Animal ID (b) (4) adverse event records (7 pages)
14. Animal ID (b) (4) adverse event records (5 pages)
15. Animal ID (b) (4) adverse event records (3 pages)
16. Animal ID (b) (4) adverse events records (3 pages)
17. Email discussion regarding Animal ID (b) (4) (2 pages)

## Attachments

FDA 482, Notice of Inspection (9/11), issued to David R. Young, DVM, PhD, Clinical Investigator, issued on 3/7/2016 (3 pages).

FDA 482, Notice of Inspection (9/11), issued to Corinne L. Young, C.V.T., L.A. Tg, Laboratory Manager, issued on 3/7/2016 (3 pages).

1. Assignment Memo, dated December 4, 2015, from Office of Foods and Veterinary Medicine (6 pages)

Karen J. Bak, Investigator
San Francisco District Office