toXcel Response to EPA E-mail request for clarification

"Mike Kelley" <Mike.Kelley@toxcel.com>
05/21/2008 10:46 AM

To: John Carley/DC/USEPA/US@EPA
Cc: "'Alan Katz'" <alan.katz@toxcel.com>, <Andrew.Pechko@Avon.com>, <Chris.Bartlett@Avon.com>, Kevin Sweeney/DC/USEPA/US@EPA, "'Nick Spero'" <nspero@icrlab.com>, <Ramez.Labib@Avon.com>, Richard Gebken/DC/USEPA/US@EPA, <rtodd@icrlab.com>, William Jordan/DC/USEPA/US@EPA, Marion Johnson/DC/USEPA/US@EPA, EQuinn@icrlab.com
Re: RE: Submission of West Nile Virus Amendment Applications for 806-29, 806-30, & 806-31

Mr. Carley,
In response to your request for clarification, I have repeated each of your questions and followed each issue with ICR's response in all caps.

Your first issue was,

> "When was the decision made to treat subjects in groups of six, instead of in groups of two as specified in the protocol? Has this change been made in the course of executing other protocols at ICR? Has there been a problem in the past with confusion of when subjects were due to enter the lab for their next round of testing?"

AS INDICATED IN THE STUDY PROTOCOL DEVIATION ON PAGE 52 OF 98 OF THE STUDY REPORT (SEE ATTACHED COPY), IT WAS DECIDED TO SPLIT THE GROUP OF 12 AVAILABLE SUBJECTS (TARGET WAS 10 SUBJECTS) INTO TWO EQUAL GROUPS OF 6 TO AVOID CONFUSION. THERE WERE SIX CAGES DEDICATED TO TWO SUBJECTS EACH AND IT WAS KNOWN THAT THREE CAGES COULD BE MANAGED AT A TIME (SIX SUBJECTS; TWO AT EACH CAGE). THE LOGISTICS OF MOVING TWO GROUPS OF SIX IN AND OUT OF THE INSECTARY WAS MORE MANAGABLE AND LESS DISRUPTIVE THAN THE LOGISTICS AND TIMING ASSOCIATED WITH MOVING AROUND SIX GROUPS OF TWO AND USING ONLY ONE CAGE AT A TIME.

THIS TYPE OF CHANGE HAS NEVER BEEN MADE IN PRIOR TESTS. THE REASON NO SUCH CHANGE WAS EVER MADE IS THAT THIS STUDY INVOLVED THE LARGEST GROUP TESTED AT ICR. MOST COMPARABLE STUDIES AT ICR INVOLVE A GROUP OF 6 SUBJECTS TOTAL. OCCASIONALLY ICR HAS CONDUCTED STUDIES USING 8 SUBJECTS, BUT THIS IS BELIEVED TO BE THE FIRST TIME THAT 12 SUBJECTS WERE INVOLVED. ICR HAS NEVER NEEDED TO MAKE SUCH A PROTOCOL DEVIATION IN THE PAST. IT WAS DEEMED TO BE A REASONABLE PRECAUTION TO ENSURE SMOOTH PERFORMANCE OF THE STUDY AND AVOID ANY POTENTIAL DISRUPTION.

Your second issue was,

> "Were two extra subjects recruited to serve as alternates in case anyone dropped out or was found to be ineligible, as specified in the protocol? If not, why not?"

YES, THE TWO EXTRA SUBJECTS WERE RECRUITED TO SERVE AS ALTERNATES. THE TARGET NUMBER OF SUBJECTS WAS 10. SINCE THERE WERE NO DROP OUTS, ALL 12 AVAILABLE SUBJECTS WERE EVALUATED.

Your final issue was,

> "Please characterize the events in the recruiting process as they occurred between the time of IRB approval and the actual day of testing. When did recruiting begin? When did each enrolled subject sign the consent form?"

THE FINAL ICD WAS AVAILABLE ON FEBRUARY 25TH. HOWEVER, ICR STARTED CALLING PEOPLE TO DETERMINE THEIR POTENTIAL AVAILABILITY FOR THE STUDY ON FEBRUARY 18-19, 2008. ON FEBRUARY 26, 2008 (THE DAY AFTER RECEIPT OF THE FINAL ICD) THOSE PEOPLE THAT INDICATED THEIR LIKELY AVAILABILITY WERE CONTACTED BY PHONE TO CONFIRM THEIR AVAILABILITY FOR THIS STUDY. THE ICD "PHONE SCRIPT" WAS READ TO EACH PERSON THAT CONFIRMED THEIR AVAILABILITY AND EACH POTENTIAL SUBJECT WAS INVITED DURING THAT CALL TO COME TO ICR TO GO OVER THE ICD IN DETAIL WITH ICR STAFF. IF A POTENTIAL SUBJECT DECIDED NOT TO TAKE ADVANTAGE OF THAT OFFER TO GO OVER THE ICD AT ICR PRIOR TO THE STUDY DATE, THEY WERE NOTIFIED THAT THEY SHOULD COME PREPARED ON THE MORNING OF THE TEST TO ASK ANY QUESTIONS AND SIGN THE CONSENT FORM IN ORDER TO PARTICIPATE IN THE STUDY. CONSENT PACKAGES WERE MAILED OUT TO ALL BUT THREE POTENTIAL SUBJECTS WHO COULD NOT RECEIVE THE PACKAGES PRIOR TO THE STUDY DATE. ALL POTENTIAL SUBJECTS AGREED TO GO OVER THE ICD, GET ANY QUESTIONS THEY MIGHT HAVE ADDRESSED, AND TO BEING PREPARED TO SIGN THE CONSENT ON THE DAY OF THE TEST. ALL SUBJECTS SIGNED THE CONSENT FORM ON THE DAY OF THE STUDY, MARCH 4, 2008.

I hope the above responses are satisfactory. If you would like to have these responses submitted in hardcopy form via document processing, please let me know. If we can be of further assistance, do not hesitate to ask.

Regards,
Mike Kelley

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-----Original Message-----

From: Carley.John@epamail.epa.gov [mailto:Carley.John@epamail.epa.gov]
Sent: Monday, May 19, 2008 3:36 PM
To: Micah Reynolds

Cc: 'Alan Katz'; Andrew.Pechko@Avon.com; Chris.Bartlett@Avon.com; Sweeney.Kevin@epamail.epa.gov; 'Mike Kelley'; 'Nick Spero'; Ramez.Labib@Avon.com; gebken.richard@epa.gov; rtodd@icrlab.com; jordan.william@epa.gov; Johnson.Marion@epamail.epa.gov
Subject: Re: Submission of West Nile Virus Amendment Applications for 806-29, 806-30, & 806-31
Importance: High

Please clarify a few points for me about the execution of ICR study A117. I need answers to the following questions to finish up my ethics review of this study:

> When was the decision made to treat subjects in groups of six, instead of in groups of two as specified in the protocol? Has this change been made in the course of executing other protocols at ICR? Has there been a problem in the past with confusion of when subjects were due to enter the lab for their next round of testing?
>
> Were two extra subjects recruited to serve as alternates in case anyone dropped out or was found to be ineligible, as specified in the protocol? If not, why not?
>
> Please characterize the events in the recruiting process as they occurred between the time of IRB approval and the actual day of testing. When did recruiting begin? When did each enrolled subject sign the consent form?

Thanks.

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