From: Woollen, Stan - OC on behalf of OC GCP Questions
Sent: Tuesday, August 09, 2005 6:17 PM
To: [Redacted]
Subject: RE: Your Voicemail Inquiry to FDA

Dear [Redacted],
I'm expecting that you will hear from my CDRH colleagues directly on those questions relating specifically to whether the IRB can direct that data be withheld. I've copied them on this inquiry as a reminder.

I don't want to preempt their reply to you, however, in the meantime, I can offer some preliminary information regarding the authority of IRBs , in general. This relates broadly to your first question below.

FDA regulations governing IRBs are found at 21 CFR 56. A copy can be found under the regulations link on our website http://www.fda.gov/oc/gcp/regulations.html

There are several sections dealing with the IRB's authority. I've excerpted portions of some pertinent sections below for your convenience. The first section 56.109 deals with IRB review in general, and the second section 56.113 deals with the IRB's authority to suspend or terminate studies:

56.109 IRB review of research.
(a) An IRB shall review and have authority to approve, require modifications in (to secure approval), or disapprove all research activities covered by these regulations.

(e) An IRB shall notify investigators and the institution in writing of its decision to approve or disapprove the proposed research activity, or of modifications required to secure IRB approval of the research activity. If the IRB decides to disapprove a research activity, it shall include in its written notification a statement of the reasons for its decision and give the investigator an opportunity to respond in person or in writing.

Sec. 56.113 Suspension or termination of IRB approval of research.
An IRB shall have authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB`s requirements or that has been associated with unexpected serious harm to subjects. Any suspension or termination of approval shall include a statement of the reasons for the IRB`s action and shall be reported promptly to the investigator, appropriate institutional officials, and the Food and Drug Administration.

As you can see the IRB does have pretty broad authority to set and enforce its standards at the institution. What the regulations don't specifically address in your situation is what authority the IRB has over the data from studies which it has disapproved or suspended. The submission of data to FDA and sponsors is governed by different regulations and it is possible that those regulations require data that is collected in your case must be submitted to the sponsor and FDA. I would expect the IRB cannot overrule these requirements. However, I'm not expert on this point and therefore you can see why I have asked CDRH to answer you questions relating to this issue.

It is also not clear to me exactly what the IRB intends or expects in declaring "data generated from four patients cannot be considered research data". This is a question that can only be worked out between you and your IRB. They can certainly have the authority to make the declaration, but I don't know what it

means. Likewise, I'm also pretty sure that FDA will not give you an answer to your 4th question due to its subjective nature.

I hope this discussion has been of some help, at least with your first question. I will defer to my colleagues in CDRH to give you their best judgment on your other issues relating to withholding and submitting data. I did say we try to answer our GCP mailbox within three days. I suppose I should have said that only applies to simple questions with easy answers. Your questions don't fall into that category:) Thank you for your patience.

Sincerely

Stan W. Woollen
Associate Director for Bioresearch Monitoring
Good Clinical Practice Programs
OSHC, Office of the Commissioner

This communication does not constitute a written advisory opinion under 21 CFR 10.85, but rather is an informal communication under 21 CFR 10.85(k) which represents the best judgment of the employee providing it. This information does not necessarily represent the formal position of FDA, and does not bind or otherwise obligate or commit the agency to the views expressed.

-----Original Message-----
From: [Redacted]
Sent: Monday, August 08, 2005 1:09 PM
To: 'Woollen, Stan - OC'
Subject: RE: Your Voicemail Inquiry to FDA

Dear Mr. Woollen:

Is this still under discussion?

[Redacted]

-----Original Message-----
From: Woollen, Stan - OC [mailto:SWoollen@OC.FDA.GOV]
Sent: Tuesday, August 02, 2005 8:30 AM
To: [Redacted]
Subject: RE: Your Voicemail Inquiry to FDA

Dear [Redacted]

Thank you for providing the details of your issues below. You have an interesting ethical/regulatory dilemma. I've referred your information to my colleagues in the Center for Devices for their consultation, especially in regards to FDA's expectations regarding the reporting of data generated under an IDE. We will respond further to your questions shortly.

Sincerely,

Stan W. Woollen
Associate Director for Bioresearch Monitoring
Good Clinical Practice Programs

OSHC, Office of the Commissioner

-----Original Message-----
From: [Redacted]
Sent: Monday, August 01, 2005 6:20 PM
To: Woollen, Stan - OC
Subject: Re: Your Voicemail Inquiry to FDA

To: Office of Good Clinical Practice
From: [Redacted]

Re: Withholding data from the sponsor of a clincial triall

From 2000 through 2004, I was the Principal Investigator at [Redacted] site for the [Redacted] multicenter trial of [Redacted]. The trial was sponsored by [Redacted]. In 2001, due to a miscommunication between me and [Redacted], I enrolled into the trial 4 patients who had [Redacted]by a physician who was not officially designated a study physician by [Redacted]. This physician had completed a training course by [Redacted] and had been approved by [Redacted]. I know this physician personally, and I approved of his participation in the trial. However, I did not obtain official approval by [Redacted] and by the IRB of this physician as a sub-investigator. After the discovery of this error, I promptly reported it to the IRB. The IRB halted the study while it conducted an audit. At the conclusion of the audit, the IRB allowed the study to continue. The IRB letter to me stated: "...the data generated from (these) four patients cannot be considered research data. However, these patients should be monitored according to protocol." Now, four years later, the study has again been audited. The report of this audit, conducted by a Panel of [Redacted], stated: "[Redacted] continued to submit follow-up data on the four patients as if they were still research subjects....In her interview with the Panel, [Redacted] (the Director of [Redacted] of [Redacted] stated that her expectations based on the findings and instructions of the IRB were that data from the four patients would have been excluded from the study research data..." The Panel concluded that I should not have submitted the data from these four patients to [Redacted].

The following questions now arise:

1. Does the IRB have the authority to declare that "data generated from four

patients cannot be considered research data" ?

2. If so, does the IRB have the authority to order that the data from the four
patients be withheld from the sponsor?

3. If so, does the IRB have the authority to order that data on the primary endpoint of the study, which is death or hospitalization, be withheld from the
sponsor?

4. Is [Redacted]'s expectation reasonable? That is, is it reasonable to
conclude that the letter from the IRB to me, stating "...the data generated from (these) four patients cannot be considered research data. However, these
patients should be monitored according to protocol" should be regarded as an instruction to me to withhold from the sponsor the data on these four patients?

Quoting "Woollen, Stan - OC" <SWoollen@OC.FDA.GOV>:

> Dear [Redacted],
>
> Dr. Lepay forwarded your voicemail to me for response. Please feel free to
> submit any GCP related questions you may have to gcpquestions@oc.fda.gov.
> You can visit our web site at http://www.fda.gov/oc/gcp/default.htm for
> one-stop shopping for GCP information from FDA. On our page you will notice
> a link at the bottom of the third column titled "Contact GCP Staff".
> Clicking on that link will take you to our contact information including the
> GCP mailbox link above. We try to answer all questions received in our box
> in less than three business days.
>
> We look forward to hearing from you.
>
> Sincerely,
>
> Stan W. Woollen
> Associate Director for Bioresearch Monitoring
> Good Clinical Practice Programs
> OSHC, Office of the Commissioner