From: Toth-Allen, Jean
Sent: Tuesday, August 22, 2006 10:18 AM
To: [Redacted]
Subject: Follow-up regarding pre-clinical studies with blood and blood components

Dear [Redacted]:

In my message of August 10, I referred you to Celia Witten, M.D., director of the Office of Cellular, Tissue, and Gene Therapies, should you have questions about "manipulated" blood products. I therefore forwarded a copy of that e-mail to Dr. Witten and she had a few concerns she wanted me to clarify with you. In addition, she suggested I look more carefully at licensing requirements (Biological License Application - BLA) with regard to blood and blood products such as plasma, red blood cells, platelets, etc. With regard to the latter, I have learned that establishments preparing whole blood and blood products do require a license, i.e., need to file a BLA. Jay Epstein, M.D., is the director of the Office of Blood Research and Review and his office is available at (301) 827-3518. The office has a Division of Blood Applications, which is headed by Dr. Alan Williams, Ph.D., and would probably be a more direct source of information in this regard. That division is available at (301) 827-3524. There is also a guidance document related to BLAs for human blood products intended for transfusion or further manufacture which is available at http://www.fda.gov/cber/gdlns/bldchanges.pdf. The guidance itself refers to changes to approved BLAs but its contents, along with its references, should give you further insight with regard to licensing requirements. I apologize for my incorrect answer in this regard.

With regard to supplying blood and/or blood products, my information regarding IRB review and informed consent for collection, maintenance, and distribution was correct. If your company is solely the supplier of these products, your responsibility with regard to the studies utilizing these products is to supply the study sponsor with the information about your collection, maintenance, and distribution procedures. As I stated previously, it is the sponsor of any study that utilizes these products who is responsible for IRB review of those studies. (If you supply any sponsor with specimens that have subject information associated with them that is traceable to a specific individual, the IRB reviewing the study would need to review informed consent procedures as well.) As your e-mail was worded, it is not completely clear as to whether your company plays any part in the studies utilizing these products, as you inquire about the need for an IND or IDE, which relates to studies with rather than supply of these products. Therefore, Dr. Witten was concerned that my response may have been incomplete in this regard, particularly should some of the studies that can be referred to as "pre-clinical" actually be toxicological studies with human subjects, as such studies would require an IND. Therefore, she wanted me to ensure that your idea of pre-clinical studies and ours is the same, i.e., research and development and animal safety studies, but none involving human subjects. If we are in agreement with this definition, I would appreciate it if you could confirm that in an e-mail.

Sorry for any confusion my previous incorrect answer with regard to licensing may have caused. Hope the information and contacts provided above assist you in that regard.

Sincerely yours,

Jean Toth-Allen, Ph.D.
Good Clinical Practices Program
OSHC, Office of the Commissioner, US FDA

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.

From: Toth-Allen, Jean
Sent: Thursday, August 10, 2006 10:39 AM
To: [Redacted]
Subject: RE: biological specimens used in research

Dear [Redacted]:

Thank you for your clarification and follow-up questions regarding biological specimens for research.

If your [Redacted] merely collects and distributes the types of biological specimens that you list, your [Redacted] does not have a responsibility with regard to the actual studies in which they are used beyond supplying the study sponsor basic information about the product supplied and the procedures used in collecting and maintaining that product. Concerns about IRB review and informed consent in any study using these specimens is the responsibility of the sponsor of the study. In any case, INDs and IDEs are only needed when any resulting product (vaccine, drug, IVD) is to be used in studies with human subjects, so pre-clinical studies do not need either. If your firm "manipulates" the specimens in any way before distribution, that would be different, and it would be best to consult with the Center for Biologics Evaluation and Research (CBER), specifically the Office of Cellular, Tissue and Gene Therapies. Celia Witten, M.D., Ph.D. is the office director and she can be reached at celia.witten@fda.hhs.gov or by phone at 301-827-6536. It is my understanding that the only possible need for a license would be for specimens that have been manipulated in some way and I believe it depends upon the nature and extent of manipulation. Dr. Witten could best address such issues.

Back to collecting, storing, and distributing specimens without manipulation - your [Redacted] is responsible for any and all procedures involved in the collection, maintenance, and distribution of these specimens. Since they are human specimens, an IRB needs to review and approve your procedures. Whether or not informed consent is needed would depend upon both the source of the specimens and what information is retained with them. For example, if the specimens are left-over specimens from routine clinical procedures and no information about the individuals is either known upon collection or retained with the specimens, it is doubtful informed consent is needed. On the other hand, if the samples are collected prospectively, informed consent from individuals "donating" the specimens would be needed. The IRB reviewing your procedures would review and approve all such informed consent documents. You may, however, have an issue with HIPAA if there is not a specific study (even though only pre-clinical) for which the specimens will be used. As presently written, HIPAA regulations require that informed consent documents describe the specific research study involved. (For information about HIPAA requirements consult with the Office of Civil Rights and/or visit their HIPAA-related site at http://www.hhs.gov/ocr/hipaa/.)

Hope this information is useful.

If you need further information and/or have additional questions, please submit them once again to the official GCP mailbox, gcpquestions@oc.fda.gov, in lieu of responding to my personal e-mail address.

Sincerely yours,

Jean Toth-Allen, Ph.D.
Good Clinical Practices Program
OSHC, Office of the Commissioner, US FDA

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From: [Redacted]
Sent: Monday, August 07, 2006 4:02 PM
To: Toth-Allen, Jean
Subject:

Dear Dr. Toth-Allen:

Thank you for your e-mail response to my inquiry dated 6/6/06. I have gathered some additional information to clarify my previous questions.

I am working with [Redacted] that collects and distributes biological products (whole blood, white blood cells, platelets and stem cells) to be used for studies. The majority of these studies are considered "pre-clinical." We use the term "pre-clinical" to describe products that are used for research and development (not animal studies).

Protocols and informed consents are approved by an IRB when studies are conducted under an IND or IDE.

We are unclear of what the requirements are when we provide biological products for "pre-clinical" studies.

We collect and distribute biological products for vaccines, drug and in-vitro diagnostics for "pre-clinical" studies. In only one of our current studies will the product be used for another human being. For these 'pre-clinical" studies do we need the following:

1. Do these studies need to be approved by an IRB?
2. Does the informed consent need to contain the required elements listed in 21 CFR 50.25?
3. Are we required to complete an IND or IDE if these products are for "pre-clinical" use?
4. All of the biological products that are collected are shipped out of state. Are these biological products required to be licensed?

Thank you,

Sincerely,

[Redacted]