

**From:** Toth-Allen, Jean  
**To:** [REDACTED]  
**Subject:** RE: Question re. Warning Letters  
**Date:** Monday, April 28, 2014 9:49:00 AM

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Dear Ms. Ž^ää&^ää

Yes, the SQA meeting was excellent as always. Please excuse my delay in responding but I attended ACRP's annual meeting this last weekend.

As you may know, FDA does not have regulatory authority outside of the U.S. Our ability to inspect a non-US entity comes from the submission of data that is generated outside of the US and is intended to be a partial or sole support for permission to conduct research or for marketing of the investigational product. While our investigators do provide a Form FDA 483 (the 483) most times when observations are noted, this is as a courtesy to the inspected party only. Observations on a 483 must be based on regulations. Since FDA regulations are not applicable outside of the US – with the presently rare exception of when a study site outside of the US is officially under an IND – the regulations are in fact not directly applicable. When observations indicate a serious breach of GCPs we can and have issued a Warned Letter (WL) to a clinical investigator outside of the US. However, it does not hold the same meaning as one issued to an investigator in the US. While much of the content of the WL in both instances – discussion of the major issues with the conduct of the study – will be the same, the possible follow up actions differ. In the US we can pursue disqualification of a clinical investigator. We cannot disqualify a non-US clinical investigator. We can, however, advise our review divisions that data from that CI should not be consider in support of an application or submission. If this is done, sponsors will be less likely to want that CI as part of their studies in the future but they would not have as strong a concern as when a CI is disqualified.

While you are welcome to send questions to FDA staff with whom you are familiar, consider sending questions regarding human subject protection (HSP) and good clinical practice (GCP) to our official GCP mai box, [gcp.questions@fda.hhs.gov](mailto:gcp.questions@fda.hhs.gov). This box is sorted each day and a response therefore does not depend on the availability of one individual. You may also find it useful to access the set of redacted GCP e-mails found at <http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/RepliestoInquiriesToFDAonGoodClinicalPractice/default.htm> since we find that many questions and concerns are repeated over time.

Sincerely yours,

Jean Toth-Allen, Ph.D.  
Office of Good Clinical Practice  
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.

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**From:** ØYXUM/XQ  
**Sent:** Thursday, April 24, 2014 12:48 AM  
**To:** Toth-Allen, Jean  
**Cc:** ØYXUM/XQ  
**Subject:** Question re. Warning Letters

Dear Mrs. Toth-Allen,

Unfortunately, I did not have a chance to connect with you at the recent SQA Meeting in Las Vegas and attend the regulatory session on the last day as I had to leave early. I hope you enjoyed the Meeting!

Today, I would like to approach you with a question that arose in the communication with a client about FDA inspections and Warning Letters. Upon checking Warning Letters, we noted that these were all addressed to US-based clinical investigators, and we wondered if the FDA would also issue Warning Letters to clinical investigators located outside the USA. We are aware the FDA 483s are indeed issued to non-US clinical investigators, but were not sure if this would also be true for Warning Letters.

I would be very happy to receive your feedback on this matter. Thank you very much in advance!

Best wishes from Europe -

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