

**From:** Sen, Goutam  
**To:** [Kevin Smyth \(KSmyth@paxvax.com\)](mailto:Kevin.Smyth@paxvax.com)  
**Subject:** Information request regarding water source used for reconstitution of your vaccine, STN: 125597  
**Date:** Wednesday, April 06, 2016 11:08:00 AM

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Dear Kevin,

The following comments pertain to our review of the following documents submitted to STN 125597\_0: the instructions for reconstitution of Vaxchora in section 2.2 of the proposed package insert; Figures 1 and 5 of the Compatibility document in module 3.2.P.2.6; and the clinical study reports in section 5.3.5.1.

- 1) Please clarify the following information regarding the administration of Vaxchora to study participants in the three phase 3 clinical studies (PXVX-VC-200-003, PXVX-VC-200-004 and PXVX-VC-200-005):
  - a. Please clarify the type(s) of bottled water used by each of the clinical sites for reconstitution of Vaxchora (i.e., purified water, spring water, artesian water, etc.). If known, please also specify the brand name/manufacturer of the water that was used.
  - b. Please clarify whether clinical sites documented (1) the time frame between removal of Vaxchora (vaccine and buffer sachets) from the freezer and reconstitution and (2) the time frame between reconstitution of Vaxchora and administration.
  - c. We note that the Investigator's Brochure does not instruct clinical sites to thaw the vaccine and buffer sachets prior to reconstitution. Please confirm whether the vaccine and buffer sachets were (or were to be) reconstituted immediately after removal from the freezer (i.e., no thaw).
  - d. We note that the Investigator's Brochure instructs clinical sites to administer the vaccine immediately after reconstitution and mixing. Please confirm how quickly Vaxchora was (or was to be) administered following reconstitution.
- 2) The comments below pertain to our review of the Compatibility document in module 3.2.P.2.6 of STN 125597\_0. We note that Figure 1 in the Compatibility document shows the impact of different sources of bottled water on drug product potency. We have the following questions and information requests regarding the data presented in this figure:
  - a. Please clarify whether the same lot of Vaxchora was used in the evaluation of each type of bottled water.
  - b. Please specify the potency of the lot(s) used in the evaluations that support Figure 1.
  - c. Please discuss the variability of the potency of the product at time zero depending on the source of water used for reconstitution.
  - d. Please clarify whether the vaccine and buffer sachets were thawed for 30 minutes prior to reconstitution (time zero). If not, please evaluate and provide a summary of the impact of different sources of bottled water on drug product potency when the vaccine and buffer sachets are thawed for 30 minutes prior to reconstitution. Please use lots at the lower end of the potency specification for these evaluations.
  - e. Please clarify the manufacturing process used for the lot(s) used in Figure 1.

Specifically, please indicate whether the bulk drug substance hold time was [REDACTED]

- 3) Please specify the potency of the lot(s) used in the evaluations that support Figure 5 of the Compatibility document in module 3.2.P.2.6.
- 4) The following are follow up comments to the telecommunication between PaxVax and OVRP on March 31, 2016, regarding PaxVax's intentions for how Vaxchora would need to be administered if approved (i.e., by a health care professional only).
  - a. We note that in order to reconstitute the vaccine and buffer sachets, the following items, which are not supplied by PaxVax, are needed: a stirrer, a measuring cup with 100 mL marked, a freezer that can maintain a temperature of -20°C, and 70% isopropyl alcohol or 10% bleach to inactivate spilled or left over vaccine for medical waste. Please discuss what research, if any, you have conducted to support that pharmacies or travel clinics have all of the items necessary to administer the vaccine as instructed. Please comment on whether any human factors studies have been conducted or considered.
  - b. Please comment on the following:
    - i. Have you considered supplying the water needed for reconstitution of Vaxchora?
    - ii. Do you have plans to change the dosage form and/or administration of Vaxchora?

Please let me know if you have any question.

Thank you,

**Goutam Sen**, Ph.D.

Scientific Reviewer

Food and Drug Administration

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**From:** Sen, Goutam

**Sent:** Tuesday, April 05, 2016 8:38 AM

**To:** Kevin Smyth (KSmyth@paxvax.com)

**Subject:** Please give me a call 301-796-2640, STN: 125597

Good morning Kevin.

Please give me a call at your earliest convenience. I need to talk to you regarding bottle water- you plan to use to reconstitute your vaccine. I am including the document you submitted in your original BLA submission, so that we will be on the same page during our conversation. We are working on our comments to be communicated, but I thought of giving you a heads-up.

Thank you,

Goutam

**Goutam Sen**, Ph.D.

Scientific Reviewer

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