

# Memo of Device Review (10/23/2007) - Rotarix

## MEMO OF DEVICE REVIEW

BLA: 125265

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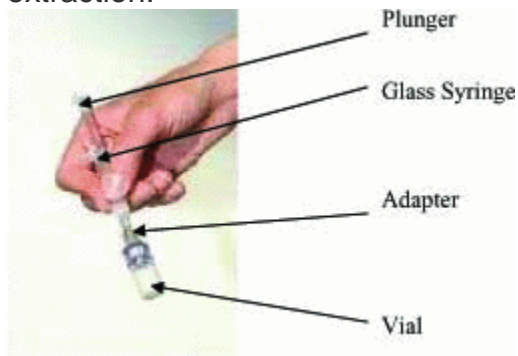
SUBJECT: Review (CON076106) of Transfer Device in STN 125265/0 Rotarix Vaccine

### General description of device:

The vaccine diluent is filled in a clean, sterile syringe. To transfer the vaccine into the syringe, a transfer adapter device is used. According to the sponsor, the reconstitution of the HRV vaccine with the diluent suspension requires the use of a transfer adapter. The transfer system consists of two plastic parts moulded together: a rigid ----- vial adapter whose spike pierces the vial stopper, and a ----- Elastomer) hose which fits tightly on the syringe tip. For the manufacturing of this transfer system based on -----

-----.

The transfer system is used for HRV lyophilised vaccine reconstitution prior to its oral administration. The sponsor states that this material is not sterilized due to the oral route of the vaccine administration and the short time of contact of the vaccine with the device. Picture below shows the syringe connected to the adapter that has pierced through a vial for extraction.



### Tests and Specifications:

The sponsor claims that it has conducted number of tests on the Transfer adapter device. The specifications and some of the tests conducted on the device are listed below:

[       ]

[       ]

[ ]

[ ]

The enteral transfer adapter is composed of 2 parts: a hose pipe and a vial adapter. The Materials are as follows: Hose pipe --->------. Vial adapter ---> ----- ------.

**Consultant's comments:**

The sponsor has conducted testing on the glass syringe, plunger stopper, plunger rod and enteral transfer adapter. However the sponsor has not provided the compositions of the components, any standards that these components comply with and labeling of these devices (syringe and the adapter). In addition, sponsor has provided only a brief description of the procedure to fill the syringe with vaccine via the adapter. Although the sponsor has stated that the vaccine would be administered orally, there is no further description on how the vaccine is given to a patient once it is in the syringe. There is no indication if these devices (adapter, syringe) are reusable, or one-time use. Sponsor should also provide an instructions set for the user.

Sponsor has conducted such tests as "-----", and "-----". However the ----- listed (-----) and these tests themselves are arbitrarily designed by the sponsor and not following any recognized standard. I have listed my deficiencies below.

**Deficiencies that require Additional Information from the Sponsor:**

1. In section 2 of Container Closure System you have stated that "*Raw materials used in the transfer device are of pharmacopeia quality in compliance with -- pharmacopeia and ISO 10993 guidelines.*" Certain materials such as ----- are mentioned in the description of the Transfer Adapter. We believe that generic class alone (e.g. -----) is not adequate because there are many formulations of material composition. Please provide a complete listing of all device materials (trade name and chemical formula) and manufacturer. Please also provide the list of materials, name of the manufacturer for glass syringes, syringe plunger stoppers, plunger rods for the syringes and the backstops for the syringes. Please also include the exact name, composition, manufacturer of the ----- used on the syringe.
2. The description, tests, specifications you have provided of the Container Closure System do not state that any biocompatibility was performed according to the ISO 10993 or an equivalent standard. Even though the syringe and the adapter may not be touching the patient, they are contacting the vaccine. Hence untested devices and their materials such as the ----- may contaminate the vaccine being administered to the patient. Please provide biocompatibility test results obtained by testing representative samples of final finished product (including the syringe and the adapter). Please also identify lot number tested and date of manufacture. Please also provide us with testing protocols with end points: Cytotoxicity, Sensitization, Irritation or Intracutaneous reactivity. The Agency recommends that you conduct biocompatibility testing as described in the guidance, Use of International Standard ISO-10993, Biological Evaluation of Medical Devices Part-1: Evaluation and Testing, <http://www.fda.gov/cdrh/g951.html>.

3. The description, tests, specifications you have provided of the Container Closure System do not describe the labeling and instructions that would be on the packages of these devices (syringe and adapter). A user should be provided sufficient information about the devices and instructions on how to use them on the packaging of the devices. The labeling on the packaging of these devices should identify if they are single-use, sterile, pyrogen-free, etc. Please provide us with the labeling and instructions of use that would be present on the packaging of your devices (syringe and the adapter).
4. In the Container Closure System section you state, *"Both tip caps and plunger rubber contains dry natural latex. The transfer adapter is latex-free."* A user or a patient can have an allergic reaction to products containing latex. Therefore in order for your device to be latex-free, please certify that your product does not contain latex, is manufactured in a latex free environment, and that the raw materials used to make your product have not been exposed to latex proteins. For devices containing natural latex, please refer to 21 CFR 801.437 User Labeling for devices that contain natural rubber.
5. In section 2 of the Container Closure System section you have provided tables containing the tests and specifications for glass syringes. FDA recommends conformance to FDA recognized standard(s) to ensure that the device has been tested according to the international consensus tests outlined in the standards. Please confirm if the glass syringe conforms to: ISO 7886-1:1993 Sterile hypodermic syringes for single use -- Part 1: Syringes for manual use, ISO 594-1 Conical fittings with a 6 % (Luer) taper for syringes, needles and certain other medical equipment -- Part 1: General requirements, and / or ISO 594-2 Conical Fittings with a 6% (Luer) Taper for Syringes, Needles, and Certain other Medical Equipment. Please also verify if the Enteral Transfer Adapter conforms to any FDA recognized standards.
6. In section 1.2 of the Container Closure System, you have stated that the vaccine is filled in a sterile syringe; however the syringe plunger rod is not sterilized. The FDA expects that the syringe, plunger stoppers, plunger rods, backstops, enteral transfer adapter (ETA) will all be sterilized since there is a possibility of contamination of the vaccine if these components are not sterile. Also the sterilization must be performed on final finished products (entire syringe and its components, and ETA). Therefore please provide us with the following:
  - a. Sterilization method description (e.g. -----)
  - b. ----, for ----- (e.g., -----)
  - c. Sterilant residuals remaining on the device. (For --, the maximum levels of residuals of ----- that remain on the device (note: not to include ---- residual level because the recognized standard, -----  
-----  
-----)
  - d. A description of the Validation Method for the sterilization cycle (not data). For example, -----cycle method, bioburden method, combination method
  - e. Sterility assurance level (SAL). (e.g., 10<sup>-6</sup> for all devices.
  - f. If you have labeled your devices as "Pyrogen Free". Please provide a description of the method used and bench testing to support your claim.