

## **SHAN5 VACCINE DELISTED FROM WHO PREQUALIFICATION**

As of 28 July 2010 the World Health Organization (WHO) has removed the Shantha Biotechnics (India) produced pentavalent Shan5 (DTwP-hepatitis B-Hib) vaccine from the list of prequalified vaccines.

This action is based on the advice of an ad hoc committee of experts, following incidents of white sediment sticking to Shan 5 vaccine vials that was difficult or impossible to resuspend (flocculation). There have been no reports of any side effects from the use of Shan5.

WHO recommends that countries continue vaccination using pentavalent vaccine from an alternative manufacturer or an alternative DTP-containing vaccine. Countries should contact WHO or UNICEF country offices (or the in-country entity facilitating the shipments or procurement of these vaccines) for assistance with ensuring sufficient supply of vaccine for continuation of immunization programmes.

### **Background**

- Shan5 is a combined, pentavalent vaccine containing diphtheria and tetanus toxoids, whole cell pertussis, recombinant DNA derived hepatitis B surface antigen, and components of *Haemophilus influenzae* type b (Hib). The vaccine is adsorbed onto aluminium salts as an adjuvant and preserved with thiomersal.
- In past months, WHO received vaccine quality complaints from Colombia, Comoros, and Nepal regarding the presence of a white sediment sticking to glass vials containing Shan5 vaccine which would not re-suspend even after vigorous shaking.
- On 19 February, WHO recommended the temporary suspension of the distribution and use of specific lots of Shan5 vaccine as a precautionary measure pending investigation.
- On 12 March, WHO recommended that the procurement and use of all lots of the Shan5 vaccine be temporarily suspended, after WHO received reports that additional lots, not included in the temporary suspension, showed a similar problem. Countries were advised to put any remaining vaccine into quarantine until further notice.
- The manufacturer was asked to provide additional data and WHO undertook independent testing in WHO-contracted laboratories.
- WHO called on an ad hoc committee of experts (from regulatory, vaccine manufacturing and immunization programme management fields) to review reports of the investigation from the manufacturer, results of WHO-commissioned tests, and the physical appearance of the Shan5 vaccine received from the countries. Samples of lots of the Shan5 vaccine received during the prequalification process and other DTP combination vaccines were also reviewed.
- On 26 April, after review of the additional data, WHO recommended the recall and destruction of all lots of the Shantha Biotechnics (India) produced pentavalent Shan5

(DTwP-hepatitis B-Hib) vaccine remaining in stock in countries. The company was requested to provide a report on the root cause of the problem and WHO undertook to re-evaluate the prequalification status of the vaccine on the basis of analysis of the report.

### **Shan5 vaccine and WHO prequalification**

The manufacturer conducted a high-quality investigation and submitted a report on the root cause of the quality issue, together with a robust plan for corrective action within the requested period of two months. The ad hoc group of experts reviewed the report and considered that the investigation report was thorough and that potential root causes were well identified. However, the implementation of corrective measures will mean that there is a break in traceability between the originally prequalified product and a revised product. WHO considers it will not be possible to link the quality, safety and immunogenicity of a product manufactured using a revised procedure to the original product. Therefore, a new application for prequalification will be required. Accordingly, Shan5 will be removed from the list of WHO prequalified products.

### **Shan5 and alternative vaccine supply**

According to updated estimates, between November 2008 and February 2010, almost 24 million doses of this vaccine were supplied to countries through UNICEF and the Pan American Health Organization (PAHO) Revolving Fund. The vaccine was also procured directly by a number of countries.

UNICEF and PAHO have been working with alternative suppliers of pentavalent vaccines and with the concerned countries to ensure that there is an adequate alternative supply of vaccines for continuation of immunization programmes.

### **Shan5 vaccine quality, safety and efficacy**

WHO does not recommend revaccination of individuals who have received the full DTP-hepatitis B-Hib vaccination schedule using Shan5. For individuals who had begun, but not completed, the schedule using Shan5, WHO recommended in its last update (26 April) that an alternative vaccine or vaccines should be used to complete the schedule.

No other vaccine quality complaints besides the flocculation described above were reported to WHO.

### **Prequalification status of other vaccines manufactured by Shanta Biotechnics (India)**

The review of the manufacturing process has ruled out as the root cause of the flocculation the manufacture of the diphtheria, hepatitis B and tetanus components. WHO will therefore maintain the tetanus toxoid Shan TT and hepatitis B Shanvac vaccines on the list of prequalified products. Also, the recently submitted application for evaluation of a cholera vaccine Shancol for prequalification will continue.

As a potential root cause is linked with the manufacture of the pertussis component, WHO has decided to also remove the tetravalent (DTwP-hepatitis B) from the list of prequalified products, and to terminate the ongoing prequalification evaluation process for a DTwP vaccine Shantrip.