
STATEMENT BY THE PAN AMERICAN HEALTH ORGANIZATION/WORLD HEALTH ORGANIZATION (PAHO/WHO) ON

FATAL ADVERSE EVENTS FOLLOWING RECEIPT OF YELLOW FEVER VACCINE PRODUCED BY BIO-MANGUINHOS, BRAZIL

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Summary of reported adverse events

In recent weeks, four fatal cases of adverse events following administration of yellow fever vaccine (17DD sub-strain) manufactured by Bio-Manguinhos, Brazil have been reported to the Pan American Health Organization/World Health Organization (PAHO/WHO).

The four deaths occurred in Peru between 6 and 24 October, 2007 in vaccinated persons ranging in age from 23 to 79 years.

All four cases reported in Peru were recipients of a single lot of vaccine (050VFA121Z), during a yellow fever vaccination campaign in the Ica Region, south of Lima. Yellow fever vaccination was started on 23 September, 2007 and was suspended by national authorities on 6 October, following the report of the first fatal case; during this period it is estimated 42,742 persons have been vaccinated with the specified lot. These four cases presented with a similar clinical picture of fever, headache, malaise and diarrhea, progressing rapidly to distributive shock and irreversible multiple organ failure. Their onset of symptoms ranged from less than 24 hours to one week after vaccination. No additional suspected cases of viscerotropic disease have been identified in Peru at this point and all other reports of adverse events following yellow fever vaccination have been characterized as mild and fully recovered.

Based on the clinical and laboratory information available to date, three of four cases are being classified as laboratory-confirmed cases of acute viscerotropic disease following yellow fever vaccination (Definite YEL-AVD); one case is probable vaccine associated viscerotropic disease pending additional laboratory confirmation on autopsy material.

An investigation of the reported cases was started by the relevant national authorities in Peru with the support of PAHO/WHO and the US Centres for Disease Prevention and Control (CDC). In addition, PAHO/WHO convened, as of 1 November, a panel of experts in yellow fever hemorrhagic disease and yellow fever vaccination, virology and epidemiology to review with the respective national authorities all the reported cases and evaluate the potential causal relationships with the vaccine.

Acute viscerotropic disease following yellow fever vaccination is a rarely reported condition first recognized in 2001; to date 37 suspected or confirmed cases have been reported globally following vaccination with both 17DD and 17D204 vaccine substrains. It most typically presents as a yellow fever-like illness with multiple organ failure, with onset of symptoms 2-5 days following receipt of yellow fever vaccines. The estimated risk for viscerotropic disease following YF vaccination ranges from 0.1 to 0.3 per 100,000 vaccinated persons overall; a higher risk has been documented in persons older than 60 years. There is currently limited understanding of the individual host factors or vaccine factors that potentially contribute to the risk of developing viscerotropic disease.

The yellow fever vaccine produced by Bio-Manguinhos is prequalified by WHO since October 2001 and supplied through the PAHO Revolving Fund and UNICEF to several countries for routine immunization, campaigns, outbreak control, and for immunization of travelers.

PAHO/WHO recommendations

The cases in Peru constitute the first reported cluster of viscerotropic disease potentially linked to a single vaccine lot. Based on the number of doses of vaccine used in Peru from 23 September to 6 October, the reporting rate of cases is approximately 10 per 100,000 vaccine doses administered, significantly higher than previously reported rates. In view of this significantly higher reporting rate of viscerotropic disease linked to the vaccine lot 05OVFA121Z used in Peru, PAHO/WHO recommend with immediate effect, the suspension of use of the Bio-Manguinhos yellow fever vaccine lot 05OVFA121Z and related lots in production, specifically 05OVFA118Z, 05OVFA119Z, 05OVFA120Z, 05OVFA122Z, 05OVFA123Z, 05OVFA124Z, 05OVFA125Z, 05OVFA126Z, till further notice. The suspension of any other lots of Bio-Manguinhos yellow fever vaccine is not necessary at this time (other than the lots specified above) as there are no data suggesting an increased risk.

PAHO/WHO recommend that all countries using the yellow fever vaccine enhance their capacity to detect severe adverse events following immunization.

Specific actions to be taken at country level:

If it is confirmed that a country has current stocks of the **specified lots** of Bio-Manguinhos yellow fever vaccine (as above), use of the vaccine should be suspended immediately and the vaccine retained under the recommended storage conditions till further recommendations are provided.

If it is confirmed that the country has **NOT received shipments of the specified lots** of yellow fever vaccine, there is NO ACTION required with regard to suspension.

ONLY if there is still concern that a country may have received yellow fever vaccine related to the suspended lots, the responsible national authorities should inform PAHO/WHO and UNICEF through their respective Country Offices of the specific lots of concern. A check will be made into these lots and the country will be advised whether these lots are affected by the suspension or not.

Further action being undertaken by PAHO/WHO, in conjunction with the relevant national authorities in Peru includes:

- Deployment of an international team of PAHO/WHO and CDC staff to Peru to assist with the ongoing investigation.
- Continuing steps to identify additional epidemiological, virological, molecular, and pathological data needed to classify the reported cases.
- Further laboratory testing of vaccine samples will be performed to help in determining the association of the reported events with the specific lots used.
- An independent review of the manufacturing and quality control process for the vaccine, as well as distribution and use of the above specified lots.
- Enhanced surveillance for potential additional cases of mild to severe viscerotropic disease and further epidemiological investigation.

The above-mentioned expert panel includes several leading national and international experts with extensive experience in investigating previously reported cases of viscerotropic disease. PAHO/WHO will continue to coordinate and rely on the expertise provided by this panel and will be issuing additional updates as critical information becomes available, as well as recommendations for further specific action.

For further information

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