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28 April 2006

MEMORANDUM CIRCULAR

No. 2006 - 0020 - A

FOR : **UNDERSECRETARIES, ASSISTANT SECRETARIES, BUREAU/ SERVICE DIRECTORS, CHD DIRECTORS, CHIEFS OF MEDICAL CENTERS & HOSPITALS AND OTHER CONCERNED OFFICES**

SUBJECT: **Destruction of any Stocks of Morupar (MMR), Morbilvax (MR) and Morubel (M) Vaccines produced by Chiron Vaccines, Italy**

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This is in relation to the Memorandum Circular No. 2006 – 0020, dated 28 March 2006, on the above subject.

Attached for information and appropriate action, is a letter from the World Health Organization (WHO) Country Representative stating that after further investigation and review of the available PMS data as well as of information supporting the hypothesis of dextran as the causative agent, confirms that there is increased allergic reactions with the Morupar® measles-mumps-rubella (MMR) vaccine.

Accordingly, the WHO advises destruction of any stocks in the country of Morupar (MMR) vaccine produced by Chiron Vaccines, Italy. The same is also being advised for other Chiron-produced vaccines specifically the Morbilvax (measles-rubella) and Morubel (measles) vaccines since these products contain similar concentrations of dextran. Attached along with this, is the briefing note on the subject from Department of Immunization, Vaccines and Biologicals of the WHO Headquarters.

Necessary dissemination of this information to all concerned Offices / Organizations is strongly recommended for their appropriate action.

For compliance.

By the authority of the Secretary of Health:

MARIO C. VILLAVERDE, MD, MPH, MPM, CESO III
Assistant Secretary

Smoking will kill you!

URGENT

WORLD HEALTH ORGANIZATION
WESTERN PACIFIC REGION

ORGANISATION MONDIALE DE LA SANTE
REGION DU PACIFIQUE OCCIDENTAL

OFFICE OF THE WHO REPRESENTATIVE IN THE PHILIPPINES
Department of Health, San Lazaro Compound, Sta. Cruz, Manila, Philippines
P.O. Box 2932, 1000 Manila, Philippines

In reply please refer to: WP/2006/0794/jb (EPI)
Prière de rappeler la référence:

Dr Ma. Virginia G. Ala
Officer-in-Charge
Bureau of International Health Cooperation
Department of Health
San Lazaro Compound
Sta. Cruz, Manila
Philippines

26 April 2006

Dear Dr Ala,

Subject: **Withdrawal of Morupar Vaccine by Chiron Vaccines, Italy**

This refers to our letter dated 24 March 2006 on the above subject.

Further investigation and review of the available PMS data as well as of information supporting the hypothesis of dextran as the causative agent confirms that there is increased allergic reactions with the Morupar vaccine.

The Headquarters, therefore, advises destruction of any stocks of Morupar (MMR), Morbilax (MR) and Morubel (Measles) vaccines produced by Chiron Vaccines, Italy, remaining in the Philippines. Attached is briefing note on the subject.

Kindly inform relevant units and agencies of this matter for their appropriate action.

Thank you.

Yours sincerely,

Dr Jean-Marc Olivé
WHO Representative

Encl.: As stated.

cc: EPI/WPRO
Dr H. Sobel

BRIEFING NOTE

Issue:	**UPDATE on withdrawal of MMR, MR and M vaccines produced by Chiron from WHO pre-qualified list (For reference: Briefing note dated 20 March)**
Date:	**20 April 2006**
To:	**Assistant Director-General, Family and Community Health/WHO and Regional Advisers**
Originator:	**Department of Immunization, Vaccines and Biologicals, (WHO/FCH)**

Background:

On 16 March, the Italian vaccine regulatory authority (Agenzia Italiana del Farmaco) announced the suspension and recall of Morupar® measles-mumps-rubella (MMR) vaccine produced by Chiron, Italy due to an observed increase in allergic reactions. This apparent increased risk, hypothesized to be related to dextran (used as a stabilizer in the vaccine), has been under review by the Global Advisory Committee on Vaccine Safety since 2005 with further data pending for final recommendations. However, in the first two months of 2006, a further increase in serious allergic reactions was reported.

Following a preliminary risk-benefit assessment of the available safety information, the Department of Immunization, Vaccines and Biologicals (IVB) decided, as a precautionary measure, to withdraw Chiron-produced MMR, measles-rubella and measles vaccines (all containing dextran) from the WHO list of pre-qualified vaccines for UN supply, until further notice. These actions were communicated to the UN supply agencies and WHO Regional Offices in a series of communications from 15 to 22 March.

Update:

IVB has reviewed additional information on the safety profile of the Chiron MMR vaccine made available to WHO, as well as possible evidence for the hypothesis of dextran as the causative agent of the observed reactions. The key conclusions are as follows:

- Comparative analyses of adverse event data for the Chiron MMR vaccine and other MMR vaccine products indicate significantly higher rates of allergic reactions reported following the Chiron vaccine.
- In particular, the data showed an increase in serious and potentially fatal allergic reactions (including anaphylaxis) following the Chiron vaccine compared to previously recognized estimates of the risk of such reactions, and compared to other vaccine products in the current analysis.
- While there is still no conclusive evidence of the causative agent and mechanism for the increased allergic reactions, the additional information reviewed lends strong support to the hypothesis of dextran as a causative agent. Dextran-related hypersensitivity reactions (not limited to vaccines) are rare and difficult to predict; further evaluation is required to determine other potential contributing factors that may have increased the risk in this instance. Data suggest the risk of such reactions may be higher with high molecular weight dextran.
- There are no data to suggest that the occurrence of allergic reactions following Morupar® may have been associated with previous sensitization with Morupar (cases occurred following 1st dose as well as 2nd dose Morupar® when the 1st dose of MMR had been given with either Morupar® or other MMR vaccine products). Furthermore, there are literature reports of other potentially common sources of dextran sensitivity, including

cross-reactive bacterial polysaccharides and traces of dextran in foodstuffs and toothpaste.

- Further safety data need to be evaluated to understand the full safety implications of the presence of dextran in Chiron M and MR vaccines.
- **The review supports, from a safety perspective, the WHO decision to withdraw the Chiron MMR, MR and M vaccines from the pre-qualified list of vaccines.**
- **Furthermore, IVB is recommending the recall and destruction of any remaining stocks of the specified Chiron vaccines that were put on hold by the previous WHO recommendation. This recommendation is being communicated to the UN supply agencies and through Regional Offices to Member States.**

Further evaluation of this safety issue is ongoing, including a comprehensive review of the presence of dextran in other routinely used vaccines and its safety implications. The outcome of this review will be reported to the Global Advisory Committee on Vaccine Safety at its June 2006 meeting for further expert review and advice to WHO.