DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Centers for Disease Control
and Prevention (CDC)
Atlanta GA 30333

JUN 18 2004

Mr. Damian A. Braga
President
Aventis Pasteur
Discovery Drive
Swiftwater, Pennsylvania 18370

Dear Mr. Braga:

Thank you for your letter regarding the recent Advisory Committee on Immunization Practices' (ACIP) recommendation that children from 6 to 23 months of age receive routine vaccinations for influenza. As you know, CDC accepted the ACIP recommendations to include the influenza vaccine in the immunization schedule for children 6-23 months of age and recommends that pregnant women also receive the vaccine. The ACIP also did not express a preference for any type of licensed influenza vaccine over another for this age group.

Aventis Pasteur is an important public health partner and critical player in the fight against vaccine preventable diseases. The issues you raise are important to us. CDC understands that, with the exception of influenza vaccines, all routinely recommended licensed pediatric vaccines that are currently being manufactured for the U.S. market contain no thimerosal as a preservative or contain significantly reduced amounts (e.g., trace amounts) of thimerosal. However, CDC continues to support the elimination of mercury from vaccines as a feasible means of reducing an infant's total exposure to mercury. CDC is committed to working with the Food and Drug Administration, other partners, and manufacturers, such as Aventis Pasteur, to assure the continued reduction or removal of thimerosal from influenza vaccine targeted for children and pregnant women as expeditiously as possible without causing interruption in the flu vaccine supply for the upcoming flu season.

I look forward to our continued partnership and working with Aventis Pasteur and other vaccine manufacturers, on this and other important vaccine issues. Please feel free to call me if you have any further thoughts or questions.

Sincerely,

Julie Louise Gerberding, M.D., M.P.H.
Director

Aventis Pasteur

Damian A. Braga
President US

April 20, 2004

Dr. Julie Louise Gerberding, MD, MPH
Director, Centers for Disease Control and Prevention
Edward R. Roybal Campus
1600 Clifton Rd., N.E.
Mail Stop D14
Atlanta, Georgia 30333

Dear Dr. Gerberding:

We are aware that the CDC may be considering a change to the recent ACIP recommendations regarding pediatric influenza guidelines that would recommend patients be immunized with preservative-free influenza vaccine. As a world leader in vaccines, Aventis Pasteur (AvP) is well aware of the need to ensure public confidence in vaccines. In particular, AvP is a proponent of our nation's efforts to transition to preservative-free vaccines for pediatric populations in order to maintain continued public confidence. While we support an orderly transition to preservative-free influenza vaccine, such a move must be carefully planned in coordination with key immunization stakeholders to ensure that the full implications of policy changes are well thought through and understood. The implications of failing to learn from recent history could prove devastating to public health.

As you may recall, in 1999, abrupt policy changes without advance input from vaccine manufacturers led to the removal of preservative in several routinely recommended pediatric vaccines. That abrupt change by policy makers caused severe vaccine shortages and resulted in unintended consequences for childhood immunization. In contemplating changes to the current ACIP recommendation, policy makers should take into account that manufacturers are five months into the planning, production and ordering cycle for this season's influenza vaccine, based on the October, 2003 ACIP recommendations. There is a high probability that an abrupt change from the current recommendation to one expressing preference for preservative-free influenza vaccine will inadvertently distort vaccine demand, and lead to a shortage of influenza vaccine nationally and undermine the success of the national influenza immunization program. Given the potential disruption to the nation's influenza vaccine supply, we believe policy makers must carefully plan for the orderly transition to preservative-free influenza vaccine for the pediatric population. We believe that the following points must be taken into consideration in any contemplated policy change:

- As the current preservative-free and preservative containing formulations of AvP's influenza vaccine are both safe and effective for use in both pediatric and adult patient

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populations, there is ample time to plan for the orderly transition to preservative-free influenza vaccine.

- Based on a 5-year rolling average for production yields, AvP will produce approximately 45 million doses of influenza vaccine available to ship by the end of October to customers. The prebooking process for influenza vaccine began on December 1, 2003. Including expected orders for pending contracts, our capacity is already fully allocated.

- Based on the October, 2003 ACIP recommendations, AvP plans to produce approximately 5 million doses of Fluzone® Preservative-free: Pediatric Dose, Influenza Virus Vaccine for the US market. This is approximately a 350% increase in our preservative-free pediatric formulation over last year's season and includes consideration for the CDC contract award. The 5 million doses represent our full capacity for the unit dose presentation necessary for preservative-free influenza vaccine.

- The already planned increase in preservative-free pediatric single-dose presentation constrains our production flexibility in both production; due to the approximate 30% loss of vaccine in every preservative-free dose manufactured, and filling; because of the need to use a single dose presentation.

- We are concerned that an abrupt change in CDC policy to recommend the use of preservative-free formulations could have fall-out in the adult market. This change could lower confidence in the adult formulation and negatively impact the adult population's immunization rates, thus increasing the morbidity and mortality related to influenza disease. If this were to occur, it could take years to restore public confidence and would result in significant delays in our efforts to achieve the Healthy People 2010 goals.

- There are several additional technical constraints which preclude further significant changes in commitments for production at this point in the year. Most importantly, the vaccine strains recommended by FDA for this season may pose some challenges in growth and yield, considering two of three strains (including the B strain) have changed from last year's formulation. As with any new strain there is always the possibility that yields may be lower than expected. Therefore, at this time we are not comfortable committing beyond our present production capacity.

- We are currently in discussions with HHS/CDC officials to establish an end of season Influenza Vaccine Strategic Reserve and large-scale production of a H5N1 influenza clinical material for evaluation by the government. Meeting the 2004-2005 season's demand, plus end of the year commitments to produce reserve doses and clinical material for the government does not leave flexibility to address such a last minute policy change.

- Finally, any substantial change to our existing production timelines could impact the scheduling of routine maintenance work on our influenza vaccine manufacturing facility. This maintenance must occur prior to the start of next season's vaccine production. AvP must be ready start production, at risk, on December 1st, in order to meet the market demand for influenza vaccine during the 2005-2006 campaign.

Aventis Pasteur supports the development of a timetable to ensure an orderly transition to a policy that expresses preference for preservative-free influenza vaccine for infants. Such a timetable would be contingent upon securing FDA approval for a new unit-dose vial presentation and should include open discussion among policy makers and stakeholders to reduce the possibility of fall-out in the adult population.

In summary, AvP supports an orderly planned transition to preservative-free influenza vaccine for the pediatric population in order to maintain public confidence in immunization. This transition must be carefully undertaken in order to avoid any supply shortages or market distortion that would undermine the national influenza immunization program. We believe that consideration of the above points is of the utmost importance when contemplating any change to policy recommendations and will help eliminate the possibility of an influenza vaccine supply disruption this year. I look forward to an opportunity to discuss these issues in more detail. Chris Grant, our Vice President, Public Policy and Government Relations, will be in contact with your office to coordinate a mutually agreeable time for us to further discuss this important topic.

Sincerely,