February 15, 2002

Sir Liam Donaldson
Chief Medical Officer
Department of Health
Richmond House
79 Whitehall
London SW1A 2NS
United Kingdom

Dear Sir Liam:

I understand that concerns about a possible link between combined measles, mumps, and rubella (MMR) vaccine and autism have intensified in the United Kingdom as a result of a recent publication by Uhlmann, et al.[1] I write to offer our scientific and medical support for the safety and use of combined MMR vaccine. As many countries around the world have found, this vaccine has controlled or virtually eliminated measles, mumps, and rubella disease, and thus greatly improved the health of infants and children In our own country, low coverage with MMR vaccine in preschool children in the years 1989 to 1991 sparked a measles epidemic that resulted in over 55,000 cases of disease and claimed more than 120 lives. Since 1996, coverage levels in children 19- to 35-months old have been approximately 90 percent, and our annual measles morbidity has declined remarkably to less than 200 cases total in the last 2 years.

Despite our success with this vaccine, we too have faced concerns related to MMR vaccine. The question about the possible link to autism, along with the suggestion that separate administration of the three vaccine components would solve the problem, have recently and extensively been reviewed in the United States. These reviews, by independent groups of experts, have concluded: (1) the available epidemiologic evidence does not support a causal link between MMR vaccine and autism, and (2) separate administration of the three components in MMR vaccine is, therefore, not warranted and may in fact harm public health.

MMR vaccine has been used widely in the United States since 1971 with no correlation between its use and the recently observed increase in autism.[2] Two independent nongovernmental groups, the Institute of Medicine (IOM) of the National Academy of Sciences and the American Academy of Pediatrics (AAP), have reviewed the evidence regarding a potential link between autism and MMR vaccine.[3,4] Both groups reviewed published and unpublished information on virologic studies, case series, and epidemiologic studies, *including* preliminary data from the recent Uhlmann, et al.[1] and Taylor, et al. articles.[5] Both the IOM and AAP independently concluded that the U.S. should continue its policy of using MMR vaccine.

The media attention and public concern toward MMR vaccine generated by the Uhlmann, et al. article is surprising from a scientific viewpoint. A commentary by Morris and Aldulaimi that accompanied the research article by Uhlmann, et al. pointed out several limitations in their research.[6] These reviewers noted that while the researchers were able to detect whether measles virus fragments were present in the pathology specimens, the study was unable to answer several critical questions on cause and effect including: What does the presence of virus fragments actually mean? What is the relationship between measles virus and developmental disorders? Did the measles virus fragments cause the disorder or do developmental disorders cause the persistence of measles virus in the bowel? Uhlmann, et al. also failed to provide critical details of the disease syndrome and baseline characteristics in "affected" children. In addition, the children in the control group were inadequately described making it difficult to determine their validity as a comparison group. For example, it was not possible to tell whether the two groups of children had been adequately matched on such variables as age, timing and type of sampling, vaccination history, reason for biopsy, and interval between vaccination and biopsy.

Our laboratory experts have also raised several important technical concerns about the research techniques used by Uhlmann and his colleagues. Clinical studies such as these must use safeguards against sample contamination and technician bias, clearly define what constitutes a positive result, and explain the rationale behind their choice of tests. Further, the methods used could not determine if the measles genomic material identified was from a previous injection with MMR vaccine, a vaccine that contained only measles vaccine virus, or was the result of a case of measles disease. Thus, in our assessment, the available virologic information presented in the Uhlmann, et al. paper does not support an association of MMR vaccination with the reported syndrome nor the need to administer separate measles, mumps, and rubella vaccines.

It is critically important that people recognize the ability of MMR vaccine to protect infants and children from once common, and potentially serious, infectious diseases. A reduction in the use of MMR vaccine, or moving to administration of single virus vaccines, not only will increase the risk of disease between scheduled immunizations, it could result in some children never obtaining the recommended vaccines. This, in turn, will increase the number of infants, children, and adults who are susceptible to these diseases and increase the likelihood of disease epidemics.

In fact, the rubella component of MMR is really our first "anti-autism" vaccine. Intra-uterine exposure to rubella (congenital rubella syndrome) is one of the few proven causes of autism. Delays in obtaining rubella vaccine could potentially fuel a rubella epidemic leading to cases of the devastating congenital rubella syndrome. It would be tragically ironic if concerns about autism leads to use of single vaccines, delays in obtaining needed immunizations, a resurgence of rubella, and, ultimately, an increase in autism.

Ultimately, our concern extends beyond measles, mumps, and rubella disease. We currently recommend that all children in the United States be protected against 11 vaccine-preventable diseases. This requires 16 to 20 injections within the first 18 months of life. Adding two more injections by separating MMR vaccine into its individual components adds another significant

impediment to completing the overall schedule. Such a change could result not only in decreases in coverage for measles, mumps, and rubella, but for other vaccines as well. Single antigen measles, mumps, and rubella vaccines are not listed as an alternative in the U.S. recommended immunization schedule.

In sum, the United States continues to recommend the use of MMR vaccine for routine vaccination of children. This recommendation is supported by the Advisory Committee on Immunization Practices (ACIP), a committee that advises the Centers for Disease Control and Prevention (CDC) on immunization policy, and by the American Academy of Pediatrics and the American Academy of Family Physicians. These three groups recently issued a joint harmonized childhood immunization schedule (http://www.cdc.gov/nip/recs/child-schedule.htm) which calls for the use of MMR vaccine.

Sincerely,

(original letter signed)

Walter A. Orenstein, M.D.
Assistant Surgeon General
Director
National Immunization Program

Enclosure

cc:
Dr. David Salisbury

[1] Uhlmann V, Martin CM, Sheils O, et al. Potential viral pathogenic mechanism for new variant inflammatory bowel disease. Molecular Pathology 2002;55:0-6.

[2] Dales L, Hammer SJ, Smith NJ. Time Trends in Autism and in MMR Immunization Coverage in California. JAMA. 2001;285:1183-1185.

[3] Institute of Medicine Immunization Safety Reviews: Measles-Mumps-Rubella Vaccine and Autism. Washington DC, National Academy Press, 2001.

[4] Halsey NA, Hyman SL, and the Conference Writing Panel. Measles-mumps-rubella vaccine and autistic spectrum disorder: Report from the New Challenges in Childhood Immunizations Conference convened in Oak Brook, IL, June 12-13, 2000. Pediatrics 2001;107(5).

[5] Taylor B, Miller E, Lingam R, et al. Measles, mumps, and rubella vaccination and bowel problems or developmental regression in children with autism: population study. BMJ 2002;324(7333). Available at http://bmj.com/cgi/content/full/324/7333/DC3.

[6] Morris A, Aldulaimi D. New evidence for a viral pathogenic mechanism for new variant inflammatory bowel disease and development disorder? Molecular Pathology 2002;55:0.