

MedImmune Vaccines is grateful for the opportunity to review and provide comment on the NVPO Pandemic Plan. Our comments reflect the perspective and experiences of a US pharmaceutical company that has recently entered the influenza vaccine market with an intranasal influenza vaccine (FluMist®). MedImmune is committed to participating in a significant way to solve the chronic influenza vaccine supply problems and to respond proactively to the pandemic threat. I am submitting for your consideration general comments on the intent and scope of the document, and also more specific comments on topics related to vaccine research, development, purchase, distribution and communication as described in the core document and various Annexes.

General Comments on the Intent and Scope of the Document

The pandemic preparedness and response plan defines the roles, responsibilities and tactical activities of key stakeholders at the federal, state and local levels. One of the key stakeholders whose role and interactions with other key stakeholders is *not* clearly defined is that of industry. The vaccine shortage situation in the 2004-05 influenza season illustrates the need to strengthen the fragile influenza vaccine manufacturing industry in the US during the interpandemic period and to emphasize its key strategic role in preparing for and responding to a pandemic threat. Therefore, MedImmune recommends that the scope of the plan be expanded to provide more attention to the vaccine industry's role in the overall strategic plan, and also that a separate Annex be written that specifically addresses tactical activities that could be undertaken by industry (with the support of federal, state and local stakeholders) during the interpandemic period. For example, public stakeholders could develop strategies that will increase and stabilize interpandemic vaccine uptake (e.g., recommendation and support for universal vaccination), which would encourage private stakeholders to maximize their supply and distribution capacity (e.g., invest in new facilities and technologies) thereby enhancing our ability to prepare for and respond to a pandemic situation.

MedImmune believes that the government needs to find ways to encourage companies to build manufacturing facilities in the U.S. There is an increasing trend for U.S.-based companies to build manufacturing plants offshore in order to gain access to a well-trained pool of potential workers as well as significant tax advantages. With this trend, comes the increased risk of the type of event we are currently experiencing, companies will face regulatory decisions that may prevent product from entering the U.S., or worse yet, in the event of a catastrophic event or the emergence of a new pandemic strain, the host country may embargo vaccine for use within its own borders.

Specific Comments on Key Decisions for Pandemic Preparedness

Vaccine distribution. The current primarily private system of vaccine distribution has the infrastructure and procedures in place to deliver millions of doses of vaccine during a period of several months. Furthermore, suppliers of injectable vaccine are able to reach high-risk individuals and the supplier of intranasal vaccine is able to reach healthy individuals. To develop a public distribution system able to target and reach each of these populations would require a sophisticated public distribution system and absolutely clear and consistent messages to the public regarding each type of vaccine being distributed. Distribution complexities likely to occur in the lead-up to a pandemic will be much greater than those in the 2004-05 influenza season, in which there was an unanticipated shortage of the inactivated vaccine. Recognizing that routine vaccine distribution requirements and targeted groups might be very different in a pandemic setting, MedImmune would favor retaining the current private distribution system until more details are available concerning the infrastructure and procedures required to implement a public distribution system for use in the event of a pandemic.

Vaccine purchase. MedImmune supports federal guarantees of vaccine purchase in the pandemic setting. Furthermore, in order to build supply capacity leading up to the pandemic, MedImmune would encourage the government to consider federal purchase of vaccine produced

in excess of vaccine actually used.

Priority groups for vaccine when supply is limited relative to potential demand.

- /// HHS is developing a list of priority groups and acknowledges that “while no law specifically addresses pandemic influenza, numerous federal and state statutes authorize relevant public health actions”. In developing the priority list, MedImmune encourages HHS to consider developing separate priority lists for injectable vaccines and intranasal vaccine based on their respective current labels, and/or to clearly designate which vaccine is subject to prioritization. This will avoid the confusion on the part of consumers and physicians as to who may be vaccinated with each vaccine and will prevent States from developing mandates that are inconsistent those of federal policy makers.
- /// MedImmune believes that HHS should consider stockpiling prototype pandemic vaccines that can be used immediately in targeted groups (e.g., in first responders) should a pandemic occur in order to provide targeted groups with some measure of protection against the actual pandemic strain. The utility of this approach would, of course, require clinical testing during the interpandemic period of prototype pandemic vaccines and assessment of the degree of heterosubtypic cross-protective immunity that they induce. MedImmune is currently working on developing pandemic vaccines using its proprietary reverse genetics technology in conjunction with the U.S. government.
- /// MedImmune believes that liability issues need to be resolved during the pandemic period.
- /// HHS notes that intellectual property issues should be resolved during the interpandemic period. Scientists associated with MedImmune were involved in the discovery of reverse genetics and, as such, the company controls certain intellectual property rights for this technology in the production of influenza vaccines. To assure public health officials had access to all applicable technology in protecting humans from pandemic strains of influenza, MedImmune proactively notified the World Health Organization in December 2003 (and subsequently notified other world health agencies) that it would grant free access to its intellectual property to government organizations and companies developing pandemic influenza vaccines *gratis* for public health purposes. For corporate manufacturers interested in using reverse genetics in the production of influenza vaccines for commercial sale, MedImmune has offered licenses to its intellectual property under reasonable terms and consistent with industry standards. MedImmune has made it clear to its commercial peers that it will waive royalties on its intellectual property for any and all pandemic influenza vaccines that are offered free of charge in the interest of public health.

MedImmune is committed to protecting public health and will continue to work closely with global public health authorities on pandemic preparedness and to ensure that reverse genetics technology is available to other manufacturers in response to a global emergency.

Vaccine development and use.

- /// The document states “it is important to ensure that resources are in place so that a pandemic vaccine can be developed as quickly as possible once a novel strains is identified”. MedImmune believes that real-time involvement of industry in informal strain surveillance informational exchanges (in addition to receiving surveillance information at formal meetings) should be encouraged because it would allow industry a “heads-up” to get facilities and materials ready to begin the manufacturing process. To develop an interpandemic or pandemic vaccine as quickly as possible, a delay of even one week in obtaining information can make a great difference in vaccine availability.

Furthermore, the first step in vaccine development involves preparation of a reassortant vaccine seed, which will most likely utilize reverse genetics methods starting with genetic material from the new pandemic strain. Although reassortants used to prepare injectable vaccine seeds are prepared by federal authorities, MedImmune produces its own reassortants for the intranasal vaccine. In order to expedite this rate-limiting first step,

mechanisms need to be in place to quickly distribute the required genetic material so that the process of vaccine manufacturing can be commenced without delay.

- ~~///~~ Use of cell culture may be required to produce the amount of vaccine required by an epidemic. However, there are both financial and regulatory hurdles impeding development and licensure of cell culture vaccines. The strategic national plan should consider mechanisms whereby these hurdles might be minimized during the interpandemic period without compromising the safety and effectiveness of vaccine produced using newer methods.
- ~~///~~ The document states “whether a live attenuated vaccine approach to a pandemic vaccine would require one or two doses has not been evaluated”. The ability to protect the population using only a single dose of vaccine would have a great impact on pandemic preparedness, and there is scientific support for the hypothesis that a single dose of live vaccine might be able to provide protection. Therefore, MedImmune is preparing a library of live attenuated vaccine seeds that can be used to prepare clinical materials in order to gather information on the immune response to a single dose of vaccine and the cross-reactive nature of that immune response.