Q&A

US puts flu vaccines on trial

The US National Institute of Allergy and Infectious Diseases (NIAID) announced last week that it will begin five clinical trials for two pandemic H1N1 influenza vaccines in early August. These trials will help inform a likely US mass-vaccination campaign beginning in September. NIAID director **Anthony Fauci** talks about what vaccines were chosen, and why.

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To increase the amount of flu vaccine available, the World Health Organization recommends using adjuvants, which boost the body's immune response to the drug. But the five trials you announced last week are for non-adjuvanted vaccines. Why?

We have planned seven priority trials. The five I announced on 22 July are for non-adjuvanted vaccines, but we also plan two more: testing GlaxoSmithKline's AS03 adjuvant with vaccine from Sanofi Pasteur and from CSL Biotherapies. We prioritized non-adjuvanted vaccines as the US government seems likely to recommend using these for vaccinating the first tier of priority groups — expected to include children and groups at higher risk of severe disease, such as those with certain underlying illnesses and pregnant women. We fully intend to proceed with trials of adjuvanted vaccines.

Will you test adjuvanted vaccines in children?

The Europeans have lots of data on the use of adjuvanted flu vaccine in the elderly, but I don't think anybody has really good data on adjuvants in children. The Department of Health and Human Services (DHHS) has therefore decided that we are not going to take the chance, and has made a policy decision that we are not going to give adjuvanted flu vaccines to kids. We don't have the time to collect substantial data.

Might not trials including at-risk groups help inform how vaccines are used?

Yes. But, as in other countries, there are many ethical constraints. We are working with both principal investigators and institutional review boards to draw up protocols for such groups. Even if the Food and Drug Administration (FDA) is considering the initial non-adjuvanted vaccines as simply a strain substitution of seasonal vaccine, it's still a new vaccine, so we want to get data from healthy adults before launching into risk groups.

What information will the NIAID get that vaccine makers won't from their own trials?

We are asking questions that will inform policy decisions likely to affect how we use vaccines, whereas the focus of vaccine makers is generally directed towards studies needed to get a licence for their vaccine. The sort of information that the FDA, DHHS and the vaccine makers told us they needed most included what levels of antigen per dose are essential to getting an adequate immune response, and whether one or two shots of vaccine will be needed.

So two trials will test both single and double shots of both 15-microgram [the amount in seasonal H1N1 vaccine] or 30-μg doses of antigen, using antigen from Sanofi Pasteur and from CSL Biotherapies. We will give the first doses in the first week or so of August, and the second dose 21 days later. We will learn very quickly after 21 days, when we draw blood, if one dose of 15 μg is enough. And if it isn't, if 30 μg is any better. And if 15 μg is enough, does 30 μg give an even better response? Shortly after 42 days, we will have data on the second doses.

Why are you testing vaccine only from Sanofi Pasteur and CSL Biotherapies, when Novartis accounts for the bulk of vaccine ordered by the United States?

Novartis has quite a sophisticated clinical-trials apparatus. The United States will purchase 45% from Novartis, 26% from Sanofi Pasteur and a little bit less than 19% from CSL Biotherapies. Novartis is able to carry the ball itself, so we made a reasonably well-based decision to fill in the gaps and get information on CSL and Sanofi Pasteur.

You also plan to test co-administration of pandemic 2009 vaccines and seasonal H1N1 vaccines. How will the immune system react to these together?

We don't know. Testing two vaccines against different H1N1s at the same time has never been done. We'll look at three test regimes: giving the pandemic 2009 vaccine before, at the same time as, or after seasonal H1N1 vaccine.

If you give the pandemic H1N1 vaccine first, will subsequently giving the seasonal H1N1 enhance the response to the original dose, or will there be antigenic competition or interference? If you give both at same time, is the body going to have a response that is enhanced against seasonal flu and not do a very good job against the pandemic vaccine, or will it actually amplify the response? And if you give pandemic vaccine after [seasonal vaccine], is that going to have an enhancing or suppressing effect? Immunologically, you can't predict the outcome.

What if we have a vaccine and then the genetics of the virus changes?

You never can predict that, but things look encouraging to me from a molecular-virological standpoint. If you look at the molecular and genetic make-up of the virus from the very first isolates in early April compared to what we are seeing now in late July, it's virtually an identical virus everywhere. So it doesn't look like it is under pressure to mutate to a significant degree. We hope it stays that way for the autumn and winter season. ■

Interview by Declan Butler

For more H1N1 coverage, see www.nature.com/swineflu.