

Interview with Rino Rappuoli (Head of Vaccines Research for Novartis Vaccines & Diagnostics)

## “We Have To Be Prepared”

On June 11, the World Health Organization (WHO) raised the worldwide pandemic alert level to Phase 6 in response to the ongoing global spread of the influenza A (H1N1) virus, meaning that a global pandemic is underway. While the WHO's decision is a reflection of the spread of the virus, not the severity of illness caused by H1N1, *Lab Times* interviewed the Global Head of Novartis' vaccines research, Rino Rappuoli, about the flu pandemic.

*Lab Times:* Dr. Rappuoli, what do you think about the media's portrayal of the swine flu pandemic? Many expected a catastrophic spreading of the infection, some were afraid even of a pandemic on the scale of the 1918 flu virus. However, so far the consequences seem not to have been too serious.

**Rino Rappuoli:** Many people say that it is not so serious, but they say this because everyone was expecting the same scenario we had from the H5N1 influenza virus that in 2005 killed about 60% of infected people. So, maybe this new infection is not serious if compared to H5N1, but it is serious if compared to normal seasonal in-

fluenza. We need a balance: it is not good to exaggerate nor to make light of such a situation.

*What about the risk of a genetic rearrangement of the virus's genome that could lead to a new and even wider wave of infection? How likely is such a scenario?*

**Rappuoli:** Such a genetic rearrangement is a risk that is typical for influenza viruses. The new H1N1 strain has already reached the United States, Australia, South-America and Chile

[editor's note: *Lab Times* conducted this interview at the beginning of June; since then the spread of H1N1 flu has yet reached over 70 countries, such as the United Kingdom,

Germany, France and other European nations]. It's a pandemic infection and that is so not only because the virus is spreading all over the world, but also because the people mainly affected are the young, under 50, as happened for the

pandemics in 1918, 1957 and 1968. Normal influenza usually concerns the elderly and children. So, mortality and hospitali-

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Rino Rappuoli,  
vaccine researcher.

zation have been not so great but the ones that die are young. The other thing that is important to think about is the big discrepancy between the number of deaths in Mexico and in the United States. A good answer for this could be that in countries such as the United States, where medicine is advanced, it is too difficult for people to die due to an influenza infection. Instead, in Mexico the public health situation is probably not ready to deal with a serious population infection. Everyone speaks about this new H1N1 as a "mild infection", but I believe that it is probably mild only for us, and not in all countries.

On May 15th, Michelle Childs, Director of Policy and Advocacy at the Campaign for Access to Essential Medicines (Doctors Without Borders/Médecins Sans Frontières), said that, "If a new pandemic will spread [...] we will have to pay our attention to the poor countries that are mainly at risk since they are the less prepared". How will it be possible to prevent such a terrible scenario, not only in poor countries but everywhere?

**Rappuoli:** Well, the good-behaviour regulations (washing your hands, staying at home for several days, etc.) that governments are adopting are vital and they are really important to try to restrain the infection from spreading. However, I am convinced that the only way for governments to be prepared is getting the right vaccines.

Novartis is working on vaccine development, both with egg-based and cell culture-based production. How is development going?

**Rappuoli:** We have received the virus genome from the CDC [the US Centers for Disease Control and Prevention]. We have already started virus propagation both in eggs and in cells, and then we will start vaccine production. From our point of view, the adjuvant MF59 is a great innovation in vaccine development. When we used this adjuvant in past years, as for the H5N1 virus infection, for example, we observed that the vaccine was not effective if administered without MF59. Moreover, this adjuvant seems to be the only way to protect from potential virus genetic drifts.

Which kind of adjuvant is the MF59 that you are using?

**Rappuoli:** There are only two adjuvants available for humans. One is composed of

## About

### Rino Rappuoli...



... was born in 1952 in Tuscany, Italy. Currently, he is the Global Head of Vaccines Research for Novartis Vaccines & Diagnostics (Siena, Italy), responsible amongst others for the development of avian and pandemic influenza vaccines. In the scientific world, Rappuoli is well known for his vaccine and immunology research. In "cellular microbiology", he has co-founded a new scientific discipline, combining cell biology and microbiology, as well as pioneering vaccine development with his "reverse vaccinology" approach (that is, screening an entire pathogenic genome using bioinformatics to find genes with attributes to act as appropriate vaccine targets).

Before joining Novartis in 2005, Rappuoli was Head of R&D at the Italian vaccine company Sclavo. After Sclavo's acquisition by US corporation Chiron in 1992, Rappuoli led the development of adjuvanted flu vaccines. He also accounted for the first recombinant bacterial vaccine against pertussis. -WK-

aluminium salts and the other is MF59, first developed and approved in Italy in 1997, that is an emulsion containing two detergents. Once injected into the body, MF59 puts the immune system on a state of alert and an intensive immunogenic response occurs. Without an adjuvant, the response would be less effective.

Is it known how this "swine flu" virus originated?

**Rappuoli:** The media call this virus "swine flu", but it is not swine at all; it is a human virus. People called it "swine" because the sequence of its hemagglutinin protein, coded by one of the eight genetic fragments that compose the viral genome, is very close to the one of the American swine flu. However, looking at other fragments, this kind of viral strain can be called "triple reassortant". The triple reassortant originated in the nineties, and it contains genetic fragments from human, swine and avian flu viruses. The H1N1 virus that today is spreading derives from this triple reassortant but with the addition

of other different genetic fragments. The H1N1 strain appeared first in 1918 and then it remained as a unique human lineage; in swine the same virus evolved into

two different strains: an Euro-Asiatic one, that kept the avian genes, and a North-American one. The actual viral strain is a sort of a combination of all of these different strains"

**"Today everyone seems to have forgotten the 2005 H5N1 virus infection. But the virus is still there and I am afraid of a global disaster. If H5N1 should rearrange with H1N1 the combination could be lethal."**

How could this "genetic rearrangement" occur?

**Rappuoli:** Well, humans move all around the world, and so do animals, especially birds.

Turning back to vaccine development. Pharmaceutical

companies have to deal with the production of the seasonal flu vaccine and the production of the new vaccine. Do you think this will be a problem?

**Rappuoli:** We are optimizing the production of the traditional one [the seasonal flu vaccine] while preparing the development of the second, so I don't really think we will have problems. There is one thing that I really would like to tell you. As we said at the beginning, we have to speak about this pandemic infection and we have to try to be prepared for everything that may happen. So, I want to tell you that today everyone seems to have forgotten the 2005 H5N1 virus infection. But the virus is still there and I am afraid of a global disaster. What I mean is that if H5N1 should rearrange with H1N1 the combination could be lethal. So, we have to be prepared.

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