Ghostly images made their way around the world in the spring of 2006—government officials and scientists in rubber boots and full-body protective suits bending over the remains of dead swans. Dead birds and lifeless fowl, the emergency slaughter of entire flocks at chicken farms, quarantine zones and police barriers. Bird flu had moved into public consciousness and, with it, the concern that the H5N1 “avian plague” virus might mutate into a form that would threaten human life. Then came the all-clear signal. The crisis disappeared as quickly as it had come. The virus passed out of sight and the pandemic did not occur. Yet.

One year later the much-feared bird flu virus reappeared, this time with much less resonance in the media. “The question is not whether there will be a pandemic, but rather when,” says Reinhard Kurth, president of the Robert Koch Institute, Berlin. In view of the genetic instability of influenza viruses, it is only a matter of time before a mutation occurs that is transmissible from human to human. Recent dramatic scenarios include the Spanish flu (1918–20), the Asian flu (1957) and the Hong Kong flu (1968), when influenza claimed millions of lives all over the world (see box next page). In addition to the human tragedy, such events bring huge financial costs to bear. Based on its experience with the epidemic respiratory illness SARS in 2003, the World Bank estimates global costs of approximately $800 billion in the event of a pandemic.

**SETTING LIMITS**

From a risk perspective, pandemics are classic catastrophe scenarios. They are similar to earthquakes and tornadoes—events “with potentially large impacts but, at the same time, low probability of occurrence,” according to Andreas Schaer of the Allianz Global Corporate & Specialty PharmChem team in Zurich. The consequences of a pandemic could be very serious because of the associated restrictions on public and economic life. “The insurance industry needs to focus its attention not only on the impacts in the areas of life, property and health insurance, but also on financial markets,” he says. “In serious events, investors would prefer to transfer their capital to assets that are believed to be more secure.”

Under such circumstances, when there is pressing need for rapid development of vaccines at the same time that clinical testing has only limited feasibility, liability issues for vaccine manufacturers take on particular significance. “Pandemics require thinking outside the box,” says Johannes Klose of the Zurich PharmChem team. “At some point, the welfare of the community at large becomes the issue. Indemnity, meanwhile, is a complicated aspect, because it is regulated differently in every country.”

**PLANNING AHEAD**

What do these concerns add up to for dealing with a pandemic? What is needed, above all, is continuous professional work on the part of government agencies, the scientific and research communities, and all stakeholders in the risk industry. The basis for such work is provided by the six-step model for risk assessment propagated by the World Health Organization (WHO). Currently the assess-
ment stands at Phase III, the beginning of the alarm phase. At this level, there is a regular exchange of information among WHO, government agencies and the scientific community. “The excitement in the media in 2006 and this bird flu, which was not transmitted to humans after all, did do some good,” says Klose. “It generated helpful political pressure.” For example, he notes, the drug industry pledged to build up its production capacity for vaccines and to keep reserve production capacity available for use in the event of large-scale diseases.

Time saved by planning and preparation is always a significant factor in the defense against a pandemic. For example, production of an adequate amount of avian flu vaccines requires that genetically modified H5N1 seed viruses be provided to WHO reference labs. Schaer notes that “approximately 20 pharmaceutical companies are doing research in this area according to the data of the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA), headquartered in Geneva, Switzerland. Nevertheless, the bottom line is that the pandemic pathogen’s genetic code is still the greatest unknown in this calculation.”

Especially in the race against time that a pandemic inherently creates, innovative research is needed. In the past year, for example, GlaxoSmithKline (GSK) submitted a “mock-up” vaccine dossier to the European Medicines Agency (EMEA). Model vaccines, which replicate the basic genetic structure of the pathogen in the broadest possible way, lay the foundation for an interim de

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<tr>
<th>DISEASE</th>
<th>TIME</th>
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<tr>
<td>Spanish flu</td>
<td>1918–20</td>
<td>40–50 million</td>
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<tr>
<td>Asian flu</td>
<td>1957</td>
<td>1–2 million</td>
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<td>Hong Kong flu</td>
<td>1968</td>
<td>ca. 1 million</td>
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Two of the three catastrophic pandemic pathogens of the last century came from the mingling of bird flu and human flu viruses. The pathogen associated with the Spanish flu developed into a human-transmissible form on its own.

Sources: WHO, BBC, globalsecurity.org

faceto license through their clinical data, providing the basis for quick licensing of an actual pandemic vaccine in a serious situation. “The license will go through in a few days, because no more clinical studies will have to be conducted before the granting of the license,” says vaccine expert Norbert Hehme.

PRODUCING VACCINES

Solutions have been found to many puzzling aspects of the H5N1 virus, which initially had been regarded as unsolvable. “As long as human-to-human transmission is not taking place on a large scale, time is on our side,” Schaer says. “On the technical front, many innovations are showing progress.” Research into transmission and vaccination, he notes, is currently taking place at the level of cell cultures.

Until recently, the production of influenza vaccines relied on fertile eggs, and production volume had been limited by capacity for inoculating these eggs. The composition of the vaccine against avian flu is already described in the seed vaccine dossiers; a broad-spectrum vaccine in the process of development and licensing,” explains Schaer. “The final work on the puzzle will entail finding and placing the last decisive piece in the general picture.” This will require no small amount of luck in challenging circumstances.

In addition to the vaccines that are intended to provide specific protection against the pathogen causing the pandemic, broad-spectrum vaccines are also in the process of being developed and licensed. The latter vaccines can be used before the outbreak of the pandemic illness, but the down-side of the broad-spectrum approach is that it does not offer specific protection against the particular virus strain.

The question is not whether there will be a pandemic, but rather when. — Reinhard Kurth | President of the Robert Koch Institute