Backgrounder:

Egg-based vs. cell-based influenza vaccine production

Influenza vaccines have been available for over 50 years. Generally, they are trivalent, i.e. they contain three different, inactivated virus strains, either whole viruses or parts or subunits of them. Because the flu virus is changing its antigenic shape constantly (either in minor drifts or in major shifts), the composition of the flu vaccine needs to be adapted to these changes regularly. The monitoring of these changes is done by the Global Influenza Surveillance Network of the World Health Organization (WHO). At the beginning of each year, the WHO makes a recommendation for the strains to be included into the vaccine for the coming influenza season.

Traditionally, influenza vaccines are produced in fertilized chicken eggs. Eleven days after fertilization, the influenza virus – each strain is grown separately – is injected into the eggs and accumulates in the fluid surrounding the embryo. A high-yielding donor strain is co-injected. The embryo becomes infected so that the virus can multiply. After several days of incubation, machines open the eggs and harvest the virus. Then the virus is carefully purified, chemically inactivated and used to produce the vaccine. On average, between one and two eggs are needed to produce one dose of vaccine. The entire production process lasts at least six months.

An alternative way of producing flu vaccine is based on cell or tissue cultures. This method of production was first described in the mid-nineties and is still in its experimental stage, yet all major players in the vaccines industry have embarked on development. Mammalian kidney cells are preferably used for these cell cultures. The virus is injected into these cells, which multiply as the virus does in them, before the the cells' outer walls are removed ,harvested, purified and inactivated. This process resembles a biotechnological fermentation, in which you move from small liter jars to huge fermenters during production. It is not unusual to produce vaccines in cell cultures; polio vaccine, for example, is made this way. Yet the development of such a cell culture-based production is a long and arduous process, namely in terms of its efficiency, standardization and validation.

The egg-based production of flu vaccines is well established and cost-effective. It works well – though with obvious disadvantages: Extensive planning (procurement of many million eggs, long timeline) is necessary that limits the flexibility in case of exponentially increasing demand. A flu pandemic could probably not be contained and defeated on egg-based procuction, because the production takes too long and eggs don't grow on demand. Cell culture based systems, however, could be rapidly expanded and scaled up in times of emergency – which also points to one potential downside of tissue culture production: the up-front costs for operational readiness of such plants (with its huge fermenters) are much higher than the costs for egg-based systems,, and the yield may be slightly slower.

Mammalian cell-based flu vaccine production may have even more benefits: potential impurities in eggs (antibiotics, other viruses) may cause sterility problems. There is also a risk of allergies against egg albumin. None of these risks exists in cells. Last but not least, the strains grown in cell cultures equal the original clinical isolates, while the growth of epidemic viruses in eggs result in variants that are antigenically distinct from the original viruses. Emerging endemic viruses sometimes do not grow at all in eggs. Virus grown in mammalian cell culture is therefore more representative of the circulating wild type virus than that grown in eggs.

While it is not yet proven that cell culture based flu vaccine products will be superior to egg-based products, they are expected to progressively capture an increasing market share starting in the future.

(Note: The term TC = tissue culture, however, is a bit misleading, because the viruses for the vaccine are not grown on the tissue but in the single cells of this tissue)