

AVIAN FLU DRUGS: PATENT QUESTIONS

The world is scrambling to defend against the threat of an influenza pandemic, which some predict could prove even more disastrous than the flu pandemic which left over 40 million people dead in 1918 -1919. If the highly pathogenic H5N1 avian flu virus mutates into a form transmissible between humans, it could trigger a public health crisis. Ensuring sufficient supplies of flu drugs is a central concern for public authorities, and one which is closely linked to the intellectual property rights which cover these drugs. Commentary in the press and among the general public, however, suggests some uncertainty as to how the international patent system applies in practice. The following answers to a few frequently asked questions seek to clarify some of the basic facts.



A microbiologist at the U.S. Center for Disease Control investigates the pathogenicity of the H5N1 virus.

Background: The two main products currently available to treat the flu virus are Tamiflu (oseltamivir) and Relenza (zanamivir). These are not vaccines, but a class of medicines called neuraminidase inhibitors, which work by limiting the spread of the influenza virus inside the body. Tamiflu has been highlighted because of its relative ease of use. As governments stockpile millions of doses of Tamiflu, wide-

spread concerns have been raised about the capacity of Roche, the Swiss pharmaceutical company that manufactures and distributes the drug, to supply the need.

First, what is the difference between Tamiflu and oseltamivir?

They are the same drug. Oseltamivir is the *generic* name of the anti-viral drug which Roche markets under its *trademark* Tamiflu.

And Roche owns the oseltamivir patent?

No. A quick search of patent databases shows that the patents covering the invention of osel-tamivir are owned by the California-based biopharmaceutical company, Gilead Sciences. (See e.g. U.S. patent no 5763483, for a "novel carbocyclic compound", filed in 1996 and in force in principle until at least 2016.) Rather than further develop and manufacture the drug within the company, Gilead opted in 1996 to license to Roche certain of the exclusive rights conferred by the patents.

What IP rights does the licensing agreement give Roche?

Gilead granted Roche a sole and exclusive license. Broadly speaking, this gives the legal right to Roche – and only to Roche – to undertake or sublicense the manufacture, sale and distribution of oseltamivir-based products covered by their patents. The text of the Gilead-Roche license is available on an open database.¹

Does Roche hold these rights worldwide?

No, because patent rights are territorial. They have legal effect only in the specific countries in which a patent was applied for and granted. Gilead never acquired a patent for oseltamivir in, for example, Thailand, Philippines, Indonesia or many other countries. So there are no oseltamivir patent rights to license or otherwise exercise in those countries.

So other drug manufacturers in those countries can freely produce and sell oseltamivir?

Legally, yes, provided there are no other rights covering the technology a manufacturer wishes to use. Indonesia was among the first of such countries to announce plans to manufacture oseltamivir. This does not infringe any patent rights, provided the drug is not subsequently exported to a country where a patent is in force.

Why aren't more countries doing this?

Patent protection is only part of the story. The manufacturing process is highly complex, and in many of the countries where oseltamivir is not patented there are no drug manufacturers with the capability or resources to produce it. There may be other economic, commercial and regulatory factors as well.

1. <http://contracts.corporate.findlaw.com/agreements/gilead/roche.lic.1996.09.27.html>
 2. See e.g. the USPTO patent database for the patents filed by Gilead: <http://www.uspto.gov/patft/index.html>
 3. For WTO's TRIPS Fact Sheet see: http://www.wto.org/english/tratop_e/trips_e/public_health_faq_e.htm

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And presumably Gilead and Roche keep the formula secret?

No. Public disclosure is central to the patent system. All patent applications have to reveal the knowledge required to reproduce the invention. So basic knowledge about how to produce oseltamivir is easily accessible through free patent information databases.² That said, Roche has, of course, in the meantime built up much additional manufacturing know-how in the production of oseltamivir.

If Roche can't meet the world's demand, and if the manufacturing capacity in countries outside the patent protection is inadequate, what are the other options?

First, Roche can voluntarily grant sublicenses permitting more companies to manufacture and sell Tamiflu. So far it has issued sublicenses to the Shanghai Pharmaceutical Group in China and to Hetero Drugs in India. (Note, this is distinct from Roche's negotiations – reported in press releases – with possible additional “partner companies” in order to expand capacity. These companies would not get a full sublicense to produce the drug independently, but would be integrated into Roche's own supply chain network, taking over specific production steps.)

Voluntary licensing may seem adequate in normal circumstances. But faced with a public health crisis like this, can governments not break the oseltamivir patents, as some have threatened?

Yes, that is also an option. But let us clarify the terminology: “Breaking the patent” actually refers to government authorities using the flexibilities permitted *within* international IP law. These allow a government in certain situations to decide to issue a compulsory license, or a government use authorization, for production of the patented product without the consent of the rights holder.

These flexibilities are defined in Article 31 of the World Trade Organization's Agreement on Trade-Related Aspects of Intellectual Property Rights



The starting material of the Tamiflu production process, shikimic acid, is extracted from the pods of the star anise, grown in mountain provinces in the south west of China.

(TRIPS)³ and in the Doha Declaration on TRIPS and Public Health, together with the subsequent decision by WTO Members regarding compulsory licenses for the supply of drugs to countries with limited manufacturing capacity.

If a government issues a compulsory license, does that negate all Roche's IP rights in that country?

No. Roche would still have the right to market its own product there. And the authorized use would probably be limited to one, specific pharmaceutical – whereas the Gilead patents actually cover a wider array of new neuraminidase inhibitors.

Moreover, the use authorized by the government would be limited to the authorized purpose and would still be subject to compensation, or to what the TRIPS Agreement calls “adequate remuneration...taking into account the economic value of the authorization.” TRIPS also sets several other conditions on the issue and use of compulsory licenses, such as the requirement normally to have first sought a voluntary license, although this provision can be waived for public non-commercial use or in times of emergency.

Note: WIPO Magazine has prepared the above to aid public understanding. It does not represent an official interpretation of the legal provisions or of the position of any of the parties mentioned.