Office of Technology Licensing
Intellectual property newsletter
St. Jude Children's Research Hospital
ALSAC • Danny Thomas, Founder
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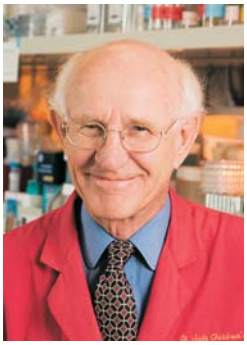
Bird Flu Vaccine



Dr. Robert Webster

Merial's vaccine, which includes reagents provided by St. Jude in the 1980's, is still effective today.

The influenza virus has received much attention lately due to recent widespread outbreak of the H5N1 avian virus among poultry in Asia. This "bird flu" has jumped from birds to humans and killed at least 60 people in Thailand, Vietnam, Cambodia and Indonesia. The existing avian H5N1 strain cannot easily transmit from human to human, but many scientists are concerned that it is only a matter of time until the virus obtains the ability to do so. When this happens, it could trigger a global pandemic, potentially killing millions of people.

Many governments and private companies worldwide are now engaged in a desperate race to make human and avian influenza vaccines to curtail the spread of this deadly virus. However, a small group of researchers including

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Research Tool Patents Take a Hit

Research tools represent one of the largest, if not the largest, categories of patented technologies held by universities and research institutions. This category encompasses a wide array of methods and materials used to identify and characterize new drugs. These research tools typically arise from basic research and are patented so their value can be captured by licensing these patent rights to pharmaceutical companies. St. Jude has patented and licensed a wide array of research tools, including cancer drug targets, drug screening methods, and animal models of human disease.

This accepted process of patenting and licensing research tools faces an uncertain future as a result of the recent U.S. Supreme Court decision in *Merck KGAA v. Integra Life Sciences I. LTD.*, 545 U.S. ___, Slip No. 03-1237 (June 13, 2005). In its decision, the Supreme Court held that the use of patented compounds in preclinical studies is protected from claims of patent infringement. The basis for this protection is 35 U.S.C. §271(e)(1). This statutory provision excludes from infringement those uses of a patented invention that are reasonably related to

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How Are Inventions Disclosed to OTL Evaluated?

In the first half of 2005, the OTL received twenty-one invention disclosures. Compared to the totals for the last three years, 35 each for 2002 and 2004 and 32 for 2003, we should see a slight increase in inventions disclosed to the OTL this year. Once the invention disclosure is submitted, what are the procedures taken toward licensing?

First, the OTL enters into discussions with the inventor(s) to obtain a better understanding of the invention. As the flow chart on page 2 shows, this meeting may take place before an invention disclosure form is submitted, especially with investigators who have never submitted an invention. The technology is evaluated based on its (1) fit with the St. Jude mission, (2) benefit to the public and

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Timing of License Income Allocations to Inventors is Changing

In January 2006, the OTL will convert its accounting system from the calendar year to the July 1-June 30 fiscal year to harmonize with other internal accounting systems. As part of this transition, inventors will receive two license income allocations in 2006. The normal distributions will be made in March for license income received during the 2005 calendar year. A second allocation will be distributed in the fall for license income received from January 1 through July 31, 2006. Beginning in 2007, one allocation per year will be made in the fall based on license income received during the previous fiscal year.

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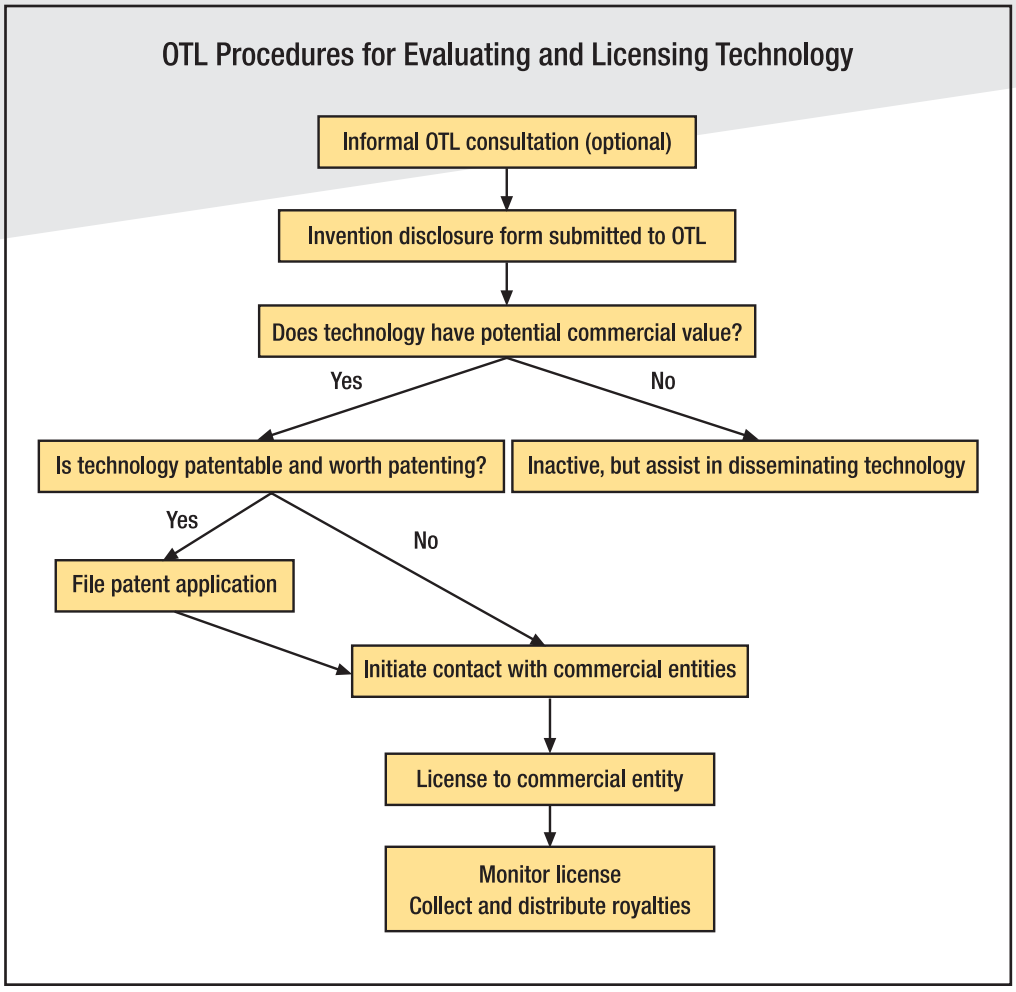
(3) commercial potential. If the invention is determined to have no commercial value, the technology is considered inactive. No further licensing activities will be undertaken, but the OTL assists the investigator in dissemination of the technology to other academic institutions via a material transfer agreement.

Is It Patentable?

If the invention is determined to meet the three criteria above, the OTL will determine the patentability of the invention. This evaluation may be undertaken internally or with the help of outside patent counsel. If it is determined that the invention is patentable, a US application is filed, preferably before the investigator discloses the technology outside St. Jude. Additional US and foreign applications may be filed, depending on the technology.



Marketing and Licensing

Some technology may be determined to be unpatentable, but still have commercial value. Such inventions include antibodies, knockout and transgenic animals, proteins and viruses. If the inventor or the OTL are aware of a company interested in the technology, the OTL will undertake negotiations with that entity to license the technology. If there are no potential licensees, the OTL will market the technology. This involves identifying companies conducting research in an area related to the technology and/or ones with similar products on the market. These companies are provided a brief description of the technology and asked to contact the OTL if interested in learning more. The technology is also listed on the OTL internet site *http://www.stjude.org/technology-licensing*.

Once the technology is licensed, the OTL will monitor the licensee for diligence obligations relating to further development of the invention. Any upfront, milestone and/or royalty payments due St. Jude are received by the OTL and a portion is allocated to inventors.

Shawn Hawkins, OTL, and Anne-Marie Colapietro, HR, represent St. Jude at the 2005 BIO Conference in Philadelphia. Virgil Holder, HR, not pictured, also attended.

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developing and submitting information to the FDA for the approval of a drug. It was enacted to allow generic drug manufacturers to test their drugs for equivalency with patented drugs during the patent term so they could get them approved and ready for marketing immediately after the patent expired.

Before this decision 35 U.S.C. §271(e)(1)had been invoked to protect a broad range of activities related to clinical research, but no one had ever tried to use it to protect preclinical activities from claims of infringement.

Many practitioners felt that preclinical activities should not be protected by this provision for a variety of reasons. In particular, the fear was expressed that extending this protection to preclinical activities would significantly devalue patents covering research tools or render them worthless.

In its decision, the Court found that this statutory provision necessarily includes certain preclinical activities which produce data that must be submitted to the FDA in an investigational new drug application (INDA) in order to receive approval to conduct clinical trials. The Court noted that this provision even protects activities that do not lead to an FDA submission, as long as there was a possibility that the activities could have led to an FDA submission when they were conducted.

While a footnote indicates that this decision does not apply to research tools, the reasoning of the Court certainly seems applicable to any invention used in preclinical research. Therefore this case provides strong ammunition against any claim of patent infringement based on activities related to preclinical drug discovery and development.

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our own Dr. Robert Webster have been conducting research in this area for many years and have already made substantial progress. Dr. Webster developed reagents more than twenty years ago that have been used to make a currently available vaccine that shows signs of protecting the avian population from the H5N1 virus.

TROVAC™ AIV H5

In the 1980's, Dr. Webster provided a clone containing the hemagglutinin (HA) gene from an H5 avian influenza strain to a small company, Virogenetics, under the terms of a standard material transfer agreement (MTA) for the development of a vaccine to be used in birds. Virogenetics inserted the HA gene into an attenuated strain of a fowl pox virus to generate an avian vaccine, TROVAC™ AIV H5. The MTA stipulated that Virogenetics could use St. Jude's reagents for internal research purposes, but would need an additional license from St. Jude in order to further develop and commercialize a vaccine. In 1988, St. Jude entered into a collaboration and license agreement with Virogenetics, under which Virogenetics paid for research in Dr. Webster's laboratory that helped characterize the vaccine and agreed to pay St. Jude royalties on the sale of TROVAC™ AIV H5.

Virogenetics eventually became a Pasteur Merieux majority owned biotechnology joint venture. In 1997, Rhone Merieux and Merck AgVet formed a joint venture to create a new animal health company called Merial. Merial is the current owner of the TROVAC™ AIV H5 vaccine. Today, Merial is a joint venture between Merck and Sanofi Aventis.

In the US, the administration of avian influenza vaccines is governed by the US Department of Agriculture. Therefore, a company must obtain a Veterinary Biological Product License in order to sell their vaccine. TROVAC™ AIV H5 received a conditional license in 1998. It is the only USDA licensed avian influenza vaccine for administration to chickens at one day of age and is fully efficacious after just one dose.

Poultry Vaccinated in the Americas and Asia

TROVAC™ AIV H5 entered the market in 1998. Over 1.6 billion doses of the TROVAC™ AIV H5 vaccine have been sold in Mexico, Guatemala and El Salvador since that time with no reported adverse reactions. In March 2005, Vietnam began testing 600,000 doses of TROVAC™ AIV H5 in chickens. The Vietnamese Ministry of Agriculture and Rural Development announced positive results of the trial in September and is allowing Ho Chi Minh City to use an additional 600,000 doses on its poultry flock. Tom Mickle, Associate Director for Merial Avian Global Enterprises anticipates that Merial will ship 12 million doses of the TROVAC™ AIV H5 vaccine to Vietnam in the first quarter of 2006. TROVAC™ AIV H5 data is also being evaluated by international agencies and experts for inclusion in international guidelines for controlling and preventing avian influenza outbreaks.

Controlling avian influenza is not St. Jude's mission. However, through licensing to industry, St. Jude's technology and expertise is being utilized to control avian influenza, which could prove instrumental in preventing the avian strain from mutating into a form capable of transmitting from human to human and causing a pandemic.

[*This is the first article of a 2 part series. The second article will describe more recent efforts of Drs. Webster, Webby and Hoffmann and their colleagues here at St. Jude to make vaccines effective against the H5N1 avian influenza*].