Office of Technology Licensing
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New Bird Flu Vaccine


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In the previous edition of this newsletter, an avian influenza vaccine that was developed using reagents provided by Robert Webster, PhD, Infectious Diseases, back in the 1980s was highlighted. More recently, Fort Dodge Animal Health, a division of Wyeth, collaborated with members of St. Jude's Virology Division to develop an avian vaccine specifically designed to protect against the H5N1 virus. On April 10, 2006, Fort Dodge announced that this vaccine, marketed as Poulvac® FluFendTM i H5N3 RG, was conditionally approved by the National Agency of Veterinary Medicine (France) for use in controlling the H5N1 virus in France. Approval was based on the superior efficacy of Poulvac®, which demonstrated the ability to reduce mortality, and virus re-isolation and shedding after challenge with highly pathogenic avian influenza viruses.

St. Jude and Fort Dodge began discussions in February 2004 and entered into a formal collaboration and license agreement in December of that year. St. Jude prepared the seed stock for the vaccine using the eight-

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How to Avoid Losing Your Patent

Inequitable conduct verdicts hurt. Here are eight steps you should take to avoid them

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During the early and mid-1990s, Purdue Pharma filed three patent applications for oxycodone formulations. The applications highlighted an unexpected finding:

It has now been surprisingly discovered that the presently claimed controlled release oxycodone formulations acceptably control pain over a substantially narrower, approximately four-fold [range] (10 to 40 mg every 12 hours--around-the-clock dosing) in approximately 90% of patients. This is in sharp contrast to the approximately eight-fold range required for approximately 90% of patients for opioid analgesics in general.

In October 2000 Purdue sued Endo Pharmaceuticals, alleging that Endo's generic drug would infringe its three patents. Endo contended that the court should not enforce the patents due to Purdue's misconduct. Even though Purdue had repeatedly relied upon the "surprising discovery" to argue for its patents, Endo argued, the company did not explain to the patent examiner that the discovery had been a product of an inventor's theory-based insight, unsupported by data. Federal district and appellate court judges inferred that Purdue had intended to deceive the patent examiner and declared Purdue's patents unenforceable. The result? The termination of rights in three patents

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Two Important Changes Related to Inventor Allocations

The OTL has converted its accounting system from the calendar year to the July 1-June 30 fiscal year to harmonize with other St. Jude accounting systems. As part of this transition, inventors will begin receiving royalty allocations in the fall instead of the spring. Since allocations for the 2005 calendar year were distributed in March, inventors will receive allocations for license income received from January 1 through June 30, 2006 this fall. Beginning in 2007, one allocation per year will be made in the fall based on license income received during the previous fiscal year.

Also beginning this fall, ***all allocations will be distributed to the inventor as personal income***. The inventor will no longer be given the option of depositing all or a portion of their allocation into an untaxed restricted St. Jude account. St. Jude has been advised by an external source that this practice could lead to unanticipated tax liabilities.

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that cover OxyContin, a drug that reportedly generated more than 70 percent of Purdue's annual revenue at one time.

Such verdicts are known as findings of inequitable conduct. They can destroy or severely impair an inventor's reputation, says J. Scott Elmer, director of the office of technology licensing for St. Jude Children's Research Hospital. "An inventor has a duty of candor, good faith and honesty to patent examiners during the process of obtaining a patent," says David G. Latwesen, a patent attorney at Wells St. John in Spokane, WA. Inequitable conduct can occur, he says, if an inventor intentionally misleads the examiner.

And the penalties can go beyond a court determination: an inventor guilty of inequitable conduct can "probably forget about raising money or participating in a start-up company," says Elmer. Technology licensing personnel and patent attorneys, he says, will be extremely skeptical of any of the inventor's new inventions. The patent-killing behavior may also bring grave consequences for the inventor's organization if it holds the now-worthless patent rights.

Want to avoid becoming the focus of a successful inequitable conduct defense? Here are eight tips from experts:

1. **Disclose Prior Art** In 1990, PerSeptive BioSystems filed a patent application for chromatography methods of separating biological molecules. While arguing for patentability, the company apparently assured a patent examiner that its inventor had not created prior art by briefly discussing his invention during a public seminar, because he had not used a poster, abstract or writing of any kind. Yet after Pharmacia Biotech alleged inequitable conduct during a patent infringement suit, a Massachusetts federal district court found in 1998 that the inventor had shown slides and had prepared an abstract distributed at the conference. Latwesen suggests that an inventor can best avoid inequitable conduct by disclosing anything that could impact a patent examiner's determination. There's no such thing as disclosing too much to your patent attorney or agent, says David Hricik, associate professor at Mercer University School of Law in Macon, GA. Joseph N. Hosteny, a patent attorney with Chicago-based law firm Niro, Scavone, Haller & Niro, agrees. "Provide the examiner with any patents, articles, public uses, etc. that the applicants or their attorneys know about," he says. "Err on the side of disclosure."
2. **Update the Examiner about Prior Art Discovered in Related Applications** An inventor may need to update the patent examiner if the inventor finds new information during patent prosecution, says Hricik. "Don't forget to call related applications to the examiner's attention," cautions Warren D. Woessner, of Schwegman, Lundberg, Woessner & Kluth in Minneapolis. Related U.S. patent applications may be assigned to different patent examiners who discover prior art relevant to the other application. Hosteny also advises patent applicants to supply their U.S. examiners with literature search results performed by examiners of counterpart patent applications filed outside the U.S. At a minimum, he says, provide your U.S. examiner with references cited against the novelty of the claimed invention.
3. **Don't Submit Partial Translations of Foreign References** When Semiconductor Energy Lab Company filed a patent application, the company also filed an information disclosure statement that listed relevant references. So far, so good. But then, the company provided the patent examiner with an untranslated 29-page Japanese reference, a concise explanation of its relevance and a one-page partial English translation. In 2000, the U.S. Court of Appeals for the Federal Circuit concluded that untranslated portions of the reference contained information more relevant to Semiconductor's claimed invention than anything else considered by the patent examiner. "If foreign references are provided," Hosteny says, "translate them. Don't use partial translations." A court can decide that patent applicants concealed material information in the untranslated portions of a foreign reference.
4. **Update Examiners about Developments in Related Patent Litigation** While a patent application slowly winds its way through the patent examination process, a related patent may be the subject of litigation. In these situations, Hosteny suggests that patent applicants should supply the patent examiner with prior art identified by the opposing party. Patent applicants may also need to update the patent examiner about any litigation decisions, he says. For example, a judge may decide that prior art narrows the scope of claims in the litigated patent, which may be similar to claims under-

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going examination in the patent office. This happened in Mallinckrodt, Inc. v. Masimo Corp., a case about claims to a pulse oximeter decided by the Federal Circuit in September 2005. Masimo had not informed its patent examiner about a judge's decision that claims in a related patent must include certain limitations to avoid prior art.

5. **Disclose Data Even if it Undercuts Patentability Arguments** A 1988 Delaware federal district court decision revealed that Merck had informed a patent examiner that cyclobenzaprine did not cause drowsiness, even though the company had new data showing that this assertion was untrue. What should an inventor do if new data casts doubt about the invention? That depends, says W. Murray Spruill, a patent attorney in Alston & Bird's Raleigh, NC office. Do the data merely show that the invention does not work quite as well as the inventor had hoped? Or, do the data contradict patentability arguments presented in the patent application or during patent prosecution? Mark J. Nuell, a patent attorney in the Falls Church, VA office of Birch, Stewart, Kolasch & Birch, says that, if an inventor obtains new data that are contrary to a prior argument for patentability, then the inventor must submit the data for the patent examiner's consideration. Spruill suggests that inventors consider the question: "If litigation reveals that patent applicants withheld the data from the examiner, then how would this impact patent claims?" Merck learned the answer to this question; it lost a patent.
6. **Help Your Patent Representative to Identify Inventors** In the PerSeptive case, a judge decided that the company – with deceptive intent – had failed to include as co-inventors researchers from a business collaborator. "Applicants for U.S. patents should do their best to name the correct inventors on an application," says Nuell. Unlike authorship of a scientific publication, inventorship is a legal determination. "The individuals involved in the project," Spruill says, "can aid their patent representatives by providing information about contributions to the claimed invention without any preconceived notion about who should be named as an inventor." The patent office allows patent applicants to correct honest mistakes about inventorship. A deliberate misrepresentation of inventorship is another matter. "Intentional omission of an inventor will result in an invalid patent," Nuell warns.
7. **Ensure That Affidavits Present the Truth** While fighting a rejection of patent claims to a glaucoma treatment, a Pharmacia inventor filed a declaration stating that a certain dose of a prior art compound does not significantly decrease intraocular pressure, a statement contradicted by an article that the inventor had co-authored. The declaration also reported a result from an experiment that the inventor had not performed. During patent prosecution, inventors may file an affidavit called a Rule 132 Declaration to support arguments against a rejection of patent claims. "Every sentence in such declarations," Woessner says, "should be examined to be sure it is the whole truth and nothing but the truth." In particular, inventors should not "provide data and represent it comes from an experiment if it does not," says Hosteny. Courts decided that misleading statements in declarations filed by Purdue Pharma and Pharmacia inventors supported inequitable conduct verdicts.
8. **Don't Write Prophetic Examples in the Past Tense** When Cetus Corporation applied for a patent on Taq enzyme, the company included a detailed protocol used to purify the enzyme. In 2004, a federal district court judge found that the description of enzyme purification had been a prophetic example written in the past tense, and that Cetus had used purification "data" in the prophetic example to argue for patentability. This supported the judge's decision that courts should no longer enforce the Taq enzyme patent.

While an actual example, which describes performed experiments, provides compelling evidence that others can make and use the invention, "a prophetic example," says Elmer, "merely describes what an applicant contemplates would happen and is much more easily challenged by a patent examiner." If an inventor writes a prophetic example in the past tense, a patent examiner will assume that it is an actual example and may give the patent application a more favorable and deferential examination than it merits. A court may decide that this represents a deliberate act of deception constituting inequitable conduct, Elmer warns.

Final words of advice from Latwesen: "The route to obtaining a good patent is not to conceal pertinent information from the PTO, but rather is to provide all pertinent information to the PTO and show that the invention is patentable on its own merits." *–Phill Jones*

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plasmid reverse genetics system developed at St. Jude by Erich Hoffmann, PhD, Infectious Diseases. Reverse genetics allows one to manipulate the pathogenic strain of the virus so that it no longer retains the capacity to cause disease, but still remains immunogenic. Reverse genetics also allows for the efficient inclusion of specific genes from different influenza viruses into one vaccine. In this particular vaccine, the hemagglutinin gene is from the H5 strain, the neuraminidase gene from a N3 strain and the other 6 genes from a PR8 laboratory strain commonly used for vaccine production. Inclusion of an N3 neuraminidase gene allows for vaccinated birds to be distinguished from birds infected with the field strain.

In addition to developing a vaccine targeted directly against the current H5N1 virus outbreak, a critical goal of this collaborative effort was to set a new standard for animal flu vaccines. The antigen content of older conventional veterinary influenza vaccines often varied from batch to batch. Since reverse genetics provides an efficient method for preparing high-yield virus, Fort Dodge and St. Jude made it a priority to develop a standardized vaccine that would consistently prevent disease symptoms as well as prevent viral shedding.

After St. Jude made the pre-master seed stock, Fort Dodge prepared prototype vaccines within an established seed-lot system and developed the conceptual vaccine candidate obtained from St. Jude into a viable large-scale commercial product. The Fort Dodge efforts culminated in successful completion of the appropriate laboratory and field safety studies, along with vaccination and challenge of immunity studies necessary to satisfy government licensing requirements. FDAH work on this vaccine continues, now focusing on obtaining the appropriate governmental authorizations for each country around the world where there is need for this vaccine. In addition to recently approving this vaccine, the French government has also requested 7 million doses of the vaccine to begin its control and eradication program. They have already begun vaccinating outdoor ducks to prevent them from contracting avian influenza from migrating birds. Additional governmental approvals are expected as Fort Dodge continues its efforts to promote the use of this vaccine as the best way to protect bird populations from the spread of this deadly virus.

Under its agreement with Fort Dodge, St. Jude will receive license income from the sales of this vaccine. As with all license income, a portion of the amount received by St. Jude will be allocated to the key researchers involved in this effort with the remaining amount retained by St. Jude to be directed toward further research.

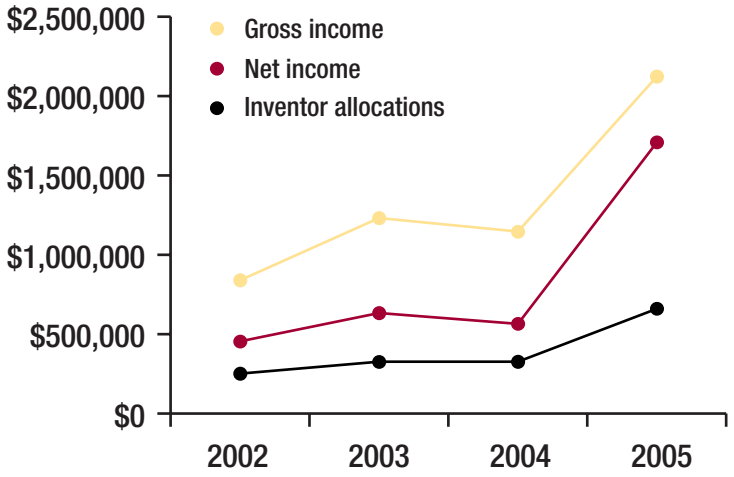
U.S. Patents issued to St. Jude during CY2005

Patent Number	Inventors	Subject	Issue Date	Reference Number
6,841,381	Webster (Robinson, Fynan)	Immunization by inoculation of DNA transcription unit	1/11/2005	SJ-91-0004B
6,849,454	Kelly, Vanin	Packaged viral vector system	2/1/2005	SJ-00-0004A
6,858,706	Tuomanen, Masure (Wizeman, Johnson, Koenig)	A polypeptide comprising the amino acid of an N-terminal choline binding protein A truncate, vaccine derived therfrom and uses thereof	2/22/2005	SJ-98-0009A
6,916,627	Kastan, Bakkenist	Critical phosphorylation site for activation of ATM kinase	7/12/2005	SJ-02-0008A
6,933,150	Sorrentino, Bunting, Schuetz, (Nakauchi)	Relationship of ABC transport proteins with hematopoietic stem cells and methods of use thereof	8/23/2005	SJ-97-0016A
6,951,754	Hoffman	DNA transfection system for the generation of infectious influenza virus	10/4/2005	SJ-00-0006A
6,969,760	Ihle, Quelle, Wittuhn, Silvennoinen	JAK kinases and regulation of cytokine signal transduction	11/29/2005	SJ-93-0001D

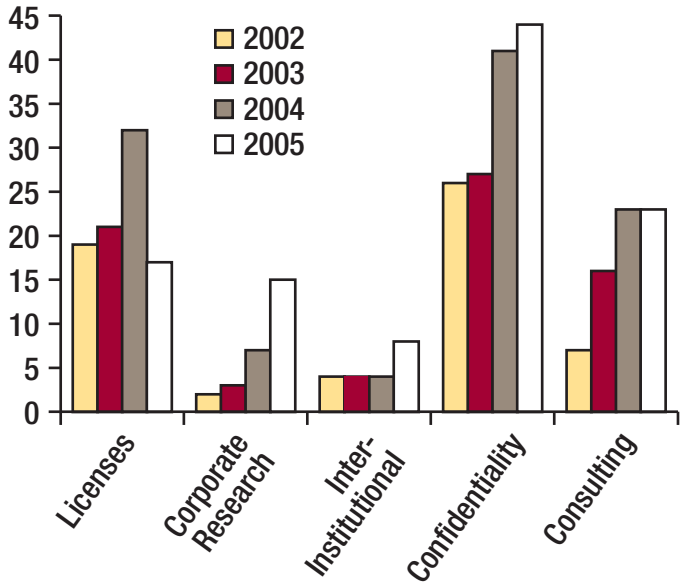
OTL Activities for the Previous Four Years

In CY2005, the OTL enjoyed its most financially productive year since the department originated in 1995, with net income of $1.7M generated from gross revenues exceeding $2M. More than $650,000 was distributed to various inventors. The number of license agreements executed in 2005 was down from previous years; however, all other agreements including corporate research, inter-institutional, confidentiality, consulting and material transfers (not shown) were up. The number of invention disclosures received in the OTL increased last year, while the number of U.S. patent applications and international applications filed decreased slightly. The number of granted U.S. and foreign patents increased slightly.

Income and Allocations (2002–2005)



OTL Agreements (2002–2005)



Patent Activity (2002–2005)