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Patient Encounters of the WiSE and Automated Kind

By Eric Grunwald

What began as an effort to reduce costs and errors by two staff members of the Faculty Practice Plan (FPP) of the Stanford University Clinic has turned into a licensing deal that promises to boldly take health care where no doctor has gone before, replacing mounds of paper with hand-held, wireless terminals.

Stanford has granted WiSE Communications, Inc. (Los Gatos) a license to the "Automated Patient Encounter System (APES)," know-how developed over a four-year period by Ray Pedden, former Director of Business Operations, and Vic Arnold, Director of Management Information Systems.

The story began approximately four years ago when the two began looking for ways to cut costs and errors in FPP's operations, mainly by reducing the redundancy in recording the information associated with patients' visits.

As Brian Kissel, the OTL Associate who negotiated the license with WiSE explains, "The doctor writes his notes, the nurse then translates those notes onto forms containing standard codes, the form is then keyed into the computer systems, and a bill is generated. The goal was to eliminate some

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Stanford staffers and APES inventors Ray Pedden (left) and Vic Arnold agree that, as Arnold says, "Stanford should think more about ways to encourage staff, because they have a lot of good ideas. It would be good for staff and good for the University, and not just financially."

Inventions that Could Help Millions not Easily Licensed

By Amy Forrest

Parasitic diseases infect approximately six hundred million people annually worldwide, mainly in the Third World, and the rate is rising. Stanford researchers have developed a virtual arsenal of inventions to diagnose and treat several of these diseases, but getting them from the lab to the people who need them has been difficult.

One invention targets schistosomiasis, a potentially fatal disease caused by water-borne parasitic flatworms that infects approximately 220 million people worldwide.

Dr. Tag Mansour of the Department of Molecular Pharmacology has developed a DNA clone that allows expression of an enzyme that can be used to screen drugs for treating the disease; if a given drug inhibits the enzyme, it will also kill the parasite.

Another invention from Dr. John Boothroyd of the Department of Microbiology targets toxoplasmosis, a disease caused by the common protozoal parasite *Toxoplasma gondii*.

According to Boothroyd, "Infection can be very dangerous to two groups of individuals: pregnant women (particularly women who have contracted the infection for the first time during pregnancy), and people whose immune systems are compromised by AIDS, lymphomas, or transplant procedures."

To address the problem, Boothroyd and Dr. Roland Buelow have developed monoclonal antibodies that can be used in an assay (a diagnostic test) to detect degrees of infection in a patient's blood sample. The number of antibodies indicate whether the infection is chronic or acute.

Says Boothroyd, "The disease is most dangerous to pregnant women if it is acute because the fetus is at greater risk for severe neurological damage." And better diagnostic procedures are crucial because "about half of the women diagnosed with

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Stanford University
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Editor
Eric Grunwald

Office of Technology Licensing
Stanford University
900 Welch Road
Suite 350
Palo Alto, CA 94304
Campus M/C: 1850
(415) 723-0651
Fax: (415) 725-7295

Director
Katharine Ku

Stanford Technology BRAINSTORM is published quarterly by Stanford University's Office of Technology Licensing (OTL) to provide information about OTL and general information of interest to the licensing community, both within and outside Stanford.

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To find out about a specific technology, or to disclose one of your own, contact us at the above address.

Patient Encounters of the WiSE Kind

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or all of those steps."

"It's a huge paper mess," summarizes Arnold – one that results in patient data not getting recorded, inappropriate billing, and the built-in costs of repitition.

The solution, he and Pedden concluded, was to capture information closer to the physician. But how? Physicians, they believed, are and should be more concerned with seeing the patient than with typing arcane billing codes into a computer.

The answer came one day at MacArthur Park restaurant. Lunching with FPP Executive Director Don Tower, Arnold and Pedden saw the waiters using hand-held, wireless devices to send orders to the kitchen. "I don't want to call a physician a waiter," chuckles Arnold, "but it's similar."

Pedden says the idea born there was to have a system that accumulates and allows access to data from multiple points. "We needed a system that provided information where it's needed, when it's needed, and how it's needed."

Easier said than done. The foremost issue was how physicians would input data. Keyboards would be unwieldy and time-consuming. Fortunately, pen-based computing — inputing data and commands into the computer by touching the screen with an inkless "pen" — had just appeared on the market.

Over the next two years Pedden and Arnold developed a hard-wired prototype, and the process culminated in an article Pedden wrote for *Healthcare Informatics* describing their efforts.

According to Pedden, "The article generated around 50 calls from all over the country, with people saying, 'Where can I get one? Where can I get one?' In and of itself, that was rewarding. That's also when we realized we had something that could be commercially valuable and went to OTL."

Both inventors were surprised by the intensity of the interest. "Nothing that Vic and I did is rocket science," says Pedden. "Here was a business problem, and here's what we needed to do about it."

Arnold recalls thinking, "This idea has to be so obvious, there must be a zillion people working on it. There were a zillion people interested, but no one was really doing anything with it." But neither inventor could say why.

Tom Brekka, president and CEO of WiSE, may have the answer. "What's missing in other efforts is the attention to integrating good software with good communication, infrastructure, and data management in the background," he says. "You can't just take existing things off the shelf, bolt them together, and hand it to the physician."

What is needed, Brekka believes, and what WiSE is developing, is a "complete infrastructure solution" that addresses everything from the response time and data integrity of the system to the look of the interface screens and the battery life of the hand-held units.

WiSE was formed in 1992 by a group of experts in high-performance wireless network links, advanced antenna designs, and roaming software capabilities allowing, for example, cellular phone callers to be handed from one subnetwork to another as they drive.

The company devoted itself to medical informatics and began contacting experts at several medical institutions, eventually leading them to Stanford and to Pedden and Arnold. "We recognized the problem, decided we could do it, and haven't looked back since," says Brekka.

Getting from the initial contact to a license was not that simple, however. Because so many parties had expressed interest, OTL's Kissel marketed the technology widely and got serious interest in a license from other companies and a few venture capital firms.

Before granting the license, says Brekka, "OTL made us meet stringent performance criteria."

But meet them WiSE did, hiring more people with experience in medical technology; securing a strategic partnership with and three million dollars in funding from AMP Corporation, a well-known company with expertise in networking and electronics; and producing a precise business plan.

And in the end, says Kissel, "A lot of people expressed interest and wanted more time to evaluate the technology, but no one except WiSE put a meaningful offer on the table."

"They were probably the hungriest," agrees inventor Arnold, adding, "WiSE has built an excellent staff. They've pulled people from some of the best, most prestigious companies in the country."

In sum the negotiations took over a year. "We had differing goals and objectives," says Kissel. "But both sides were very creative and adapted to changing conditions and situations to come up with solutions."

Part of the difficulty was that the technology

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A Sampling of Licenses Granted by OTL in the Last Quarter

Docket(s)	Title(s)	Uses	Licensee(s)	License Type
S74-043	"Cohen-Boyer Recombinant Technology"	DNA Cloning – Production of proteins Total number of DNA licensees: 297	Glentech; Agennix; Pharmaceutical Peptides; LXR Biotechnology; Sanford Scientific; Betaseed; Immtek; Ingenex; Operon Technologies; Alko, Ltd.; Miller Brewing; Biogenetic Services; Mercator Genetics; Megan Animal Health.	Non-exclusive
S82-007A	"Expression of interferon..."	Gene amplification	Schering AG	Exclusive
S82-037, S92-160	"Monoclonal Antibodies..." "Anti-P-Selectin Antibodies"	Research reagents	Boehringer Ingelheim	Non-exclusive
S89-139	"Novel Insect Steroid..."	Protein regulation	Rhone Poulenc	Non-exclusive
S90-037	"Paraxia" (Software)	Laser testing/analysis	Sciopt	Field Exclusive
S91-007	"Human Biology for Middle Schools Project"	Student curriculum	Addison-Wesley	Exclusive
S92-068	"Genomic Mismatch Scanning"	Gene mapping	Millenium Inc.	Non-exclusive
S92-106	"Use of tRNA Genes to Stabilize the Inheritance"	Research tool, DNA vaccines	Life Technologies, Inc. Latham Labs	Field Exclusive Field Exclusive
S93-132, S94-006	"Novel Human cDNA..." "Ligand (ACT-4-L)..."	Protein encoding	Cantab Pharmaceuticals	Option

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acute toxoplasmosis will choose to have an abortion although there is only about a 10-15% chance the fetus was infected." The antibodies can also be used to generate methods to prevent or control the disease.

Boothroyd has also worked with Drs. Dominique Soldati and Kami Kim to develop a way to create attenuated parasites for use as vaccines against toxoplasmosis, other infectious agents, and even cancer cells.

Tag Mansour has also found a group of phosphorus-containing chemicals that block the primary energy source of *Toxoplasma gondii*, thereby inhibiting the onset of toxoplasmosis. These "inhibitors" may have the same effect on related parasites, such as those causing amoebic dysentery, intestinal disturbance, and genital infections.

While a serious problem, though, "toxoplasmosis doesn't hold a candle to the millions of people dying of malaria," says Boothroyd. The World Health Organization (WHO) estimates between three and five hundred million clinical cases of malaria each year, resulting in between one and a half and three million deaths. Most cases (90%) occur in Africa, and about one million of the deaths are African children under five.

To combat this killer, Drs. Kasturi Haldar and Sabine Lauer of Microbiology and Immunology have developed a method of chemotherapy for infections caused by malaria. Haldar says their therapy is similar to current malarial therapies in that it targets the asexual development cycle of the parasite "which causes the symptoms of the disease—the cyclical fevers—that have led to the popular notion of malaria."

But while current chemotherapies "target the digestive food vacuole or inhibit DNA synthesis in the parasite," she says, "we have identified a completely new target in the cell."

One major obstacle in treating malaria, however, is that the parasite consistently develops resistance to therapy. "The original resistance to the anti-malarial drug, chloroquine, took five to seven years to document well," Haldar explains. "But now we see drug resistance in a few years. Patterns of resistance develop more quickly as many therapeutics are being tried simultaneously." Haldar and Lauer's new chemotherapy may be significant in keeping the disease at bay.

The mutation of diseases is also the subject of an invention by Drs. James Mullins and Eric Delwart, who have developed an assay that can rapidly track strains of diseases and the way they respond to therapy.

The assay alerts researchers that parasites are mutating in an infected population and allows them to follow and possibly inhibit the mutation.

The assay can also be used to create vaccines, evaluate the effects of anti-microbial therapies, detect and type tumors, and screen for genetic diseases. Ideal targets are AIDS, cancer, and tuberculosis.

Mary Albertson, the OTL Associate currently concluding negotiations with the WHO for a royalty-free license to the technology, is excited about its potential for commercializa-

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OTL Fiscal Year 1993-94
Preliminary Figures

Total Income: $38.19 M
Cohen-Boyer DNA Patents:
Total Income: $23.55 M
New Licenses: 62
New License Income: $0.43 M
All Other Technologies:
Total Income: $14.63 M
New Licenses: 73
New License Income: $1.83 M
Companies in which Stanford took equity: 10
OTL Budget: $2.1 M

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tion. "It is a phenomenal opportunity to disseminate this technology in the broadest possible manner, particularly in Third World countries," she says.

Albertson says the technology is valuable to the WHO's Vaccine Development Unit of the Global Program on AIDS, but due to the variety of the invention's potential applications, it could benefit multiple markets.

Licensing the invention to the WHO is a great opportunity, explains OTL Director Kathy Ku, because "unfortunately, OTL rarely has the chance to license technology to service organizations suited both to developing them and to reaching the markets they will benefit most."

Several Stanford professors, including Dr. Gary Schoolnik, shown here in Chiapas, Mexico, have invented ways to fight Third World diseases, but OTL has a hard time licensing them. Story begins on page 1.

Ku says licensing such technologies has historically been difficult, because the countries in which they have the greatest potential are unable to offer financial incentives to the companies or organizations with the resources to develop treatments.

"These diseases often strike hardest in Third World countries where funding for their prevention and treatment is scarce," says Ku.

"Although Stanford may have the means, we can't cure malaria without licensees with the resources to reach markets that are literally dying for these innovations."

Luis Mejia, the OTL Senior Associate trying to license the other technologies described above, says the ideal licensee for inventions of this kind is "a major pharmaceutical company with the global wherewithal to broadly disseminate drugs to address these diseases."

Unfortunately, he continues, "the profit margin is small when dealing with developing countries. And Third World governments have a hard time enforcing systems of patent protection, which also acts as a disincentive to licensing."

Ku, however, remains optimistic about the possibility of long term success. "We look forward to finding licensees willing to join us in the commitment to commercializing these inventions," she says.

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was not patented. "It was our ideas that needed protection," says Arnold. "Brian zeroed right in on that. It took a long time, but everyone got a better deal in the long run." Both sides evenutally agreed on a royalty based on a percentage of gross sales.

"What's really nice," adds Pedden, "is that...I don't have to worry about negotiations or any of the other issues."

Since concluding the agreement, WiSE has taken Pedden and Arnold's ideas and advanced them significantly, developing the RF (radio frequency) wireless communication technology and an advanced software interface.

WiSE's overall product is called the "WiSE-Med System," and the latest prototype of the handheld unit looks like something out of *Star Trek*: a sleek, black, hand-held, wireless, pen-based computer terminal the size of a notebook that a clinician can carry anywhere in his or her facility.

With it, the clinician can access scheduling information and patient histories, write and retrieve hand-written notes, order tests, and generate the correct billing, all without assistance or paper.

Brekka says the most significant challenges for WiSE have been developing the RF network infrastructure and clinical cache, endowing the system with "think speed" (fast response time), and ensuring the integrity of the data on the system.

"The first time data are lost on the system will be the last time the system is used," Brekka says frankly. WiSE has therefore built in several layers of safeguards and is guaranteeing no loss of data within five seconds of input, thus making all information almost immediately available to users.

WiSE is currently working with Stanford's OBGYN department to make sure the system meets the everyday needs of clinicians. Pedden and Arnold have identified almost a half million dollars that can be saved annually in OBGYN with the APES and $2.6 million per year clinic-wide. "That will more than pay for the system," says Arnold.

Office of Technology Licensing
Stanford University
900 Welch Road, Suite 350
Palo Alto, CA 94304-1850

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