CenterWatch

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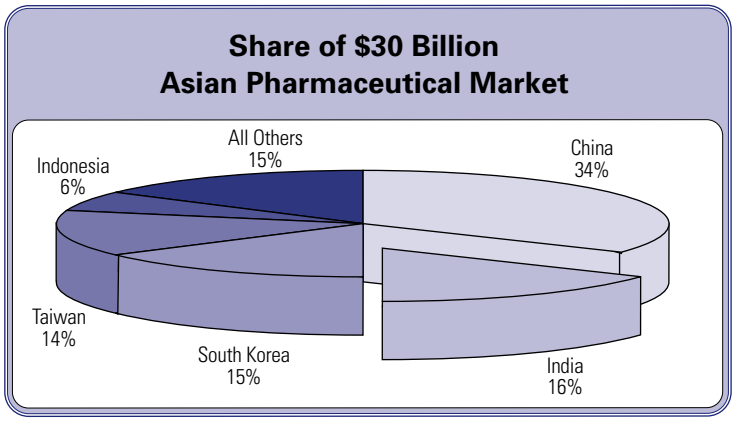
Lifting India's Barriers to Clinical Trials

▶ Broad regulatory reforms, a sizable and growing pharmaceutical market, combined with highly attractive professional and patient populations, make India a compelling new region for conducting global clinical trials.

▶ Within the past 24 months, sponsors, CROs and SMOs have increased their presence in India. CenterWatch finds that more than a dozen full service CROs and two SMOs operating in India have ambitious plans to expand there.



Source: IMS Health, 2003

Despite a history of regulatory constraints and a lack of infrastructure, India has long had several prize attributes for clinical drug development. India has a huge, treatment-naïve population of heterogeneous Caucasians with diseases of both the industrialized and third world. It is home to more than 1 billion people, including 30 million with cardiovascular disease, 25 million with type 2 diabetes, and 10 million with major psychiatric disorders. Large, extended families also still live in proximity to one another, making them attractive recruits for genetic linkage studies. And India's pharmaceutical market is the second largest in Asia, growing by more than 9% annually.

Soon, the barriers that have turned sponsors away from conducting clinical trials in India will be removed, making India one of the most important new markets for clinical research. "In recent years, we have seen considerable growth in the number of clinical studies being conducted in the country," said Chandrashekhar Potkar, Pfizer's director of clinical studies in India. "More and more pharmaceutical companies and CROs—multinational as well as domestic—are exploring clinical development in India." A key reason is that the government's "overall approach and attitude has been very positive," Potkar said.

Health care in India is provided by approximately 600,000 physicians, virtually all of whom are English speaking, computer literate and practice Western-style medicine. "There

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AHCs Face a Tightening NIH Funding Supply

▶ NIH funding growth has abruptly plateaued to less than a planned 2% in 2004. AHC clinical trial offices, many devoted to securing a share of rapidly growing NIH funding, may now be forced to re-orient their emphasis to industry-sponsored programs.

▶ Although designed to attract government funding, during the past five years, clinical trial offices have added capabilities and services that potentially position them well to secure more industry sponsors.

For biopharmaceutical companies, a doubling of the NIH budget between 1998 and 2003 has been both a curse and a blessing. During that time period—as NIH funding has grown 15% annually from $13.7 billion to $27.2 billion—academic health centers (AHCs) have found a growing source of funding to pursue government research

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Month in Review

Editor's Note: Full text articles of these stories appeared last month in *CWWeekly*. For more information about these articles, please refer to the following *CWWeekly* issues: Volume 7, Numbers 24–27.

Sites

Montreal-based **MDS Pharma Services**, a provider of drug discovery and development services, has expanded its early clinical research business by acquiring the Clinical Research Center (CRC), a phase I through IV facility in New Orleans. The center specializes in renal, hepatic, hypertension, diabetes, acute pain and osteoarthritis research. The site includes a new 16,000-square-foot facility with up to 100 beds for phase I studies, located near both Louisiana State University Medical Center and Tulane University School of Medicine. The site has 60 employees. The acquisition, whose financial terms were not disclosed, does not include two satellite sites. Founded by Gilbert McMahon in 1968, the well-known site was bought by private investors, Frantzen & Voelker Investments and MNS Venture in August 1997.

Sound Medical Research, a Toronto-based site management organization (SMO) that had big expansion plans for Canada, the United States and globally, has shut down. One company official confirmed the closing and a message on Sound Medical's voice message stated it had "temporarily suspended its services as of July 7, 2003." Sound Medical becomes the second Canada-based SMO to fail within the last year. Canadian Medical Laboratories sold off the remainder of its SMO division, Novoquest, in March 2003 after determining that the subsidiary wasn't growing fast enough.

Regulatory

Federal investigators found that three studies at 40 hospitals, coordinated at **Massachusetts General Hospital**, **Vanderbilt University** and the **Cleveland Clinic**, enrolled patients with acute respiratory distress syndrome without warning them that the study might increase their risk of death. However, the federal Office for Human Research Protections (OHRP) determined that 1,800 patients enrolled did not receive substandard care.

CROs

Philadelphia-based **ReSearch Pharmaceutical Services** (RPS), a hybrid staffing company and contract research organization (CRO), has acquired CRO, Research Scientists, Inc. (RSI), that also has its own electronic data capture (EDC) system. Based in Sherman Oaks, Calif., RSI was founded by John Hedberg and has 10 employees. A key part of the agreement is TrakWare, a clinical technology system that offers web-based EDC and clinical project management database capabilities. Financial terms of the deal were not disclosed.

Parexel has expanded its clinical pharmacology research (CPRU) unit located in Baltimore, Md. Situated on the seventh floor of the Harbor Hospital Center, the CPRU has increased in size from 11,000 square feet to 23,000 square feet and more than doubled its beds from 24 to 52 in two years.

Framingham, Mass.-based **Averion** and **Imform GmbH**, a German CRO, have signed an alliance agreement. The agreement will involve joint marketing efforts and a mutual contracting of complementary services from both companies.

CentreStage Europe

SMO Aremel Takes on the French Market

New site management organization (SMO) Aremel is now operating one private hospital-based site in Nantes, France, and has plans for growth by opening another two sites by next month.

Aremel's founding offers sponsors an SMO model that is new to France but has been in place in the U.S. for several years now. Aremel employs a study broker/trial management SMO model and focuses on phases II–III clinical trials. The company charges investigators a percentage of the revenues they receive for conducting clinical trials. The SMO also charges sponsors fees for centralized services, including hours worked by clinical research technicians who are full-time employees of Aremel. The technicians are placed at the site to perform administrative tasks associated with the conduct of the clinical trial, such as filling out case report forms, and are responsible for other technical and logistical aspects of the trial. As such, the technician enables the investigator to focus on clinical care.

Aremel also provides necessary equipment and central lab services to sites. Local clinical research technicians are managed centrally by the Paris-based Head of Operations, Frédérique Thoby-Valentin, Pharm. D., formerly with GlaxoSmithKline.

Aremel's first site—Les Nouvelles Cliniques Nantaises, in Nantes—began conducting clinical trials several months ago. The Aremel model utilizes sites that are private for-profit hospitals. Its investigator network is made up exclusively of specialists, rather than general practitioners. Aremel's first site has 120 specialists in therapeutic areas that include cardiology, gastroenterology, respiratory, orthopedics and ophthalmology. The site is currently running 12 active cardiology trials but will be expanding into other therapeutic areas.

Aremel has established an exclusive partnership with Générale de Santé (GdS), a leading group of private hospitals in France with 4,000 specialists and 127 private hospitals. GdS generated more than €1 billion [$1.1 billion] in revenue in 2002. Aremel's arrangement with GdS prevents GdS from opening clinical research structures without Aremel for the next two years.

In September, Aremel will open the CHP Saint-Martin site with 100 specialists, in Caen, Normandy, and the Hôpital Privé d'Antony site—located just outside Paris—with 240 specialists. Both are part of GdS. These sites are currently running 25 and 30 clinical trials, respectively.

The Advantage of Hindsight

The SMO market in France has been dormant for the past several years following the demise of several SMOs in the late 1990's (e.g., ProTest and CICI). Larger organizations, such as Euraxi and MG Recherche, today operate as general practitioner (GP) networks with 5,000 and 650 GPs, respectively, and a focus on phases IIIb and IV trials. There are also smaller, regional GP and specialist networks, but these GP networks, large and small, do not qualify as SMOs in the strictest sense because centralized support mechanisms for these physician investigators are largely absent.

Founder and CEO Christian Le Teurnier, M.D., told *CenterWatch* that there was one main obstacle to investigators' conducting clinical research smoothly in France—lack of time, resulting from fundamental flaws in their organization. "Physicians were longing for supportive structures capable of helping them conduct clinical trials and improve their performance. Sponsors are also waiting for better organized and more professional clinical investigation structures." Dr. Le Teurnier also believes the Aremel model will be successful because the SMO "does not disrupt French medical habits. The investigator sees the patient at his or her regular office."

In a sense, Aremel has risen out of the ashes of ProTest's and CICI's respective failures. Michel Wurm, M.D., consultant to Aremel and founder of ProTest, said, "Both CICI and ProTest represented too harsh a break with the medical habits of this country. As opposed to what happened previously, investigators are now ready to do it because they realize that they cannot run a clinical trial on their own."

Dr. Le Teurnier told *CenterWatch*, "Both ProTest and CICI grew because of venture capital at a time of euphoria. They then found themselves short of fuel when the euphoria declined. As a subsidiary of a group [Ideal Medical Product], we fund our development with the group's money, and not from unpredictable VCs."

Aremel has deliberately chosen to limit its scope to SMO activities. "We do not intend to compete with CROs by placing monitors at sites. The hybrid nature of ProTest and CICI in this regard raised CROs' suspicions, if not animosity," explained Dr. Le Teurnier.

Dr. Wurm stressed that the regulatory climate in France has always been conducive to the SMO market because the setup time is very short. "There is no IND [Investigational New Drug Application] to ask for, you just have to declare to the Agence Française de Securité Sanitaire des Produits de Santé [French regulatory agency] that you are launching a clinical trial, and one ethics committee approval is sufficient," he said.

A Look Ahead

In general, European SMOs are struggling to gain recognition as a valuable asset in the

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Aremel

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clinical trial process. Although SMOs are being used by many biopharmaceutical companies, they constitute only a minor percentage of total clinical trial work. The only Western European country where the concept has been truly embraced is the U.K. where the top two SMOs—Profiad and Synexus—have reported revenue growth and profitability this year. France's past two SMO failures could be difficult for Aremel to transcend. The company will have to convince sponsors that it will be there for the long haul and that it provides benefits that exceed what GP networks offer.

Aremel plans to grow cautiously with minimal expenditures and a primary focus in the first year on testing the concept. Dr. Wurm concluded, "What we want to do now is leverage the advantages that France offers the conduct of clinical trials, using necessary structures at the lowest possible cost for everybody. France is definitely a kind of El Dorado for clinical trials if we can create the appropriate structures."

—Sara Gambrill

Publisher's Note: *CenterWatch publishes* Guide Pratique de la Recherche Clinique à l'Usage des Investigateurs, *a manual for clinical investigators interested in beginning and expanding their involvement in clinical trials in France. Authored by Dr. Michel Wurm, the book can be found and purchased on www.centerwatch.com.*

Clinical Trials in India

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are also hospitals aplenty in India's urban centers, serving 85% of the population's specialty healthcare needs," said Nermeen Varawalla, M.D., managing director of U.K.-based CRO PerinClinical. Many of these centers are equipped with sophisticated technology such as linear accelerators, gamma cameras and spiral CT scans. Most of the major institutions also have established their own ethics committee and adopted formal guidelines put out by the Indian Council of Medical Research.

Unleashing Regulatory Reforms

"Regulatory reforms are the primary drivers making the environment for clinical research more conducive than ever before," added Varawalla. "The Drug Controller General of India (DCGI)—equivalent to the Food and Drug Administration—recently said that conforming to ICH-prescribed GCP guidelines is mandatory for all clinical research done in India."

"Previously, there was no provision in drug laws for global studies," explained Vijai Kumar, M.D., president of Neeman Medical International (Asia), a site management organization (SMO) based in New Delhi (NMIA). "Ethics committees were weak. Few physicians doing studies of any type were GCP-trained. There was no data exclusivity. Clinical drug development was marked by red tape and long startup times."

Regulatory reforms include elimination of a requirement that drug trials in India be "a phase ahead of the rest of the world," said Varawalla. "In the past, if a trial in Miami was at phase III, then you had to do a phase II trial in India and get permission from the DCGI to scale up to phase III. The DCGI endeavored to protect the safety and well-being of Indian patients. The phase lag regulation is now being weaned away." In some instances, phase II trial data from elsewhere can be used to "go right to phase III in India," she said. Next year, the DCGI is also expected to ease an historical requirement for companies to conduct phase I studies in India or to demonstrate "special value" to the nation's health care.

As of earlier this year, the high importation duty on clinical trial materials (55% of value) is also gone, said Kumar. A ruling on data exclusivity takes effect at the end of this year, ensuring that information provided to the DCGI will no longer be used to approve a competitor's product. "This is all part of the buildup to 2005, when India committed to following WTO [World Trade Organization] regulations to the tee," added Varawalla. "At that point, biopharmaceutical products—not just processes—will have full patent protection."

Consistent with WTO guidelines effective in 2005, India will also offer 10-year tax concessions on revenue to companies making research and development investments there. These incentives are expected to substantially increase R&D activities of both multinational and domestic biopharmaceutical companies. Analysts are projecting that total clinical research spending in India will increase by more than 30% annually through 2010.

India's Vital Statistics

Population	1.05 Billion
Annual population growth rate	1.8%
Health expenditure as a percent of GDP	4.9%
Number of practicing physicians	600,000
Number of hospitals	14,000
Average life expectancy	51.4 years
Infant mortality rates (deaths per 1,000 live births)	90
Top diseases	HIV/AIDS Tuberculosis Malaria

Source: WHO, 2003; World Bank, 2003

"The practical implication of all of this is that you can get DCGI approvals in India that are far less bureaucratic and fairly straightforward with compressed timelines," said Varawalla. "You can get DCGI approval within 12 weeks, for example, and ethics committee approval in three to six weeks, like the rest of the world."

Increasing Infrastructure

"What India has most lacked is global clinical trial expertise, training and quality assurance," said Varawalla. "The Indian pharmaceutical industry is based essentially on copying innovative drugs." Most of India's 20,000 biopharmaceutical companies are no more than small manufacturing units, explained Pfizer's Potkar. "About 300 have country-wide sales and marketing organizations. Less than 1% of global clinical trials take place in India, compared to approximately 82% in the U.S. and Western Europe," he said.

But the trend is clearly upward. NMIA's Kumar estimates that the number of applications filed with the DCGI for drugs being studied globally has increased over the past four years from six to about 25. "All of India presently has no more than about 200 active, GCP-trained investigators—indicative of an industry still in its infancy," he said. ICH GCP trials to date probably number no more than 50, added Sunil Wadhwani, co-founder and CEO of IGate, a hybrid SMO that entered the clinical research business earlier this year.

Management consultancies are certainly optimistic, Potkar added. They estimate that the revenue potential for contract clinical research services—including services provided by CROs, investigative sites, couriers and clinical labs—will reach $75 million in 2005 and $300 plus million in 2010. For 2002, analysts reported that India's clinical trials industry generated revenues of $30 million, said Varawalla.

"At this time, the clinical trials market in India mostly consists of local registration phase III trials," said Arun Bhatt, M.D., president of clinical development for Chembiotek Research International, a new CRO in Mumbai. "Estimates are that, all told, about 200 phase III trials and 50 phase IV trials are now being done each year in India," he said. Typically, only the post-marketing studies are done in the offices of private practice physicians.

"Most Indian pharmaceutical companies still work small, locally legislated trials," said Bhatt. "Every company that wants to register a new drug in India has to conduct a phase III study in 100 patients. Post-marketing studies are also mandatory on all drugs approved here. A lot of those are coming up in India now."

For a new therapeutic area, many of India's potential clinical investigators aren't necessarily GCP-trained and may not spend the requisite amount of time with study patients, said Potkar. "This may not necessarily be considered negative. But it does require a major investment in training during study startup," Potkar said. Focused efforts are also "necessary for ethics committee constitution, operations and training of ethics committee members," Potkar added.

India has 14,000 general hospitals, with 700,000 beds and more than 150 of those hospitals have served as sites for clinical trials in the past, added Potkar, the majority being academic medical centers. "These have good research infrastructure. For new sites, the sponsor is required to invest in research infrastructure," Potkar said. "We estimate that no more than 30% of studies are being done at private hospitals and clinics."

More and more hospitals desire to attract clinical research for the revenue. But it is physicians who are "driving hospitals to upgrade themselves to be industry-friendly," said Kumar, including putting ethics committees in place and trial conduct procedures in writing. There are several published reports claiming that India-based universities are anxious to help global pharmaceutical and biotechnology companies put down research roots in the country. The University of Pune, for instance, is providing easier access to its human resources pool.

With regard to study volunteer recruitment, India has quite a bit to boast about. It can offer the pharmaceutical industry "three times more patients at about 30% less cost than traditional geographic areas," said Kumar. "This is largely a function of lower medical manpower costs. There are also at least seven well-developed central lab facilities certified by the College of American Pathologists. These include the SRL Ranbaxy, based in Mumbai, and Biocon, based in Bangalore."

"Most importantly, patients can be recruited three to four times faster for trials than in the West," claimed Varawalla. "For cancer studies, speed of recruitment is seven times faster because of unmet need and the fact that patients are keen to take part in these trials." Clinical data from India is

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India's Clinical Trials Market

2002 industry spending on CRO services and investigator grants	$30 to $35 million
Estimated number of active ICH-GCP clinical studies conducted in 2002	40 to 50
Estimated number of active GCP-trained principal investigators in 2002	200 to 250
2010 projected industry spending on CRO services and investigator grants	$250 to $300 million

Source: CenterWatch, 2003; Company reports and interviews

Clinical Trials in India

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readily accepted by the FDA and the European Agency for Evaluation of Medicinal Products (EMEA)," she said.

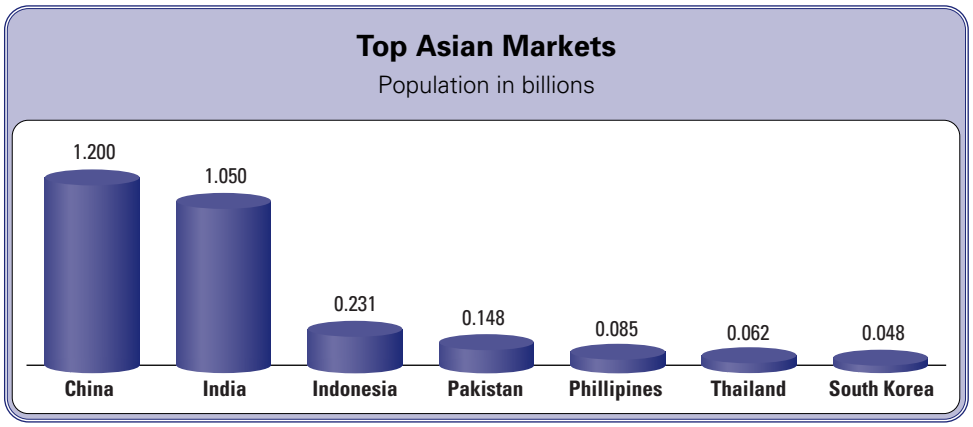
Sponsors Swarming

Pfizer alone spent $3 million in India in 2002, compared with an average of $1.5 million annually during the prior seven years. "Pfizer was the first company to establish a dedicated clinical research operation in 1994-95," said Potkar. Pfizer has now conducted nearly 40 phase II-IV studies in various therapeutic areas. Drugs are currently being tested in India for menopause, breast cancer and schizophrenia, he said, including some university-sponsored studies. A malaria study that will involve four to six sites and 300 patients is also being planned.

"The objective was to start with a biometrics operation to capitalize on the time difference between India and the U.S. Subsequently, clinical operations were considered on such grounds as therapeutic diversity and English-speaking physicians." The company anticipates that its Indian scientists will continue to provide technical support as Pfizer extends its clinical trial research into other parts of Southeast Asia.

"Bristol-Myers Squibb and Merck are noticeably absent and the only two multinationals without any sort of operating division in India," said Kumar. Other U.S. and European pharmaceutical and biotechnology companies have approached India cautiously.

"Pfizer is the only multinational doing a lot of studies, and even they do it off and on," said Bhatt. The next most active sponsor is reported to be Eli Lilly, which is managing 17 large and small phase II and III trials—many in oncology—underway in India. Lilly is also conducting post-marketing studies of its insulin products there.



Source: *World Fact Book*, 2003

Wyeth is contemplating a few major studies in India, said Kumar. Some smaller companies, such as Targacept, are also "very interested" in India. While AstraZeneca isn't doing trials here, it has set up an R&D unit in Bangalore with a staff of 70 looking at new treatments for tuberculosis, said Varawalla. "Aventis and Novartis have also begun to contribute patients from India for global clinical trials," she added.

"India, up to now, has also had an exemption from international intellectual property rights protection and pricing," said Varawalla. "As a result, Indian generic companies have not respected product patents. Driven by the huge success in India of the information technology and software industries, however, the government is keen on ensuring intellectual property protection. This is another indication of the progress India has made to play by international rules."

A CRO Invasion

A growing number of contract research organizations are now on the scene to help unlock India's clinical development potential. CenterWatch estimates that more than a dozen full-service CROs—local and international—have established offices in India, primarily in Bangalore and Mumbai. Two years ago, there were only three or four CROs operating there. Quintiles is the largest CRO operating in India based on project volume.

ClinTec, an international CRO based in Germany, has an office in Bangalore that has been in operation for about a year, reported Samiq Hussain, general manager of ClinTec India International. "During that time, we have won two clinical trial projects in India and we are currently negotiating several others. We have also managed to conduct three ICH GCP training programs," he said.

Icon Clinical Research and Omnicare Clinical Research are just now establishing a presence in India as is Covance. Potkar puts the total CRO count at closer to 50 if niche service providers are included. "CROs offer various types of services, including bioequivalence, monitoring, project management and central laboratory," Potkar said.

Small but global CROs, including PharmaNet and Pharm-Olam, have India offices "in the embryonic stages," said Varawalla. "Other CROs are looking at India, and the local CROs are primarily engaged in bioequivalence studies," she said.

Chembiotek Research International plans to offer a full menu of services when it becomes operational by the end of this year, said Bhatt, a former medical director for Novartis in India. "We've hired a small team

of three to cover regulatory affairs, project management and quality assurance monitoring. We'll hire a team of CRAs depending on need and how many we can afford. The plan is to eventually focus on cancer or a chronic disease like diabetes. But it's not possible to start like that," Bhatt said.

A year ago, Varawalla founded PerinClinical to focus solely on India by tapping international clinical development expertise in London. Maintaining a base in the U.K. was also viewed as key to driving business development and managing customer relations. "We wanted to give clients a confidence factor and reduce the perceived risk. It makes the whole sales process easier," she said.

In its London headquarters, PerinClinical has a staff of four covering training, quality assurance and business development. In Mumbai, it has an administrative head and a medical advisory group composed of 20 GCP-trained physicians who "represent the leading specialists in India in a range of therapeutic areas," she said. The physicians, all of whom are available to serve as PIs on trials, provide access to hospitals and patients—and more investigators as needed. "We have decided to restrict ourselves to four big cities—Mumbai, Bangalore, New Delhi and Chennai—because of the sophistication of the healthcare delivery system there," Varawalla said.

For trial monitoring, PerinClinical has established "a series of relationships and alliances with preferred suppliers," said Varawalla. "With our closest relationship, the supplier has a GCP-trained clinical staff of 24." The majority are M.D.s. The rest are science graduates.

PerinClinical currently has seven "fairly major proposals" in the works, the first of which is an oncology trial set to begin in December. It is responsible for providing 250 patients across the study's two arms. Among the sites the CRO plans to use is 441-bed Tata Memorial Hospital in Mumbai, a leading cancer specialty hospital. It treats 25,000 cancer patients a year from India and neighboring countries; attends to 1,000 outpatients every day; performs 10,000 major operations and 5,000 radiation and chemotherapy treatments per year; and has state-of-the-art treatment and diagnostic facilities, said Varawalla. "We have relationships at places equivalent to Tata for the other major areas we specialize in: cardiology, metabolic diseases, infectious diseases, neurology, psychology, and genetic studies," she explained.

CROs Operating in India

Name	Location
ClinWorld	Bangalore
Clin Tec	Bangalore
Covance	Mumbai (recently opened)
DiagnoSearch	Mumbai
Icon	Bangalore (recently opened)
Lotus Labs	Bangalore
Omnicare	Bangalore
PerinClinical	Mumbai
PharmaNet	Bangalore
Pharm-Olam	Bangalore
Quintiles	Ahmadabad
Reliance Clinical Services	Mumbai
Siro Clinpharm	Mumbai

Source: CenterWatch, 2003

Networks of Sites

Similar efforts to put India on the global map of clinical research come from Neeman Medical International (Asia), an early entrant SMO operating in India with a volume that is second perhaps only to Quintiles. "It was formed just after the creation of Neeman Worldwide in 1999. Its objective is to take companies into India and help them go global," said Kumar.

Since becoming operational in May 2001, "NMIA has participated in nine phase I through III global clinical trials involving 821 subjects," said Kumar. "The trials, all active, involve 24 trained investigators at 24, mostly public, hospitals. They cover the therapeutic areas of infectious disease, nutrition, psychiatry, oncology, ophthalmology, diabetes, lipid disorders and dermatology. We have retained 99.5% of the subjects enrolled," boasted Kumar. "It's not that Indian patients are any more compliant than their contemporaries elsewhere in the world. It's that clinical research coordinators (CRCs) are medically astute and well trained in all aspects of ICH and FDA guidelines."

"NMIA employs 12 certified clinical research coordinators—all trained physicians dedicated 100% to coordinator responsibilities—in New Delhi, Mumbai, Bangalore, Hyderabad, Chennai, Pune and Nagpur. They help ensure all pre-screening activities are completed before the first patient is enrolled. This is especially important for patients with chronic conditions," added Kumar. "Coordinators can help the PIs go through the patient database to identify likely candidates and complete any qualifying procedures that need to be done. There's no inertia. We begin enrollment the day the site initiation visit is over." Once the study is underway, coordinators also help with administering informed consent, scheduling patient visits, transcribing the case report form and ensuring all the information matches up with what's in the source documentation. "There's no need for data clarification when the monitor is here for a visit," he said.

Kumar explained that three NMIA employees work in quality control, training and central pharmacies in New Delhi and Mumbai where trial supplies are shipped,

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stored and monitored, said Kumar. Another seven work in business development, operations and finance. NMIA also maintains a database of more than 500 investigators across therapeutic specialties, 110 of whom the company has GCP-trained. To date, NMIA has also trained 60 ethics committee members in Mumbai, New Delhi and Hyderabad.

One of the newest entrants to the global clinical trials market in India is Pittsburgh-based information technology outsourcing company IGate, which already has a strong presence in India. "On the IT side, we serve several pharmaceutical companies as clients, so it was a natural extension for us," said Wadhwani. "So much of clinical research is IT-related."

IGate entered clinical research outsourcing via two recent acquisitions—Pittsburgh Clinical Research Network (PCRN), a Pittsburgh-based SMO, and DiagnoSearch, a 50-employee, Mumbai-based CRO with seven years of experience conducting trials in India. IGate acquired 90% of the 15-employee SMO. The other 10% ownership is being retained by the University of Pittsburgh Medical Center, with whom ICRI will partner to train investigators and build operations, said Wadhwani. "With the U.S. acquisition, we got domain expertise, a good management team and contacts with pharmaceutical companies," he said. As PCRN, the SMO managed over 140 clinical trials.

DiagnoSearch, which was acquired *in toto*, is providing IGate with access to more than 100 investigators across India as a means to accelerate patient recruitment for large global clinical trials, said Wadhwani. "We found the leading company doing clinical trials management work in the country for international companies such as Pfizer, Eli Lilly and Bayer," he said. The investigator network covers seven key therapeutic areas: cancer, diabetes, arthritis, asthma, cardiology, CNS and infectious diseases, including vaccines. "We expect to expand aggressively to include as many as 300 investigators within the next six to 12 months. Another seven to nine offices are also expected to be added, doubling the employee count," he said.

Source: IMS Health

The newly named IGate Clinical Research International (ICRI), which includes both the SMO and CRO acquisitions, is "positioned to be a lead player in India," said Wadhwani. "We will then expand into China, Eastern Europe and Latin America." ICRI already has several clinical trial projects underway and others are about to open.

Opportunity is Knocking

Analysts project that by 2008, up to 30% of global clinical trial activities will take place outside of the U.S. and Western Europe due to high demand for study subjects and well-trained clinical research professionals. China, Eastern Europe and Latin America are several key markets earmarked for rapid growth in clinical research grants. According to Varawalla, many speculate that India will capture 10% of the global clinical research market within five years.

"Sponsors will look to outsource in India, particularly biotechnology and small pharmaceutical companies that don't want to invest in their own clinical capabilities. Clinical research outsourcing in India is driven in part by India's superb IT, telecommunications and Internet connectivity. CROs in India will have to grow more than 100% per year to match the aspirations of serving 10% of global clinical trials," warned Varawalla.

Kumar said he expects India will have 400 GCP-trained investigators by next year and an exponential growth in patients. "My personal ambition is [for NMIA] to have at least 50 investigators within the next 12 months, each contributing at least 50 patients," he said. "By that time, the number of CROs will likely have at least doubled, to more than 20."

Wadhwani is also optimistic. "In two to three years it will be difficult to find a global clinical trial where India does not play a key role," he said. "Sponsors will have three big service needs: access to a network of trained investigators and a pool of patients, someone on the ground in India to manage trials, and assistance in handling regulatory affairs."

"India's largest challenge resides in the need for all CROs to deliver the highest quality work in order to create a spotless

reputation in the clinical research arena," said Vasudeo Ginde, ICRI's managing director. "Unfortunately, with limited barriers to entry and many sensing the significant growth opportunity of the clinical research field in India, a growing number of CROs with no prior training and experience in clinical research are setting up operation. This represents a significant risk for India's reputation."

The need for SMOs is actually greater than the need for CROs in a country such as India, Kumar said. "As the investigator base increases, sponsors will need more assistance managing the investigative site. If the site functions well, monitoring won't need to be so intensive."

Pfizer's Potkar doesn't fully agree. "The SMO concept is relatively new and is still gathering momentum. A few large private hospitals are self-sufficient in regards to research planning and conduct through an SMO-type structure," he said. Bhatt is equally reserved. "At the moment, sponsors don't have much need for SMOs. Recruitment is not a problem," Bhatt said.

Potkar concluded, "The clinical trials that have been conducted in India thus far have gone well. For the majority of studies, patient enrollment is a key advantage. This helps compress the development timeline. Data quality is usually excellent and depends heavily on the sponsor commitment to monitoring and quality control activities. Numerous audits in India are a testimony to level of quality, and data from clinical studies in India have been successfully filed with international regulatory agencies. Product patents and data exclusivity are the two key areas that now need attention and resolution. The potential realized at present is a fraction of the possible in India."

—Deborah Borfitz

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and to support the overall mission of their teaching institutions. AHCs have also used this funding source to grow their clinical research capabilities and to more effectively service their large networks of physician faculty and study support personnel.

Many AHCs initially made investments in their clinical research capabilities in order to compete more effectively against for-profit investigative sites for industry-sponsored study grants. Continued investments during the past five years, however, have been made with the primary intent to enhance the attractiveness of AHCs to government funding sources, and to address growing concerns—including those from regulatory agencies and the public—about study volunteer safety and institutional compliance.

"The same infrastructure of a central clinical trials office that we built initially with the major focus on industry, we're applying to NIH-sponsored research," said Mark S. Paller, M.D., professor of Medicine and assistant vice president for research at the University of Minnesota. "We had an office that was all industry-sponsored, now we've moved toward a more even industry and government split."

"We really haven't been out soliciting industry sponsors actively or aggressively," continued Paller, in comments that are consistently being heard across a large percentage of academic institutions. "The growth that we've had has been either continued business with sponsors who know us, or people who seek us out because of our reputation. But we haven't been actively seeking growth in the same way that we did, say, five years ago when we first started," he said.

An NIH Orientation

Today, an estimated 70% of the nearly 130 AHCs have central offices that support their institution's clinical research activities. In a growing number of institutions, these central offices now support government- and industry-funded studies. These offices typically provide a variety of administrative, quality assurance and educational services including: budget preparation; contract negotiation; identification and assistance securing study grants; study coordinator training and support; investigator training; assistance with regulatory requirements and the institutional review board; patient recruitment support, project and data management assistance.

Yet, the incentives for AHC faculty and staff to conduct industry-sponsored research are far less compelling—the money is less attractive, the research viewed as commercial and less interesting. Although most institutions acknowledge that they want to include industry study grants as part of their

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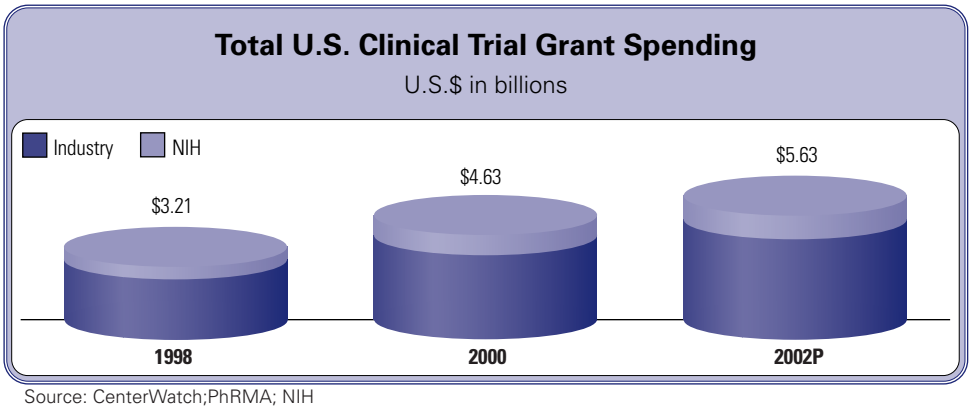

Source: CenterWatch;PhRMA; NIH

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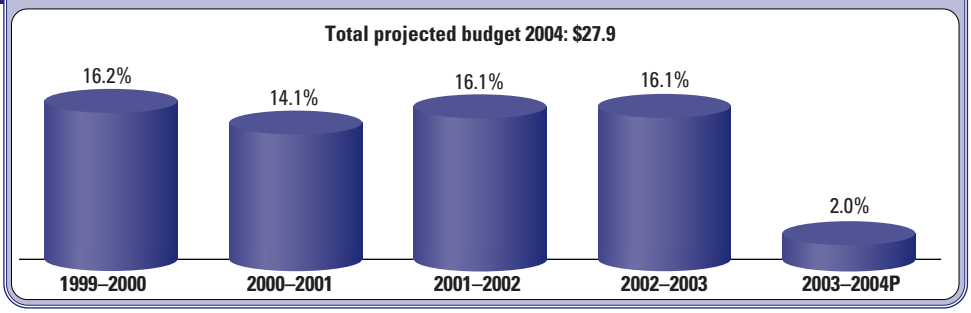
overall mix of projects, many have not invested the time and resources to nurture and build their relationships with industry sponsors of clinical trials.

In a recent survey of more than 30 major academic institutions, CenterWatch finds that, with few exceptions, AHCs have had flat to negative growth in industry-sponsored clinical trial funding during the past several years. Johns Hopkins University, New York University and Temple University, for example, report modest to no growth in 2003 funding. The University of Rochester—once a top growing AHC, reports declining dollars from industry sponsors since 2001. And the University of Pennsylvania—one of the largest AHCs involved in industry-funded clinical trials—reports an 11% decline between 2001 and 2002. UPenn expects flat growth in 2003.

"The perception of the academic institutions remains that government work has much more potential for revenue and prestige," Eileen Hilton, M.D., president and CEO of Biomedical Research Alliance of New York (BRANY) told *CenterWatch*. "For BRANY institutions, most of the research revenue is coming in from federal sources. It is a much larger number of dollars and it is growing at a higher rate than the clinical trials dollars from industry," she said.

NIH Funding Growth Abruptly Halted

Annual Growth



Source: NIH

"We want to have more NIH dollars, and we do want to have more clinical research dollars," said Tesheia Johnson, assistant dean for Clinical Trials Research at the University of Vermont. "But we really want good science to be done in research. We'd prefer to look at things that have no absolute funding value as it relates to a patent. As the NIH has grown its funding, with a much larger percentage going to clinical research, institutions are being forced to help investigators go after NIH money. That money is out there, it's available, and it better supports our mission," she said.

"From our perspective, industry-funded studies have offered steady growth, but not meteoric growth," said Constance Stubbs, director of Administration and Finance for Massachusetts General Hospital's (MGH) Clinical Research Program—a part of the Harvard Medical School system. MGH boasts having grown its industry-sponsored grant funding 12% annually since 1995 to $15 million in 2002. "But a doubling of NIH-funding has been a meteoric rise. We're very, very pleased with the NIH side," she said.

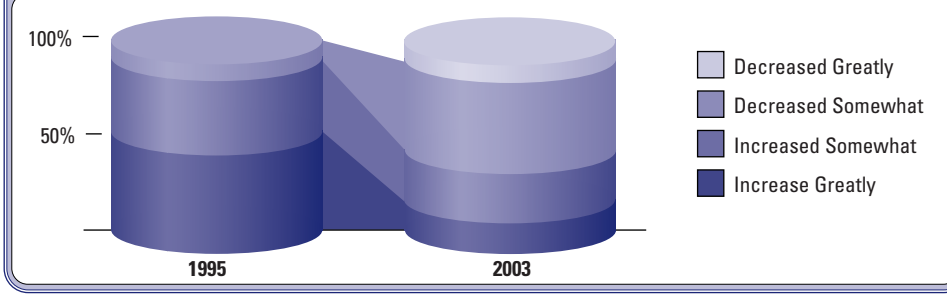
"It's harder to get promotions out of industry-funded studies when you don't own all the data, there are limited publication rights, there are multiple centers. Given the choice, investigators will often gravitate to the NIH-funded investigator-initiated study," said Stubbs.

"You really need to do both," said Marcia Markowitz, director of University of Pennsylvania's Office of Human Research. "Years ago, a number of schools said—and Penn was not one of them—we're going to gear ourselves more towards NIH. That's when NIH received an infusion of research money. Penn never did that. We want to continue our research in both areas," she said.

Several institutions—New York University and the University of Medicine and Dentistry of New Jersey, for example—report that they continue to invest in staff and facilities to support industry-sponsored clinical research. Based on reports from a large number of AHCs, however, few institutions have substantially increased investment to attract industry funding.

"Many AHCs are shifting to more federal funding," said David L. Hom, director of the Clinical Research Group at the University of Medicine and Dentistry of New Jersey (UMDNJ). "We've been actively seeking industry trials to help investigators develop relationships with industry and to gain experience in trial participation. Our new president has said that we need to reach out and partner more with industry, particularly given our proximity to them here in New Jersey," he said.

"Over the past three years, the importance of industry-sponsored clinical research to your institution has..."



Source: CenterWatch Surveys of Academic Health Centers

Continued Erosion

With many AHCs placing greater emphasis on securing government-funded study grants, the market for industry-sponsored

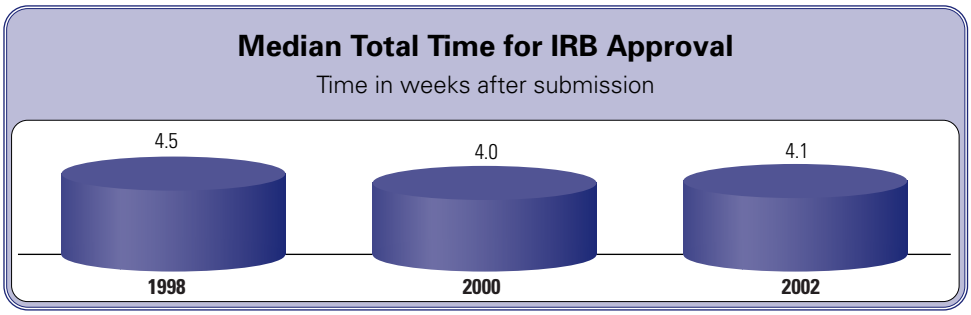
clinical trial grants has continued to shift to the for-profit sector. This comes despite industry's interest in engaging AHC-based physicians to help accelerate the commercialization of their drugs. Sponsors largely believe that AHCs offer unmatched access to an experienced and sizable pool of physician faculty and research professionals, and to large patient populations. But many AHCs have done little to attract industry.

A majority of clinical trial offices have done little to become more competitive. Institutional review board approval times at academic institutions, for example, have actually worsened during the past two years. It still takes a local IRB more than one-month to approve a submission. And less than one in four institutions claim to have used a central or independent IRB. Small staff and limited resources within clinical trial offices have all contributed to the erosion of market share for AHCs.

CenterWatch estimates that more than $1.7 billion went to clinical investigators involved in conducting clinical trials on a part-time basis—a 37% market share of total grants from biopharmaceutical and medical device companies. The part-time investigative site market segment—comprising sites that derive the majority (85% or more) of their revenue from clinical practice—has been growing steadily. In 2002, this highly fragmented and transient group has surpassed academic health centers as the largest market segment.

Approximately $1.6 billion in industry funding for clinical trials went to AHCs in 2002, representing a 35% share of the market for industry-sponsored clinical trials.

An estimated $1.3 billion or 28% of industry grants went to investigators conducting trials among dedicated sites and site management organizations (SMOs). The dedicated site segment has grown substantially—from a 19% share of the total industry-sponsored clinical grants market to 29% in 2003—in part due to stealing market share from AHCs. Approximately $270 million went to investigative sites within SMO networks—representing 14% annual growth since 2001.



Source: CenterWatch Surveys of Academic Health Centers

"Universities have been losing a lot of dollars to the private sites," said Soo Bang, director of the Office of Clinical Trials at New York University. "Big academic medical centers are looking pretty much to maintain their market share of industry-sponsored clinical trials. But that's a passive way to face the competition from private sites."

NIH Funding Hits a Wall

Biopharmaceutical companies may likely see a dramatic shift in AHC focus given the Bush Administration's plans to essentially halt new growth in the 2004 NIH budget. Between 2000 and 2002, NIH clinical trial grant spending grew by more than 16% compared to industry's 9% during that same period. Like hitting a wall, the NIH Budget, at $27.3 billion in 2003, will only rise 2% to $27.8 billion in 2004. This is well below the growth in biopharmaceutical company spending for clinical research—expected to exceed $35 billion in 2003.

Last year, approximately $7.7 billion was spent by major pharmaceutical companies to fund phase I-III activities. In contrast, the NIH spent $5.3 billion on all clinical research activities (e.g., biomedical, epidemiological, behavioral studies and laboratory work involving human tissue samples) in 2002—including $1.1 billion spent on clinical trials specifically. The NIH spends about one-third as much as does industry on clinical research designed specifically to evaluate new medicines and devices.

Facing rising costs and a sharp decline in NIH funding growth, many AHCs will need to pursue more aggressive approaches to attracting and securing industry-sponsored clinical research grants in order to meet their financial requirements.

Fortunately, clinical trial offices—the majority of which have been building up their capabilities and services to primarily target government funded programs—appear better positioned to aggressively pursue industry-sponsored research than they did several years ago. Centralized clinical trial offices have taken a hard look at addressing shortages of well-trained investigators and study coordinators. Many AHCs have improved compliance and patient recruitment support. Some have invested in the development of sophisticated information systems. And many central offices have improved their ability to meet administrative needs. Consider some of the following examples:

Investigator Training and Support

Having encountered resistance from established physician faculty over the years, many clinical trial offices have focused on providing flexible support and education for novice clinical investigators. As a result,

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AHCs are playing a large and growing role in preparing new clinical research professionals.

"As a small office with limited resources, we spend a lot of our time focusing on new investigators. These people are unfamiliar with the clinical research process and they most need our services," said William Hirschhorn, director of the Office of Clinical Trials at Temple University.

"We usually target the beginning investigator who can't afford to hire their own research team, is just starting out and needs some help with a part-time person," agreed Adrian Dobs, M.D., medical director of the Clinical Trials Unit, at Johns Hopkins University. "We offer a piece-meal of services—coordinator support, regulatory support, office space and technical support—and this flexibility has become a big growth area for us," she said,

"We're responsible for enhancing and furthering all educational portions and aspects related to the need for clinical research training," said Markowitz. We focus on improving logistics and processes, and of course making sure everyone is following research regulations. All of our training is free. We provide training through mentoring, one-on-one, group sessions, classrooms, workshops. We do web-assisted presentations, as well as web-based learning, and paper-based learning when necessary. We also maintain documentation of the education and training that's provided," she added.

"We have a new investigator subcommittee," said Bang, "that fosters and mentors young investigators to help them become career clinical researchers. We hope our investigators will participate in industry-sponsored trials. Then we hope to get them to write their own protocols and get those protocols funded either through industry or NIH."

Better Administrative Support

Faculty investigators have increasingly turned to their clinical trial offices for assistance in managing financial and operational aspects of clinical research. AHC central offices have continued to add these administrative services—some of which involve increasingly sophisticated information systems support.

"Cash management is an area that requires a lot of attention," said UVM's Johnson. "We're developing a central system that manages it once it gets into the institution. This not only helps our financial management, but also assists with audits and compliance," she said.

"The Research Operations and Development area that I head up is responsible for developing and implementing processes that will help the researchers with their study feasibilities, their standardizing budgets, giving them tools in which to develop their budgets," said Markowitz. "We've developed an in-house budget development tool. We're implementing a web-based system to track all non-clinical research. We have developed an online protocol tool to help write a protocol. And we've developed online consent forms," she said.

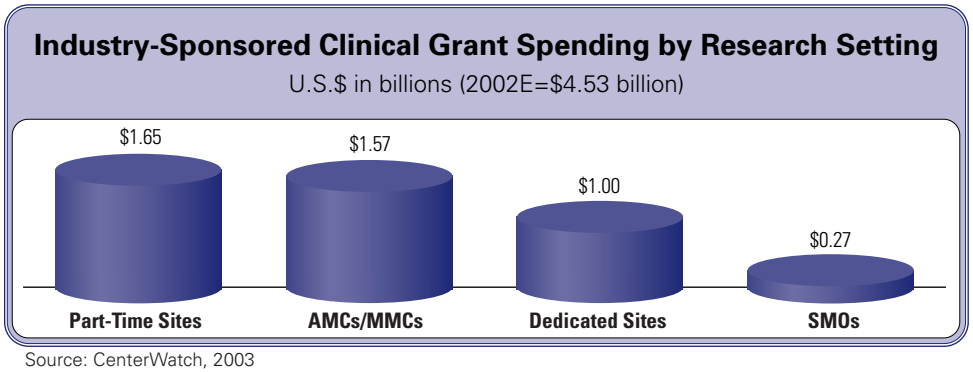
"We provide a unique service where we assist investigators in developing a recruitment plan," said Stubbs of MGH, "We work to help them understand how they are going to find patients for their studies. We help our investigators find funding sources through internal and external web sites. This year, we also have a full-blown study coordinator orientation program every month, for coordinators who are new to the institution," she said.

Streamlining IRB and Compliance Services

Almost universally, AHCs report a strong commitment to ensuring higher levels of compliance. This commitment, in part, comes in the wake of IRB suspensions in the late 1990s, rising growth in the incidence of noncompliant practices, and the highly publicized and tragic deaths of study volunteers. Although to date IRB review and approval times have not come down, many AHCs are determined to change this fact.

"Our Regulatory Compliance Division has six monitors plus a director," said Markowitz of UPenn. "They provide assistance on investigator-initiated studies. They'll do compliance monitoring, both for-cause and not-for-cause. They can help with the document preparation, especially when it comes to investigator-initiated protocols, consent forms, how to do an IND submission. They work very closely with federal regulatory agencies," she said.

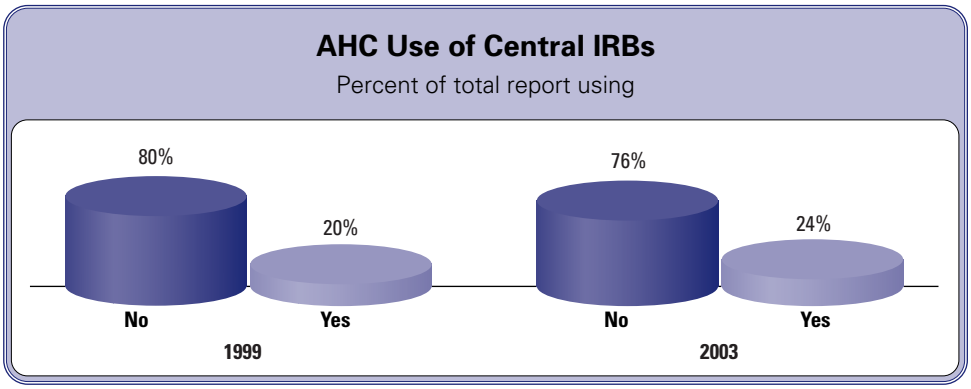
"We're working particularly closely with the university because this is where our institutional review board is housed," said



Source: CenterWatch, 2003

Markowitz. "We're looking to streamline the internal infrastructure processes necessary to perform clinical research more effectively. We're also a part of MACRO [Multi-Academic Clinical Research Organization] where we're able to utilize one IRB for five academic institutional members."

"We're looking at many of the things that have driven industry away from academic medical centers: all the red tape and the time delays," said Johnson of UVM. "We're looking very closely at our IRB timeline. We actually are increasing the frequency of our IRB meetings."



Source: AAMC, 2003; CenterWatch, 1999

Patient Recruitment Assistance

Similar to offering more flexible and sophisticated administrative services, a large percentage of clinical trial offices report that they have invested in improving services and systems to support patient recruitment.

"Our Research Patient Data Registry is a fabulous new informatics tools that we've developed that draws on all the databases in the hospital," said Stubbs. "We are able to integrate how many patients we have that meet a certain profile—either by their clinical lab values, or their diagnosis, or their age, or any number of descriptors—so that we can establish whether we have the population to do a particular study. Then once there's IRB approval to drill down on those, we can do the searches for those patients electronically. We also have an external web site for patients who are trying to learn about and find a trial. And this has a feed to the CenterWatch listings of clinical trials," she said.

"At the end of July, we're also launching a research subject volunteer program registry called RSVP for Health," added Kay Ryan, director of Clinical Research Operations at MGH. "We're doing a major advertising blitz throughout Greater Boston—to colleges, newspapers, large employer groups—encouraging persons who are interested in learning about a trial in specific areas to register either online or through a call center, so that we can really inform them about trials coming up in their specific interest field," she said.

"We think that's going to be a tremendous tool for speeding enrollment for a trial. If we're approached by industry, for a trivial cost we would be able to look at our own patient base and this self-directed registry," explained Ryan.

"At Penn we also have a patient informatics service, where we have information on all patients that have come through our health system—at any of our hospitals, outpatient clinics, private practitioners. We're able to provide information—no names of course—but demographic information on patient populations. That information is available to our faculty, and will be available to industry later this year," said Markowitz.

"We are actively offering subject recruitment assistance and subject education programs to our investigators," said Bang of NYU. "We're presently evaluating vendors so that we can have a centralized management system that will entail searchable patient databases to help us recruit quicker for research projects."

Industry Isn't Helping

The historical growth in NIH funding is not entirely to blame for AHCs' focusing on securing and supporting government funded clinical research. Most AHCs told *CenterWatch* that industry clinical trial budgets are less attractive, that often they don't cover the full cost of conducting the project, and that biopharmaceutical companies are taking far longer to pay their grants—even longer than it is taking the government.

"Industry trials are a great deal of work, with so much time dedicated to contract and budget negotiations and project delays, when the money is actually fairly small," said Dobs of Johns Hopkins. "Although the NIH grants may be more difficult to write, the budget administration of it is fairly straightforward, the work that has to be done by research administration is fairly straightforward. So there's a sense that NIH is really providing most of the money and it's much easier to get that money. It can be a real aggravation to work with industry," she said.

"When we first formed our Clinical Research Institute," explained Bill Kelvie, director, clinical research practices, Clinical Research Institute at the University of Rochester, "We were pursuing grants from pharma to supplement investigator incomes and to bring more dollars into the institution. But why do a pharmaceutical company study with 25% indirect rate when you could do a federally funded study at a 57% indirect rate?" he asked.

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"NIH grants and contracts are usually for multi-year arrangements. So, right now we participate in a couple of multi-center NIH trials," said Hom of UMDNJ. "For NIH grants, although we contract on an annual basis, we're promised that the trial will last for as long as five years. That's a guarantee, a promise that the NIH fulfills," he said.

"It's more advantageous for us to have a long-term commitment than the short piecemeal project that we get from industry, where we enroll five patients for eighteen months and then the contract is over and we have to find a replacement protocol. It's demotivating for our faculty. They look for security and a commitment to support their position for multiple years, rather than the chance of getting laid off because of hitting a trough in funding," said Hom.

"A five-year grant is great because you do the work and you're awarded the next year," said Ryan. "When a principal investigator works on a short-term study, they have to push that boulder up the hill each year. A four- or five-year grant within a field of expertise is a critical way to ensure advancement," she said.

"There are many aspects of industry-sponsored studies that make them more difficult for us," said Paller of UMinn. "Having different sponsors using different CROs has not made life any easier for us. And having to use a sponsor's consent form when the approval has to be local, it just doesn't work. Given the large differences within and between institutions, we're not making any progress in having a universal contract We've run faster and harder to make sure that we can turn contracts around quickly, but I don't think we've really streamlined the process to any great extent."

"I will say this in favor of industry grants," added Paller. "When you're talking about the NIH, it's not a sure thing that you're going to get the grant. It's a lot easier for us to very quickly assess whether we'll be successful in securing an industry grant. We can put together a rough budget pretty quickly and estimate whether we're going to have the population to recruit from pretty quickly. With the NIH, it's the whole peer review process, and you don't know for 12 months whether you're going to get a grant or not," he said.

Where They Left Off

With NIH funding growth coming to an abrupt halt, a large and growing number of AHCs appear interested in picking up where they left off in the middle 1990s. Facing strong financial pressure and the need to leverage their clinical research support capabilities, many institutions will try again to more actively increase their share of industry-sponsored research. Although the economic incentives are similar to those they have faced in the past, AHCs seem better positioned to compete for industry projects at this time. The question is—has there been too much erosion for industry to be more responsive to AHC overtures? Can AHCs begin courting industry again when academic institutions have been lukewarm dance partners for the past five years?

"While the NIH budget doubled, we all grew more confident. But the number of grants didn't double," explained Stubbs of MGH. "The length of time of the grants expanded, and the average size of each grant increased."

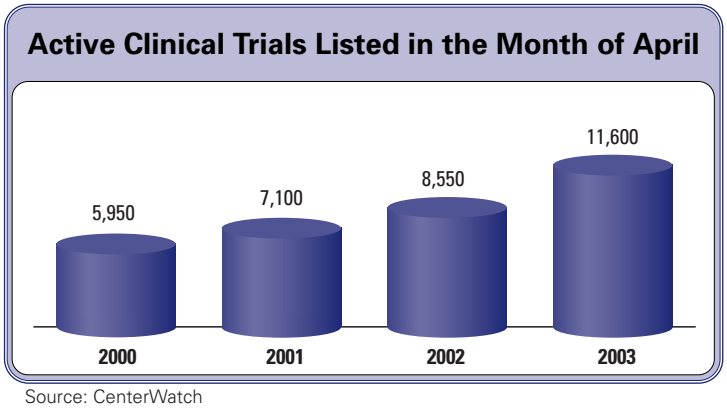
"Now, that's all over and done. The people who were funded while NIH funding was growing are not going to get renewed. There's a scramble right now in the appropriations committee because the NIH can't possibly continue funding all of the grants. And that is going to make for a really tough and challenging time for academic health centers."

—CenterWatch Editorial

CenterWatch Web Services

Companies are posting more trial listings on CenterWatch than ever before. The figures to the right represent the number of actively enrolling industry-sponsored clinical trials listed on the Center-Watch web site in the month of April from each of past 4 years.

Posting clinical trial listings on Center-Watch is easy and new listings are guaranteed to be posted within two business days. For more information please contact Matt McKinley at (617) 856-5373 or matthew.mckinley@centerwatch.com



Source: CenterWatch

Eye On: Alzheimer's Disease

Alzheimer's disease (AD) is the most common form of dementia, or loss of normal brain function, including thought, memory and language. This degenerative condition is named after Dr. Alois Alzheimer, who discovered the hallmark neuropathological feature of amyloid plaques and neurofibrillary tangles in 1906.

Cognitive dysfunction in AD is linked to neurotransmitter abnormalities, especially those involving acetylcholine. The widely held amyloid cascade hypothesis assumes that beta-amyloid protein deposits found in plaques are toxic to the brain. However, neurofibrillary tangles, inflammation, free radicals, and impaired cerebral metabolism may all play some role in the pathogenesis of AD, either alone or in combination.

Up to 4 million Americans currently have AD. Onset is usually after age 60, and risk doubles every five years beyond age 65. Prevalence is 3% at ages 65 to 74, and nearly 50% at age 85 and older. Average survival is eight to 10 years after diagnosis but may be as long as 20 years.

In addition to age, family history is another major risk factor. However, familial AD, which usually occurs between the ages of 30 and 60, is relatively uncommon. The apolipoprotein E (apoE) gene has three forms, one of which is protective against AD, and another of which increases the risk of sporadic AD. Other genetic mutations may increase risk, while environmental risk factors may include head injury, low educational level and toxic exposure.

Although there is currently no cure for AD, available drugs such as tacrine (Cognex), donepezil (Aricept), rivastigmine (Exelon), or galantamine (Reminyl) may help prevent some symptoms from becoming worse for a limited time during the early and middle stages of AD. Drugs such as tacrine and donepezil are acetylcholinesterase (AChE) inhibitors, which increase the duration of action of acetylcholine at cholinergic synapses.

Behavioral symptoms of AD, such as sleeplessness, agitation, wandering, anxiety and depression, may respond to sedatives, antidepressants and antipsychotic agents, although these drugs may worsen cognitive function and should be used cautiously.

On the theory that inflammation in the brain may contribute to neuronal damage in AD, trials are ongoing of nonsteroidal anti-inflammatory drugs such as rofecoxib (Vioxx) and naproxen (Aleve). Nutritional trials are underway with vitamin E, which may slow degeneration in AD by about 7 months, and ginkgo biloba, which may help treat AD symptoms.

Despite high hopes that estrogen therapy would reduce the risk of AD or even reverse symptoms in postmenopausal women, formal trials have been disappointing. One study showed that estrogen does not slow the progression of already diagnosed AD, and another trial of estrogen and progestin showed that women over age 65 had twice the rate of dementia, including AD, compared with the control group. Trials are also underway for substances used to reduce cardiovascular risk, including statin drugs, folic acid, B6 and B12 vitamins.

CenterWatch has identified a pipeline of 29 drugs in various stages of development for AD, many of which target neurotransmitter abnormalities.

Forest Laboratories has submitted a new drug application (NDA) for memantine, which attenuates disturbances in glutamatergic neurotransmission by modulating rapid, voltage-dependent interactions with N-methyl-D-aspartate (NMDA) receptors.

In Germany, memantine has been marketed for dementia syndrome for more than 10 years. Two European placebo-controlled studies in 418 patients suggested rapid, enduring improvement in the cognitive, psychological, social and motor impairments of dementia, which improved quality of life. Post-marketing surveillance of 531 German patients with advanced dementia revealed improvement in the overall clinical picture in 77% of patients receiving memantine and stabilization in 17%.

In a U.S. study of 252 patients, 10 mg memantine twice daily for six months significantly improved cognition, activities of daily living, and overall clinical status while reducing demands on caregivers. Adverse events were comparable to those in the placebo group, but response rates were two to three times higher.

Aricept (donepezil hydrochloride, E2020), is already approved for mild to moderate AD and is now in phase III testing by Eisai for severe AD. In a placebo-controlled, randomized trial of 145 community-dwelling patients with severe AD not requiring total nursing care, those receiving 5-10 mg Aricept had statistically significant improvement or stabilization on a measure of global function and in activities of daily living, while placebo-treated patients had functional decline. Overall improvement in behavioral disturbances was also significantly greater than in the placebo group.

Completion rates for the study were 90% in the Aricept group and 86% in the placebo group. The most common reason for discontinuation was adverse events, which occurred in 7% of the Aricept group and in 5% of the placebo group. Common treatment-emergent adverse events, which were mostly mild or moderate, were hostility, headache, diarrhea, confusion, fecal incontinence, somnolence, vomiting, back pain, flatulence, rash and urinary tract infection.

Another AChE inhibitor, in phase III testing by Takeda Pharmaceuticals, is zanapezil (TAK-147). In animal models, TAK-147 ameliorates impairments of learning and

Alzheimer's Disease

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memory without producing peripheral side effects, and it also activates the monoaminergic systems and energy metabolism. Because of its nerve growth factor (NGF)-like neurotrophic activity on central cholinergic neurons, it may prevent or slow disease progression as well as improving clinical symptoms via AChE inhibition.

Ganstigmine (CHF2819) is a novel AChE inhibitor derived from genserine, for which animal models suggest significant neuroprotection independent from its cholinergic activity. Chiesi Farmaceutici is currently in phase II testing of ganstigmine in once daily dosing. In a randomized, double-blind, placebo-controlled trial in 29 patients with probable AD, this drug was well tolerated within a dosing range of 5 to 10 mg.

Phenserine, in phase IIb testing by Axonyx, is a highly selective, reversible AChE inhibitor. Pre-clinical data released in May suggest that phenserine also reduces production of amyloid precursor protein (APP), the precursor of the neurotoxic amyloid beta-peptide (A-beta). Because of this dual mechanism of action, phenserine has the potential to improve memory as well as to slow AD progression.

Another drug targeting A-beta production is a gamma-secretase inhibitor, in phase II development by Bristol-Myers Squibb. This drug blocks the protease that cleaves APP to produce A-beta.

Telluride Pharmaceutical is in phase II/III development of Memex (nicotinamide adenine dinucleotide; NADH), which may stimulate cellular ATP production as well as endogenous L-dopa biosynthesis. In theory, helping AD patients regain their normal cellular energy production capacity may alleviate symptoms or even slow progression.

Based on a novel approach, the COGNIShunt System, in phase III testing by Eunoe, is a cerebrospinal fluid (CSF) shunt designed to increase CSF flow and clear neurotoxic cytokines and other neurotoxins that may contribute to AD progression. Phase I and II trials showed that the procedure and COGNIShunt System were safe and well tolerated in AD, without symptoms of overdrainage and with stabilization of mental function in shunted patients. CSF levels of potentially neurotoxic proteins associated with AD lesions, such as MAP-Tau and (beta)-Amyloid (1-42), decreased in shunted patients and remained low for twelve months.

Rather than targeting the cause of AD, Neurodex (AVP-923) decreases symptoms of pseudobulbar affect or emotional lability. This combination of dextromethorphan and an enzyme inhibitor that sustains elevated levels of dextromethorphan is in phase III testing by Avanir. Episodes of uncontrolled laughter or tearfulness unrelated to social context are not physically harmful, but they are distressing to both patients and their caregivers.

Although there is still no cure for AD, many drugs in the pipeline aim to improve memory loss or other symptoms through interventions in cholinergic or other neurotransmitter systems. Most promising in theory appear to be those agents with a dual cholinergic and neuroprotective effect, as these agents offer the potential to halt degeneration while improving cognitive function. Additional approaches target energy metabolism, inflammation or A-beta. However, trials of vaccine directed against A-beta were halted due to adverse effects.

—Laurie Barclay, M.D.

In the Pipeline: Alzheimer's Disease

Drug	Company	Contact	Additional Information
Phase I			
SB 271046	GlaxoSmithKline	(919) 483-2100 www.gsk.com	5-hydroxytryptamine 6 (5HT6) receptor antagonist
ZT-1	Debiopharm and H3 Pharma	+41 (0) 21 321 0111 www.debiopharm.com	acetylcholinesterase (AChE) inhibitor
HCT 1026, NO-flurbiprofen	NicOx SA	+33 (0)4 9238 7020 www.nicox.com	nitric oxide-releasing derivative of the NSAID, flurbiprofen
Apan	Praecis Pharmaceuticals	(781) 795-4100 www.praecis.com	interferes with the aggregation of beta-amyloid peptide (phase Ib)
SL 25.1188*	Sanofi-Synthelabo Pharmaceuticals	(33) 1 53 77 4000 www.sanofi-synthelabo.com	monoamine oxidase B inhibitor
TV-3326	Teva Pharmaceutical Industries	(800) 221-4026 www.tevaneuro.com	MAO-inhibitor with anti-acetylcholinesterase activity and neuroprotective activity

Drug	Company	Contact	Additional Information
Phase II			
phenserine*	Axonyx	(212) 645-7704 www.axonyx.com	highly selective, reversible acetylcholinesterase inhibitor (phase IIb)
gamma-secretase inhibitor	Bristol-Myers Squibb	(609) 252-4000 www.bms.com	protease that cleaves amyloid precursor protein, producing amyloid beta-peptide
ganstigmine, CHF 2819	Chiesi Farmaceutici	(00 39) 0521 2791 www.chiesigroup.com	cholinesterase inhibitor
Ampalex, CX-516	Cortex Pharmaceuticals	(949) 727-3157 www.cortexpharm.com	ampakine (AMPA) receptor enhancer
AN-1792, AIP-001*	Elan Pharmaceutical Research and Wyeth	(858) 457 2553 www.elanpharmaceuticals.com	vaccine composed of the ß-amyloid protein (trials halted due to adverse events)
737552, S-8510	GlaxoSmithKline	(919) 483-2100 www.gsk.com	benzodiazepine inverse antagonist
NS-2330	NeuroSearch A/S and Boehringer Ingelheim	+45 4460 8000 www.neurosearch.com	monoamine reuptake inhibitor (phase IIb)
Lipitor (atorvastatin calcium)	Pfizer	(212) 573-2323 www.pfizer.com	HMG-CoA reductase inhibitor
PYM50028	Phytopharm and Yamanouchi Pharmaceutical	+44 (0)1480 437697 www.phytopharm.com	synthetic neuroprotective and neuroregenerative agent (part of the P58 program for AD)
SR 57667*	Sanofi-Synthelabo Pharmaceuticals	(33) 1 53 77 4000 www.sanofi-synthelabo.com	
xaliproden, SR 57746A*	Sanofi-Synthelabo Pharmaceuticals	(33) 1 53 77 4000 www.sanofi-synthelabo.com	non-peptide compound that activates the synthesis of endogenous neurotrophins
Neotrofin, leteprinim potassium (AIT-082)	Spectrum Pharmaceuticals	(949) 788-6700 www.spectrumpharm.com	composed of the purine compound hypoxanthine (all clinical trials on hold)
Drug: Huperzine-A	Savient Pharmaceuticals	(732) 418-9300 www.savientpharma.com	acetylcholinesterase inhibitor
rasagiline mesylate, TVP-1012	Teva Pharmaceutical Industries	(800)221-4026 www.tevaneuro.com	monoamine oxidase B (MAO-B) inhibitor
leuprolide acetate	Voyager Pharmaceutical	(919) 846-4880 www.voyagerpharma.com	antigonadotropin
Phase II Completed			
dapsone	Immune Network	(604) 312-7488 www.immunenetwork.com	anti-inflammatory anti-microbial antibiotic
Alzhemed	Neurochem	(514) 337-4646 www.neurochem.com	small sulfonated molecule; prevents association of glycosaminoglycans with amyloid-beta peptide
Phase II/III			
Memex, nicotinomide adenine dinucleotide (NADH)*	Telluride Pharmaceutical	(908) 369-1800 www.tellpharm.com	treatment for Alzheimer's disease
Phase III			
Neurodex, AVP-923*	Avanir Pharm aceuticals	(858) 622-5200 www.avanir.com	combination of dextromethorphan and an enzyme inhibitor (for the treatment of pseudobulbar affect in neurodegenerative disorders)

Drug	Company	Contact	Additional Information
Aricept, donepezil hydrochloride (E2020)	Eisai	(201) 692-1100 www.eisai.com	reversible inhibitor of the enzyme acetylcholinesterase (approved for mild to moderate Alzheimer's; in trials for severe Alzheimer's)
COGNIShunt System	Eunoe	(888) 469-6463 www.eunoe-inc.com	Cerebrospinal fluid (CSF) shunt to clear neurotoxins that may contribute to Alzheimer's progression (pivotal device-based trial)
zanapezil, TAK-147	Takeda Pharmaceuticals	(847) 383-3000 www.takedapharm.com	acetylcholinesterase inhibitor
NDA Submitted			
memantine	Forest Laboratories	Chuck Triano (212) 224-6714	modulates N-methyl-D-aspartate (NMDA) receptor activity

* Denotes a drug for which CenterWatch could not confirm its status

Note: If you would like further information on any drug listed above, or to review our comprehensive database of drugs in development, please visit www.centerwatch.com.

TrialWatch

TrialWatch is designed to help sponsors and CROs identify a pool of investigators for their upcoming trials. Each sponsor that is listed here has confirmed that it will be actively selecting sites during the next few weeks, and would like to receive inquiries from investigative sites. Sponsors and CROs that would like to use this service should contact Tamar Skowronski at (617) 856-5974 or email tamar.skowronski@centerwatch.com. Visit our web site at www.centerwatch.com/professional/trialwatch.html to use TrialWatch online.

For investigators, this listing provides prequalified leads for clinical grants. **Please note: Unless a phone or fax number is given, do not call the sponsor or CRO**. Sponsors have provided this information to *CenterWatch* with the understanding that investigative sites will mail cover letters, CVs and other information about their facilities, staff and patients. Please inform the sponsor or CRO that you learned of the project through *CenterWatch.*

All Phases: *Still Seeking Investigators*

Global Pharmaceutical Services, Inc.
Garland Johnson
4159 N. 37th St.
Galesburg, MI 49053
Email: garlandj@iserv.net

Drug name: Not applicable
Specialty: All specialty areas
Indication: All indications
Notes: GPSI is seeking clinics/hospitals in Michigan that are conducting clinical studies. Capabilities may include Phases I through IV trials and all pharmaceutical areas of specialization. We are familiar with the large facilities (i.e. hospitals associated with UMich and Wayne State), but we want to identify other facilities in the state.

Genomics Collaborative
Susan Flynn, Director of Clinical Affairs
99 Erie Street
Cambridge, MA 02139
Fax: (617) 864-1281
Email: sflynn@genomicsinc.com

Drug name: Not Applicable (Interview with blood draw)
Specialty: Hemostasis-Thrombosis Clinics, Vascular, Pulmonology, Internal Medicine, Family Practice
Indication: Deep Vein Thrombosis (DVT)
Notes:
1. Physicians involved in direct care of patients diagnosed with DVT and matched controls without DVT.
2. Patient must be cancer free for three months post diagnosis of DVT.
3. Study Title: A multi-center case-control clinical study to identify genotypic factors in symptomatic patients who develop de novo deep vein thrombosis (DVT).

Please do not contact by telephone!

Lemuria Bio-Technologies, LLC
Terri Halstead or Jeffrey McConnell
21758 Walnut Ave.
Grand Terrace, CA 92313
Email: lemuriabiotechnologies@yahoo.com
Web site: www.lemuriabiotechnolgies.com

Drug name: Not available
Specialty: Physician working with HIV and/or studying HIV, including virologists
Indication: HIV/AIDS

Notes: This is a unique, non-toxic break through product for the treatment of HIV/AIDS. The active ingredients are delivered by suppository. There are several purified herbal constituents as well as a non-toxic chelating agent.

Phase I: *Still Seeking Investigators*

BioCell Technology LLC
Terry Howell
5000 Birch Street
West Tower, Suite 4000
Newport Beach, CA 92660
Email: terry@biocelltechnology.com

Drug name: BioCell Collagen II (dietary ingredient)
Specialty: Dermatology, Musculoskeletal
Indication: Skin health
Notes: BioCell Collagen II is a unique dietary ingredient naturally containing Hyaluronic Acid and Chondroitin Sulfate. We would like to determine how much of each element is absorbed into the blood and also to measure when peak absorption occurs.
Please do not contact by telephone!

BioCure Technologies
Jamie Oliver
1054 Washington St., Suite. 102
Raleigh, NC 27605
Email: joliver@biocuretech.us

Drug name: M4N
Specialty: Oncology-Otolaryngology
Indication: Recurrent Head & Neck Cancer
Notes: Looking for two additional sites. Treatment is intra-tumoral injection. PK is < 8 hr.

Genesis Group International
Walter Drimer
100 West Road, Suite 300
Towson, MD 21204
Email: wdrimer@genesisgroupinternational.com

Drug name: Not available
Specialty: Phase I capabilities
Indication: Not applicable
Please do not contact by telephone!

Johnson & Johnson PRD
Juli Zappa
30 Cattano Avenue, Apt. 2D-204
Morristown, NJ 07960
Email: jzappa2@prdus.jnj.com
Drug name: various
Specialty: Phase I units
Indication: Schizophrenia; sarcoma; HIV; healthy-patient studies
Notes: Seeking M.D.s with some Phase I research experience who are able to utilize central IRB for patient studies as well as healthy-volunteer studies. Sites should be located in the Northeast region—as far North as Canada, as far West as Indiana, and as far South as Virginia.

Phase I/II: *New Leads*

Sunol Molecular Corp.
Bee Huang
2810 N. Commerce Parkway
Miramar, FL 33025
Email: byhuang@sunolmolecular.com

Drug name: Sunol CH-36
Specialty: Physicians in infectious diseases
Indication: ALI (Acute Lung Injury)
Notes: We would prefer to consider centers in Florida or East coast. We would expand to wider area in the later phases.
Please do not contact by telephone!

Phase II: *New Leads*

Quintiles, Inc.
Catherine Johnson
5927 S. Miami Blvd.
Durham, NC 27703
Email: catherine.johnson@quintiles.com

Drug name: Not available
Specialty: Nephrologists with dialysis patients
Indication: Vascular Graft Occlusion in Dialysis Patients with AV Graft
Please do not contact by telephone!

Phase II: *Still Seeking Investigators*

Cephalon, Inc.
Rosanne Stevenson
145 Brandywine Pkwy
West Chester, PA 19308
Email: rstevens@cephalon.com

Drug name: Not available
Specialty: Pediatric Specialists in Pain, Pain Management, or Anesthesia. Also specialists in Cancer, Sickle Cell, or Burns related to the treatment of pediatric pain.
Indication: Pediatric breakthrough pain
Notes: Trial to commence in October.

Discovery Laboratories
Timothy J Gregory, Ph.D.
350 South Main St., Suite 307
Doylestown, PA 18901
Phone: (215) 340-4699, x119
Fax: (215) 340-6479
Email: gregory@discoverylabs.com

Drug name: Surfaxin (lucinactant)
Specialty: Pulmonary, Respiratory, Critical care medicine, Trauma
Indication: Acute Respiratory Distress Syndrome (ARDS)
Notes: A multicenter, randomized, controlled trial comparing the safety and effectiveness of Surfaxin, delivered via bronchopulmonary segmental lavage, to standard care

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ILEX Pharmaceuticals, L.P.
Gary Gonzales
4545 Horizon Hill Blvd.
San Antonio, TX 78229-2263
Email: ggonzales@ilexonc.com

Drug name: CAMPATH
Specialty: Neurology
Indication: Multiple Sclerosis

ILEX Pharmaceuticals
Mark Mayle
4545 Horizon Hill Blvd.
San Antonio, TX 78229-2263
Email: mmayle@ilexonc.com

Drug name: CAMPATH + Rituxan
Specialty: Oncology
Indication: Non-Hodgkin's Lymphoma
Notes: Second line therapy

Immusol
10790 Roselle Street
San Diego, CA 92121
Email: mitchell@immusol.com

Drug name: VitrenASE(TM)
Specialty: Ophthalmology
Indication: Proliferative Vitreoretinopathy

RxKinetix
Vicki J. Abbas
1172 Century Drive, Suite 260
Louisville, CO 80027
Email: vjabbas@rxkinetix.com

Drug name: RK-0202
Specialty: Oncology
Indication: Oral mucositis due to cancer treatment
Notes: Alternate contact: Laurie Armijo, (303) 926-1900

Sention Inc.
Jim Crichton
Clinical Research Associate
1 Richmond Square, 3rd Floor
Providence, RI 02906
jcrichton@sentionpharma.com

Drug name: C105
Specialty: Neurosurgery, Neurology, or physicians specializing in Memory Impairment
Indication: Memory Impairment in Subjects with Treated Anterior Communicating Artery Aneurysm
Notes: The purpose of this clinical research study is to evaluate an investigational medication that may improve memory in people who have been treated with this specific aneurysm.

Wyeth Research
Louise Rochon
87 Cambridge Park Drive
Cambridge, MA 02140
Email: lrochon@wyeth.com

Drug name: Not available
Specialty: Oncology
Indication: Non small cell lung cancer

Phase IIb: *New Leads*

Almirall Prodesfarma S.A.
Beatriz Palacios
Cardener, 68
08024 Barcelona, Spain
Email: bpalacio@almirallprodesfarma.com

Drugname: Not available
Specialty: Pulmonary / respiratory
Indication: COPD

Phase IIb: *Still Seeking Investigators*

UCSD Stroke Center
Janet Werner
200 W. Arbor Dr.
OPC 3rd Fl. Ste 3
San Diego, Ca 92103-8466
Email: jdwerner@ucsd.edu
Drug name: Repinotan
Specialty: Neurologist
Indication: Acute Ischemic Stroke
Notes: t-PA can be given but not required; 4.5 hour window

Phase II/III: *New Leads*

Pfizer Inc.
Cheryl A. Oprisko
50 Peqout Ave
MS 6025- B2239
New London, CT 06320
Email: cheryl_a_oprisko@groton.pfizer.com

Drug name: Not available
Indication: Pediatric Bipolar and Schizophrenic Disorders
Specialty: Research Experience, Pediatric Psychiatric Specialty and/or works along with sub-investigators with the same pediatric specialty
Please do not contact by telephone!

Phase II/III: *Still Seeking Investigators*

Peachtree Clinical Research
Gail Trauco
510 Huddleston Road.
Fayetteville, GA 30214
Email: gtrauco@peachtreeclinicalresearch.com

Drug name: Surfaxin
Specialty: Neonatology
Indication: Infant Respiratory Distress Syndrome
Notes: NICU Phase I-III experience investigational sites needed ASAP.

Phase III: *New Leads*

JBA Research
Natalie Lawrence
1045 East 3900 South
Salt Lake City, UT 84124
Email: nlawrence@jbaresearch.com

Drug name: Not Available
Specialty: Endocrinology for diabetes
Indication: Painful Diabetic Neuropathy
Notes: Patient Population: 18 or older; type 1 or type 2 diabetes with symptoms of distal diabetic neuropathy for at least 6 months; at least moderate pain

Otsuka Maryland Research Institute, Inc.
Terri Goldberg, MPM
2440 Research Boulevard
Rockville, MD 20850
Email: terrig@otsuka.com

Drug name: Tolvaptan
Indication: Chronic hyponatremia of any origin
Specialty: Nephrology, Endocrinology, Psychiatry, Gastrointestinal, Cardiology
Notes: International Trial—U.S., Canada, Europe

Phase III: *Still Seeking Investigators*

Aeterna Laboratories
Isabelle Coté
1405 Boul. Parc-Technologique
Quebec, Quebec
Canada, G1P4P5
Email: isabelle.cote@aeterna.com

Drug name: Neovastat
Specialty: Community Oncologist, Academic Oncologist, Radio-oncologist
Indication: Non-small cell lung cancer
Please do not contact by telephone!

Bracco Diagnostis, Inc.
Pamela Seaman
107 College Road East
Princeton, NJ 08543
Email: pamela.seaman@diag.bracco.com

Device name: Multihance
Specialty: Neuroradiologist in associaton with vascular surgeons
Indication: Imaging Contrast
Notes: MRA vs DSA in Carotid Artery Stenosis
Please do not contact by telephone!

Cell Therapeutics, Inc.
Jeffrey Phillips
PPD, Inc.
3151 S. 17th Street
Wilmington, NC 28412
Email: jeffrey.phillips@wilm.ppdi.com

Drug name: Xyotax
Specialty: Oncology
Indication: Non-small cell lung cancer
Notes: Qualified investigators may inquire about any or all of the following three studies:
1. The primary objectives are to compare the overall survival of patients treated with study drug to that of gemcitabine or vinorelbine.
2. The primary objectives are to compare the overall survival of patients treated with study drug as a single agent or study drug in combinations with carboplatin to that of paclitaxel in combination with carboplatin.
3. The primary objectives are to compare the overall survival of patients treated with study drug to that of docetaxel.

Cellegy Pharmaceuticals, Inc.
Matthew Hauffe
349 Oyster Point Blvd., Suite 200
South San Francisco, CA 94080
Email: mhauffe@cellegy.com

Drugname: Not available
Specialty: 1. Colon and rectal surgeon;
2. Gastroenterologist
Indication: Chronic Anal Fissures

Delcath Systems
James Bartley
1100 Summer Street
Stamford, CT 06905
Email: jbartley@delcath.com

Drug name: Doxorubicin
Specialty: Oncology, Interventional radiology
Indication: Cancer (melanoma)
Notes: Delivery system for the isolated hepatic arterial infusion of chemotherapy to patients with metastatic liver tumors.

Discovery Laboratories
Valerie Parker, Sr. Clinical Project Coordinator
350 South Main Street, Suite 307
Doylestown, PA 18901
Email: vparker@discoverylabs.com

Drug name: Surfaxin
Specialty: Neonatology
Indication: Respiratory distress syndrome
Notes: 1. International study
2. Study group—premature infants

Discovery Laboratories
Evette Riegel, Clinical Research Associate
350 South Main Street, Suite 307
Doylestown, PA 18901
Email: eriegel@discoverylabs.com
Drug name: Surfaxin
Specialty: Neonatology
Indication: Meconium aspiration syndrome (MAS)
Notes: Phase III multicenter trial comparing safety and effectiveness of bronchoalveolar lavage with Surfaxin to standard care, for the treatment of MAS in newborn (term) infants

Eximias Pharmaceutical Corporation
Peggy Senico, RN, BSN
1055 Westlakes Drive, Suite 200
Berwyn, PA 19312
Email: psenico@eximiaspharm.com

Drug name: Thymitaq
Specialty: Oncologist
Indication: Hepatocellular carcinoma
Notes: 1. Seeking sites able to treat 3–4 subjects per year
2. Treatment is for unresectable or recurrent disease.

ILEX Pharmaceuticals
Scott Bergin
4545 Horizon Hill Blvd.
San Antonio, TX 78229-2263
Email: sbergin@ilexonc.com

Drug name: CAMPATH
Specialty: Oncology
Indication: B-cell chronic lymphocytic leukemia (B-CLL)
Notes: First line therapy; familiarity with Chlorambucil

ILEX Pharmaceuticals
Mark Mayle
4545 Horizon Hill Blvd.
San Antonio, TX 78229-2263
Email: mmayle@ilexonc.com

Drug name: CAMPATH + Fludara
Specialty: Oncology
Indication: B-cell chronic lymphocytic leukemia (B-CLL)
Notes: Second line therapy

Imaging Diagnostic Systems
Gary Bishop
6531 NW 18th Court
Plantation, FL 33313
Email: bishop@imds.com

Device name: CTLM-Computed Tomography Laser mammography
Specialty: Radiologist specializing in mammography
Indication: Breast cancer
Notes: 1. Laser mammography device images vasculature and lesions without compression or x-radiation.
2. In final phases of FDA modular submission.

Medical Research Management
Jill Matzat
5825 Eagle Cay Lane
Coconut Creek, FL 33073
Email: jmatzat@cra-training.com

Drug name: Not available
Specialty: Infectious disease and/or experience with HIV research
Indication: HIV
Notes: East Coast sites preferred

OSI Pharmaceuticals
Jack Cavness, Pharm.D.
Mgr. Medical Information Services
2860 Wilderness Place
Boulder, CO 80301
Phone: (800) 572-1932
Email: medical-information@osip.com

Drug name: Tarceva (erlotinib HCl)
Specialty: Oncology
Indication: Non-small cell lung cancer

Pacific Clinical Center
Kimberly Panizzon
17337 Ventura Blvd., Suite #226
Encino, CA 91316
Email: pacific_clinical@yahoo.com

Drug name: Not available
Specialty: Rheumatology
Indication: Arthritis
Notes: Investigator must be Board certified and located in the Los Angeles area.

Pacific Clinical Center
Kimberly Panizzon
17337 Ventura Blvd., Suite #226
Encino, CA 91316
Email: pacific_clinical@yahoo.com

Drug name: Not available
Specialty: Pulmonology
Indication: Asthma
Notes: Investigator must be Board certified and located in the Los Angeles area.

PharmaNet
Greg Collins
1787 Sentry Parkway West
Building 16, Suite 100
Blue Bell, PA 19422
Email: gcollins@pharmanet.com
Drug name: Oral antibiotic
Specialty: Oncology, hematology, infectious disease
Indication: Vancomycin-resistant enterococcus (VRE) prevention in neutropenic oncology patients identified as asymptomatic carriers of VRE

PRA International
Jenni Smith
16400 College Blvd.
Lenexa, KS 66219
Email: smithjennifer@praintl.com

Drug name: Atamestane
Specialty: Oncologists with experience in research who see patients with breast cancer
Indication: Metastatic breast cancer

Research Testing Laboratories
John Marinaro, M.S./Director
255 Great Neck Road, Suite 150
Great Neck, NY 11021
Email: jmarinaro@rtlab.com

Drug name: An oral antibiotic
Specialty: Gastroenterology, Oncology, Infectious Diseases
Indication: Pseudomembranous Colitis
Notes: Patients must have laboratory evidence of C. difficile toxins A or B and will probably be hospitalized. Contact Anne Mui at (516) 773-7788 x49 or John Marinaro at x52.

Unither Pharmaceuticals
Judy Whitman
15 Walnut Street
Wellesley, MA 02481
Email: jwhitman@unither.com

Drug name: OvaRex
Specialty: Gynecologic Oncologist; Medical Oncologist
Indication: Stage III/IV Ovarian Cancer
Notes: This is a randomized, double blind placebo controlled consolidation trial following successful front line treatment. Results from a phase II trial in an identical patient population showed a doubling in time to progression were recently presented at ASCO. These results are available for your review. Please contact us for more information.

University of Medicine and Dentistry of New Jersey
Patrick Pullicino, MD, Ph.D.
185 South Orange Avenue
Department of Neurosciences
Newark, NJ 07103
Email: ruzyckma@umdnj.edu

Drug name: Warfarin versus aspirin
Specialty: Heart failure cardiologist and neurologist at each site to collaborate on enrollment
Indication: Warfarin versus aspirin in Reduced Cardiac Ejection Fraction—WARCEF Study
Notes:
1. WARCEF is an NIH-funded study.
2. Federal wide assurance number required for participation.
3. Seeking responses from investigative sites only. No CROs please.

Please do not contact by telephone!

VITEX
Candida Fratazzi, MD
134 Coolidge Avenue
Watertown, MA 02472
Email: candida.fratazzi@vitechnologies.com

Drug name: INACTINE—treated pathogen reduced red blood cell concentrates
Specialty: Anesthesiologist, Surgeon
Indication: Coronary Artery Bypass Graft (CABG) in patients with prior CABG
Notes: The INACTINE technology addresses both the infectious disease and immunological risks of blood transfusions. Inactine inactivates viruses, parasites, lymphocytes and bacteria, and removes cytokines involved in febrile transfusion reactions, TRALI antibodies, prion proteins and plasma proteins or allergens from red blood cells.

VITEX
Candida Fratazzi, MD
134 Coolidge Avenue
Watertown, MA 02472
Email: candida.fratazzi@vitechnologies.com

Drug name: INACTINE – treated pathogen reduced red blood cell concentrates
Specialty: Hematology, Oncology
Indication: Red blood cell transfusion therapy for the treatment of thalassemia and sickle cell disease
Notes: The INACTINE technology addresses both the infectious disease and immunological risks of blood transfusions. Inactine inactivates viruses, parasites, lymphocytes and bacteria, and removes cytokines involved in febrile transfusion reactions, TRALI antibodies, prion proteins and plasma proteins or allergens from red blood cells.

Phase IIIb: *Still Seeking Investigators*

PRA International
Keisha Rhoden
4 Industrial Way West
Eatontown, New Jersey 07724
Email: rhodenkeisha@praintl.com

Drug name: Not available
Specialty: Pediatric Nephrologist, Pediatric Cardiologist, Pediatric Endocrinologist, Pediatrician
Indication: Pediatric Hypertension (ages 6–16)

Notes: Preference given to sites with demonstrated pediatric hypertension experience, central or rapid local IRB approval ability, and access to an African-American population. Consideration will be given to sites that are committed to the study and have adequate experience with pediatric research.

Phase IV: *Still Seeking Investigators*

Boehringer Ingelheim Pharmaceuticals
Tashia Cruciani
900 Ridgebury Road
Ridgefield, CT 06877
Phone: (800) 344-4095, x 7785
Email: tcrucian@rdg.boehringer-ingelheim.com

Drug name: tenecteplase
Specialty: Interventional cardiologists
Indication: Myocardial infarction

CareStat
Erika Stone
180 Wells Avenue
Newton, MA 02459-3353
Phone: (617) 618-5144
Email: estone@carestat.com

Drug name: Not available
Specialty: Nephrology
Indication: Anemia with Chronic Kidney Disease
Notes: The ideal subjects for these studies are newly referred patients.

Genaissance Pharmaceuticals
Heidi Whalen
5 Science Park
New Haven, CT 06511
Email: h.whalen@genaissance.com

Drug name: Not available
Specialty: Psychiatry
Indication: Schizophrenia, Mood disorders
Notes: Looking for patients that have had clozapine-induced agranulocytosis anytime in the past. Will open sites that can enroll 1-2 patients that have had agranulocytosis.

Parexel International
Cathy Ford, Clinical Operations Assistant
Rose Tree Corporate Center
1400 N. Providence Rd., Suite 2000
Media, PA 19063
Phone: (610) 565-2622, x2153
Email: catherine.ford@parexel.com

Drug name: Not available
Specialty: Neurosurgeons, anesthesiologists, orthopedic surgeons
Indication: Patients undergoing elective spinal surgery with anticipated perioperative blood loss of two units

Opportunities Underway

Frequently, sponsors seek additional investigators once a trial is underway. This section provides investigative sites with a listing of large phase II through IV programs that have recently been initiated. Sites can use this information to track ongoing studies that may offer grant opportunities. **Please do not contact these companies as they are not actively seeking candidate sites.**

Indication	Sponsor	Drug/Device	Date Trials Initiated	Number of Sites Initiated	Expected Number of Evaluable Patients
Phase I					
cancer and other diseases	Exelixis	XL784	June 2003	Multi	70
Phase II					
Parkinson's/Alzheimer's disease	NeuroSearch/ Boehringer Ingelheim	NS2330	June 2003	Multi	900
Phase IIa					
excessive scarring	Procyon Biopharma	Fibrostat	June 2003	7	200
Phase IIb					
non-small cell lung cancer	Titan Pharmaceuticals	Pivanex plus docetaxel	August 2003	50	225
rheumatoid arthritis	Vertex Pharmaceuticals	pralnacasan	August 2003	Multi	400
Phase III					
traumatic brain injury	Pharmos	dexanabinol	August 2003	15	900
low-back pain	Pain Therapeutics	Oxytrex	August 2003	Multi	700
chronic heart failure	Vasogen	immune modulation therapy	August 2003	100	2,000

I would like to thank two pharmaceutical companies who recently contacted me to sign up for corporate-wide subscriptions to our monthly newsletter. One company had been distributing an electronic copy of our monthly newsletter to more than 85 readers—yet the company only had paid for one subscription. As many of you know, it is an infringement of federal copyright laws to make and disseminate paper and electronic copies of the *CenterWatch* newsletter or any of our publications. Ultimately, copyright infringement harms our ability to provide the level of coverage that you expect from our editorial and research staff. Contact me at (617) 856-5940 or kenneth.getz@centerwatch.com for information about our discounted and flexible corporate and multi-reader subscriptions. We also offer a program through the Copyright Clearance Center for those of you wishing to make copies of individual pages from our newsletters and books.

Traffic to the CenterWatch web site was very strong this past month. Approximately 1,000 active new trials were listed on the CenterWatch service bringing the total number of industry-sponsored trial listings to nearly 11,500. Through our many online affiliations and print distribution channels, clinical trials listed on the CenterWatch web service reached 969,000 unique visitors—the majority of whom were patients—last month. If you are interested in listing your clinical trials on our web service; wish to learn more about our FDAMA section 113 compliance assistance program for sponsors; or would like to feature your research center or CRO services on the profile page section of our web site, please contact Dan McDonald at (617) 856-5961 or daniel.mcdonald@centerwatch.com.

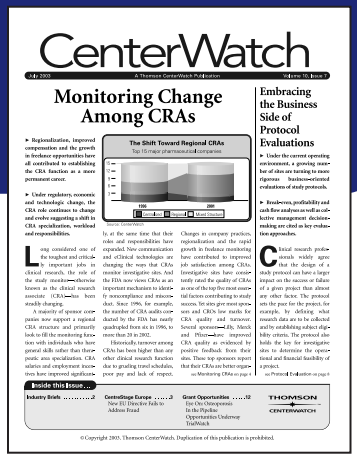
July was also a very active period for sales of our many CME- and CE-accredited publications. Academic institutions, in particular, have been busily preparing for their fall semester courses. Please contact Rick Lavallee at (617) 856-5224 to learn more about our accredited training manuals. Sales of our *2003 CenterWatch Directory of the Clinical Trials Industry* were also very strong as many organizations—CROs and investigative sites—are eager to find new contract and study grant leads during this challenging economic period. Please visit www.centerwatch.com for information, reviews and sample pages from our publications.

As always, we welcome your feedback on ways we can continue to provide useful and valuable clinical research information. Our very best wishes for a productive and relaxing rest-of-summer!

—Ken Getz

Coming Soon…

- **Investigative Sites Update Their Evaluations of CROs**
- **Eye On: Crohn's Disease**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