ARVO® News
The Association for Research in Vision and Ophthalmology
SUMMER/FALL 2011 SPECIAL ADVERTISING REPORT

Contract Research Organizations

From transactional to strategic partnering

In the 1980s, when a biotech or pharmaceutical company hired a contract research organization (CRO), it was on a project-by-project basis because internal resources were at full capacity, typical of outsourcing practices of the period. A decade later, this relationship took a different turn, as the pharmaceutical industry sought to balance climbing expenses, for research and development with the number of new drugs being submitted for approval.

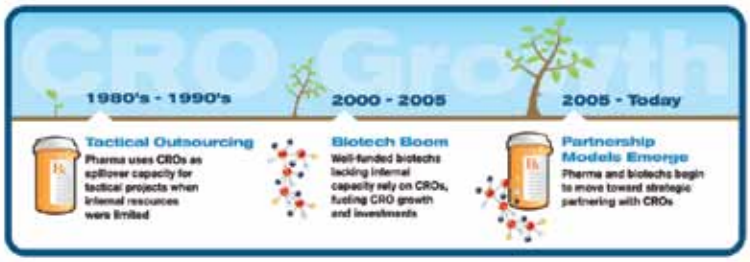
Based on a report by the U.S. States Government Accountability Office (GAO), from 1993 to 2004, R&D expenses increased from about $16 billion to about $40 billion — an increase of 147%. Over that same period, the number of drug applications for new molecular entities increased only 7%. Big pharma, biotech companies and academic institutions saw CROs as the solution and started turning over a larger number of noncritical studies to offsite experts to lower their costs.

Services now include:

- Product development
- Formulation and manufacturing
- Clinical trial management (preclinical through phase IV)
- Clinical, medical and safety monitoring
- Preclinical, toxicology and clinical laboratory services for processing trial samples
- Data management, biostatistics and biomedical writing services, especially in preparation for an FDA new drug application

"The strategic model creates deeper relationships on both sides, which results in better service,

See **Partnering,** page 3



Reprinted from "Strategic Outsourcing Partnerships: Innovative Solutions for Improving R&D Productivity in the Biopharmaceutical Industry," Covance 2009.

A case study in strategic partnering

Iris Pharma frequently acts as a development partner, actively collaborating with clients on varied drug and device development projects. In a recent example, the sponsor, a mid-size European pharma, requested Iris Pharma to develop novel gel-based formulations of anti-glaucomateous timolol.

Iris Pharma's direct responsibilities were the design and execution of the ocular pharmacokinetic, ocular tolerability and efficacy rabbit studies to support the identification of the optimal formulation. Iris Pharma study directors and management worked closely with the sponsor project leader and R&D senior management. In regular teleconferences and face-to-face meetings, both sides reviewed results and progress, and mapped out quarterly plans. In addition, to control costs and timelines, the CRO took on the development of a reliable snapshot test, presented in part in a poster at the 2009 ARVO Annual Meeting, to rapidly screen formulations at early stages of development, instead of conducting time-consuming full ocular pharmacokinetic studies.

Iris Pharma recommended a formulation for ocular GLP studies that the CRO conducted to enable a first-in-man study. The product is now marketed in Europe. ■

Partnering with academia

Academic-industry partnerships — encompassing large and small bio/pharmaceutical firms, academic research centers and CROs — are becoming increasingly vital as a model for drug development.

"Academic groups represent about 12% of our work, a fairly sizable chunk, and this includes groups from various countries."
—Paul Milne, IDDI

"Working with institutions and academic groups is important to Iris Pharma and is a growing part of our business. For instance, [we have] a close relationship with both preclinical and clinical scientists at the Institut de la Vision in Paris where Iris Pharma has an office.

"On one hand, it allows [us] to stay on top of the latest scientific and technological development in ophthalmology. On the other, Iris Pharma helps institutions and academic centers assemble drug development and business plans. Iris Pharma provides support in the selection of the indications and targets with the optimal chance of success. We particularly offer our institutional sponsors a drug development methodology and the tools that they usually do not have in house to demonstrate that their concept or early-stage product can become a drug or device."
— Philippe Margaron, Iris Pharma

Since 1989

EACH EYE HAS ITS IRIS

Specific focus on ophthalmology and highly skilled staff for your drug & medical device development

PRECLINICAL RESEARCH
CLINICAL TRIALS
BIOANALYSIS
PRECLINICAL FORMULATION
CONSULTING

www.iris-pharma.com

iris PHARMA

A GLOBAL SERVICE PROVIDER OF PRECLINICAL AND CLINICAL RESEARCH IN OPHTHALMOLOGY

Partnering, continued from page 1

consistent communication and stronger commitments," explains Mark Vezina, scientific director, ocular and neuroscience at Charles River. "Strategic relationships often have governance committees comprised of individuals from operations to the executive level, which ensures that programs stay on track."

By merging the wide range and depth of pre-clinical and clinical experience, a successful strategic alliance can bring a fresh perspective to the ophthalmic drug and medical device development process. "Scientists with the CRO become part of the client's team because there is more knowledge sharing, which creates a greater level of trust," adds Vezina.

The significant shift from transactional to strategic outsourcing by sponsors in the U.S. as well as global CRO markets sparked the latest movement toward preferred partnerships — with pharmaceutical companies agreeing to outsource services to select CROs for a fixed period of time. Drug company sponsors are benefitting from preferred CRO partnerships by gaining access to exclusive technology, expertise, guaranteed delivery timelines and preferential pricing.

"Preferred provider process is more specifically structured and used for outsourcing by big pharmas," says IDDI's chief executive officer, Damien Tremolet. "With the globalization approach, [the industry] used to favor full service CROs. We now see a trend of preferred provider agreements to niche companies focusing on specialized services with the aim for clinical trial sponsors to optimize drug development, reduce risk of failures and keep costs under control." ■

CROs and global growth

As drug and medical device developers have expanded their research presence substantially in the last decade, CROs are also expanding their global outsourcing to meet clients' needs.

"Research development in ophthalmology is much more globally connected between small and big companies than when our company was created in 1989," reports Pierre-Paul Elena, PhD, founder and CEO of France-based Iris Pharma. "We had only French clients and now we are working with the industry in almost all of the countries — China, Japan, Australia, Europe, Israel and countries in North America."

According to clinicaltrials.gov, approximately 53% of clinical trials are performed in the U.S. 24% in Europe and 23% in Asia, Latin America, Africa and Australia.

Damien Tremolet, chief executive officer of Belgim- based IDDI, explains that "as a high added-value niche partner to the biopharma industry, the U.S. market remains the first and leading market for IDDI with growing demands and business." As a result, decision centers for R&D are moving to the U.S., where it has had an office in Cambridge, Mass., since 2001 and in 2011 expanded to Houston, Texas.

While the U.S. continues to be the largest source of pharmaceutical research and development, emerging locations are increasingly providing opportunities for quality R&D. Frost & Sullivan, a leading growth-partnership company, reports the size of the global CRO market is estimated to reach $27 billion in 2011 with a compound annual growth rate (CAGR) of 15%, primarily driven by Asia and Easter Europe. Among the key drivers:

- Cost efficiency in lower cost countries
- A growing global biotechnology sector

Based on Frost & Sullivan reporting, the Chinese CRO market grew at a CAGR of 27.2% from $380 million in 2007 to $615 million in 2009, and is projected to grow at a CAGR of 20.7% to $1.3 billion in 2013 — outpacing the growth of the global industry. The Chinese pharmaceutical market is reported as one of the fastest growing in the world and is estimated to be the third largest by 2020.

In its "R&D Strategies Report 2007," Datamonitor reported India, along with China, as one of the most popular emerging countries for outsourcing CRO activity. After the U.S., India is home to the largest number of FDA approved plants. This trend is driven by easy access to the patient pool and diverse disease profiles in the patient population, government support and cost savings.

Compared to the West, the cost of carrying out clinical trials in China is 15% less for Phase I and 20% less for Phase II/III. In India, Phase I studies are estimated at 50% less and 60% less in Phase II and III studies, compared to the West.

While lower economic costs and a larger patient population are principal growth drivers, so too are the increasing breadth of R&D service offerings and a growing domestic pharmaceutical market.

"As an industry, we have shifted our focus from therapeutic areas that have proven medicines to targeting unmet medical need in very complex diseases," explains Mark Vezina, scientific director, Ocular and Neuroscience at Charles River. "The days of the "me too" drugs are gone. Today, we are seeing a focus on developing innovative, quality medicines."

Vezina points out that the growth of ocular therapy, a relatively new area compared to more established ones such as oncology or the central nervous system, is due to a vast unmet need.

"We are continuing to see clients outsource their discovery chemistry work to companies in Asia," reports Vezina. "There is evidence that companies in Asia want to demonstrate their ability to produce novel molecules via the bio-better route rather than being copiers of others' designs." ■

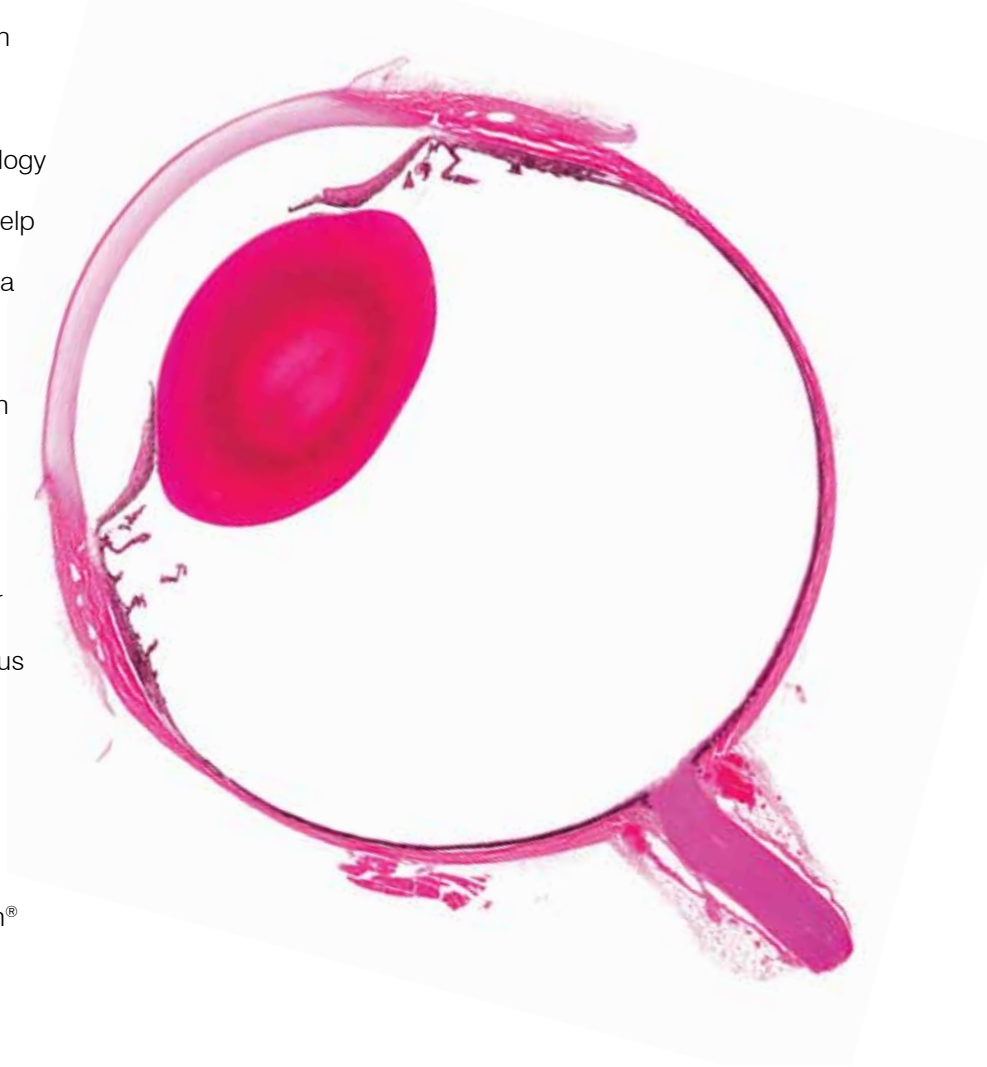
Frost & Sullivan report the size of the global CRO market is estimated to reach $27 billion in 2011 with a compound annual growth rate (CAGR) of 15%, primarily driven by significant growth in Asia and Eastern Europe.

Ocular Research and Toxicology

For almost 20 years, Charles River Preclinical Services has been conducting safety studies to support regulatory approval of ocular therapeutics as well as the evaluation of off-target ocular effects of compounds intended for other indications. We have experience with all classes of compounds and offer multiple species, dose routes and specialized technology and equipment. Our experienced team can help navigate regulatory expectations and design a study or program that fits your needs.

Our goal is to provide an integrated approach to ophthalmology research.

- ***In vitro* Ocular Irritation Assay**
- **Validated pharmacology/efficacy models**
- **Ocular biodistribution**
- **GLP ocular toxicology using state-of-the-art technology**
- **Customized ocular pathology evaluations**



For more information on all that Charles River has to offer, call is at 1.877.CRIVER.1 or visit us at www.criver.com.

Join our 'Ocular Research' group on LinkedIn® professional networking services.

charles river | preclinical services

1.877.CRIVER.1
www.criver.com

Directory of selected CROs

from among ARVO advertisers and exhibitors

Appletree AG
Theaterstrasse 29
P.O. Box CH - 8400
Winterthur,
SWITZERLAND
+41 52 209 06 40
Fax: +41 52 209 06 50
www.appletree-ag.ch

Biological Test Center
2525 McGaw Ave.
Irvine, CA 92614
949.660.2416
Fax: 949.660.3404
www.biologicaltestcenter.com

bioRASI
3440 Hollywood Blvd.
Hollywood, FL 33021
786.388.0700
Fax: 786.388.6044
www.biorasi.com

Calvert Laboratories Inc.
130 Discovery Dr.
Scott Township, PA
18447
570.586.2411
Fax: 570.586.3450
www.calvertlabs.com

Cayman Chemical Company
1180 E. Ellsworth Rd.
Ann Arbor, MI 48108
800.364.9897
Fax: 734.971.3420
www.caymanchem.com

Cetero Research
2000 Regency Pkwy.
Ste. 255
Cary, NC 27518
877.723.8376
Fax: 919.468.6850
www.cetero.com

Charles River
251 Ballardvale St.
Willmington, MA 01887
781.222.6000
Fax: 978.988.9236
www.criver.com
See ad in this insert

Comparative Biosciences Inc.
786 Lucerne Dr.
Sunnyvale, CA 94085
408.738.9260
Fax: 408.738.9278
www.compbio.com

Covance Inc.
3301 Kinsman Blvd.
Madison, WI 53704
888.541.7377
Fax: 608.335.9530
www.covance.com

IDDI
30 Avenue Provenciale
Ottignies-LLN 1340
BELGIUM
011.321.061.4444;
Fax: 011.321.061.8888
www.iddi.com
See ad in this insert

inGenious Targeting Laboratory
25 Health Sciences Dr.
Ste. 117
Stony Brook, NY 11790
631.444.6803;
Fax: 631.840.1044
http://genetargeting.com

Integral BioSystems LLC
2 Bonnievale Dr.
Bedford, MA 01730
781.879.4677
Fax: 781.275.9232
www.integralbiosystems.com

Iris Pharma
Allee Hector Pintus
La Gaude Alpes Maritimes
06610 FRANCE
33.493.594.959
Fax: 33.493.594.950
www.iris-pharma.com
See ad in this insert

JANIX
27101 Aliso Creek Rd.
Ste. 100
Aliso Viejo, CA 92656
949.251.9800
Fax: 949.252.7766
www.janix.com

MPI Research
54943 N. Main St.
Mattawan, MI 49071
269.668.3336
Fax: 269.668.4151
www.mpiresearch.com

Ocean Ridge Biosciences
10475 Riverside Dr.
Ste. 1
Palm Beach Gardens, FL
33410
561.427.7845
Fax: 561.740.8710
www.oceanridgebio.com

Oculos Clinical Research
400 N. Ashley Dr.
Ste. 1950
Tampa, FL 33602
855.777.2283 ext. 801
Fax: 855.777.2283
www.oculoscr.com

Ora Inc.
300 Brickstone Square
Andover, MA 01810
978.685.8900
Fax: 978.689.0020
www.oraclinical.com

Precision Vision Inc.
944 First St.
La Salle, IL 61301
815.223.2022
Fax: 815.223.2224
www.precision-vision.com

Preclinical Surgical Services
Medical Center Blvd.
Winston Salem, NC
27157
336.713.7399
Fax: 336.713.1404
www.preclinicalsurgical-services.com

Promedica International
3100 Bristol St.
Ste. 250
Costa Mesa, CA 92626
714.460.7363 ext. 11
Fax: 714.460.7364
www.promedica-intl.com

Statistics & Data Corp. (SDC)
21 E. 6th St.
Ste. 110
Tempe, AZ 85281
480.632.5468
Fax: 480.632.5469
www.sdcclinical.com

Toxikon Corporation
15 Wiggins Ave.
Bedford, MA 01730
781.275.3330
Fax: 781.271.1136
www.toxikon.com

TrialRunners
128 W. Villard
Dickinson, ND 58601
701.483.3558
Fax: 701.486.1556
www.trialrunners.com

Published by:

ARVO

The Association for Research in Vision and Ophthalmology
1801 Rockville Pike, Suite 400 | Rockville, MD 20852–5622 | **www.arvo.org**

Technology in the hands of the CRO

In recent years, the pharmaceutical and biotechnology industry has called for CROs to take a greater role in IT management, and industry analysts are projecting that IT decision-making will move away altogether from the sponsor into the care of the CRO.

CROs are already finding that more often, clients are looking to them as a service provider of data management solutions and are basing their decisions on the capability and robustness of the electronic systems chosen by the CRO.

This has become especially vital for the regulatory submission process. "There is an increasing need for regulatory statistical support, advanced statistical design, statistical validation of biomarkers for use in the clinic and cost-effective and integrated electronic data capture solutions," confirms IDDI CEO Damien Tremolet.

The competitive pressure to shorten the clinical trial cycle by collecting quality data more quickly and accelerating the availability of the data have led to the growth of electronic data capture (EDC) and other systems. As a result, CROs are playing a key role in providing solutions that are imperative for time-controlled data collection during many early-stage clinical studies.

"This is one of the most significant changes I've seen in the industry," says founder and CEO of Iris Pharma, Pierre-Paul Elena, PhD. "After designing a compound, clients want to know if the compound is active in humans. They want to be in the recruitment stage, onto Phase II as soon as possible; you have to have electronic data capture technologies set in place." ■

A case study in electronic data capture

A new ophthalmic drug entered a Phase I trial to assess its safety and tolerability in dry age-related macular degeneration. Per the sponsor's requirements, IDDI designed the paper CRF and set up its Oracle-based data management system to collect clinical data using a full proof double data entry process. As the collection of CRFs impacted heavily on the study logistics at site and delayed the data entry process while several patients were already enrolled, the sponsor challenged the data management team to switch the data collection process to electronic data capture.

Since IDDI's Data management suite allows a hybrid deployment (paper or EDC), the changes were limited to the enhancement of existing entry forms and edit checks for a user-friendly remote data entry process and the design of additional tracking reports. A date for stopping paper forms usage was defined. IDDI trained the sites and monitors and enabled the electronic data capture feature five weeks after the request, when all paper CRFs were collected.

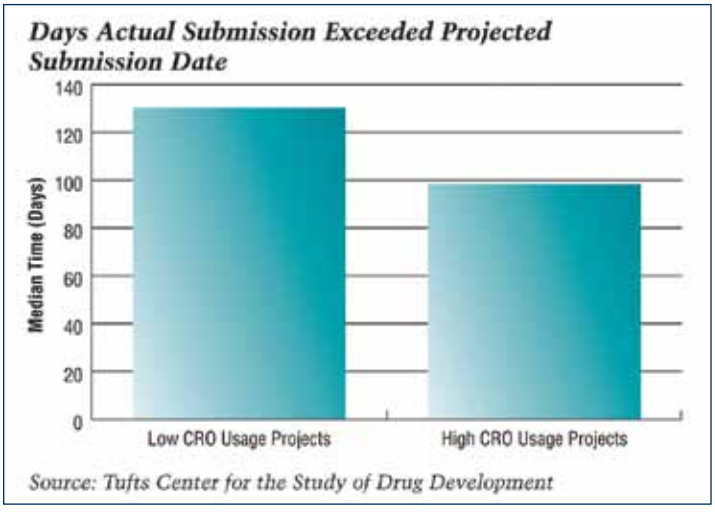
Client response: "Switching from paper CRFs to EDC not only significantly reduced the time taken to issue and respond to queries, it also allowed us to lock our database two weeks after the last patient visit. This would not have been possible with paper CRFs. IDDI made the process of switching from paper to electronic CRFs mid-study easy for us and easy for our sites." ■

CROs reduce development time at equal quality

According to an independent study by Tufts Center for the Study of Drug Development, clinical outsourcing results in faster development times at comparable quality. The study's key findings show that:

- According to sponsors, projects with high CRO usage stay closer to schedule: in general, high CRO usage projects are submitted more than 30 days closer to their projected submission date than are low CRO usage projects.
  - Median time from projected to actual submission date for low CRO usage projects was 130.5 days.
  - Median time for high CRO usage projects was 98.3 days. Although pivotal trials involving high CRO usage tend to be larger than those with low CRO usage, they are completed faster, especially during the study close-out period.
- While CRO usage is associated with faster development speed, performance quality is comparable between low and high CRO users.
- No statistically significant differences between low and high CRO usage were found when comparing time from new drug application submission to approval.
- There was no difference in investigative site compliance with good clinical practice guidelines between high and low CRO usage projects.

For the purpose of this study, low CRO usage is defined as drug sponsors spending less than 40% of their total clinical program budget on CRO services; high CRO usage is defined as drug sponsors spending more than 60% of their total budget on CRO services. ■



Source: Tufts Center for the Study of Drug Development