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CROs: Preclinical moves forward

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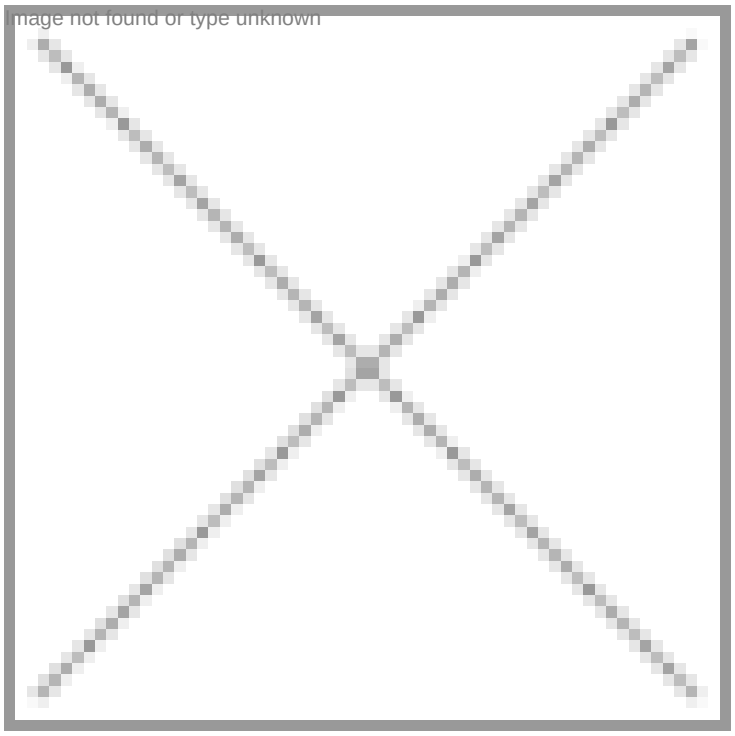

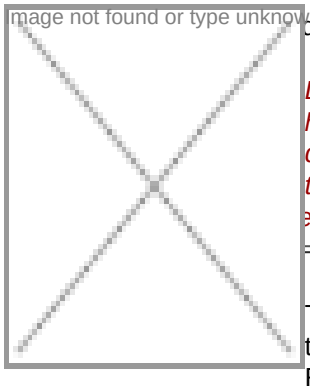

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The pharmaceutical industry is undergoing a significant change right from drug development, tightening of regulations, to restructuring, all in the midst of the economic downturn. The drop in the R&D spending in the last few financial quarters has not only taken a toll on the contract research organization (CRO) industry but also provided a unique opportunity.

The increasing costs and falling productivity, are driving pharmaceutical companies to outsource an increasing range of functions to CROs, in search of time and cost savings. This produced strong double-digit growth in the sector between 2003 and 2008. The global CRO market was estimated at 65,506 crore ($14 billion) in 2006 and it grew at an annual rate of 14-16 percent, to reach 112,326 crore ($24 billion) in 2010, and is expected to reach 163,865 crore ($35 billion) by 2015, according to Market Insights report.

Contract research is a relatively nascent service industry in India. Like all other service industries in its infancy, CRO industry also faces unique challenges, which when addressed, provides huge opportunities. In 1990s, India saw the development of

contract research. The Indian Patents (Amendment) Act of 2005 triggered the Indian pharmaceutical industry to invest in innovation, that led to the development of a local market for research personnel. The process of harmonization of research regulations led by the international conference on harmonization (ICH) since 1990, also provided an impetus for increase in the growth of research activities in the country. Contract research has been a product of this growth in research activities, that has led to the establishment of small and large drug development service companies in preclinical and clinical domains.

Genesis of preclinical CROs

Over a decade ago, global CROs were seen as service providers for pharmaceutical companies who generated routine data at the request of client companies, and did not contribute to the overall strategy of their drug development. This process underwent a critical change in the 1990s, when large global CROs were set up, and started attracting highly-qualified scientists. These, in-turn, led to the development of the CROs as center for scientific excellence in drug development.

The inflection point was when these CROs instead of conducting work for their clients, were also able to guide them through the entire drug development process. With this, the dynamics of interaction between CROs and pharmaceuticals changed in the recent times, from service providers to working partners. The CROs with good scientific profiles had gained massive experience and were able to capture the majority of the preclinical market.

Indian CROs currently find themselves in the same position as the global CROs were, about a decade ago. All trends suggest that the Indian CROs are in the phase of significant upward movement. As of today, partnerships with overseas companies have progressed beyond synthesis and solid dosage formulations. What began as project-by-project outsourcing, is giving way to long-term relations.

It is widely believed that Indian CROs will build a strong presence as the economic recession ends, since global companies will rethink aggressively towards cost-effective operations in R&D. Also, a substantial growth in the preclinical outsourcing market is predicted from 2011 onwards, due to the implementation of Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) legislation and ever tightening controls on chemical, fertilizers, cosmetics and food safety.

Further, the expectation that organization for economic cooperation and development (OECD) will soon approve the Indian GLP program, should provide the necessary impetus to preclinical services from India. These factors are expected to be the key drivers of the preclinical market for Indian CROs.

Preclinical outsourcing in chemistry.

The outsourcing of chemistry to India began in 1998, and has matured today with many of the large pharmaceutical companies working with CROs on an exclusive basis. The business models followed have included setting up of joint facilities and venture companies. The outsourced chemistry is expected to excee 19,678 crore ($4.2 billion) in fiscal 2009-10. The business is ready for the next stage, where larger revenues could come from more value-added services such as lead generation and hit-to-lead selection.

Preclinical outsourcing in biology

Preclinical outsourcing in biology is certainly at an exciting point where serious deliberations and focused actions will determine where the business will reach in the next few years. Until now the growth in biology has been relatively slower than in chemistry, as there has been a general perception that India is not competitive in the biology space. Some of these factors have come in the way of capturing significant foothold in he 23,430 crore ($5 billion) worth biological contract research market (Kalorama Information).

There has been a consistent effort from Indian biology-focused CROs in the last couple of years to change this perception and capture the untapped business. Indian CROs, in the last five to eight years, have made significant investments in infrastructure, technology and talent to attract business. The biology-focused CROs have expanded their services to include recombinant DNA/protein-based activities, focused screening of small molecules, and absorption, distribution, metabolism, excretion, and toxicity (ADMET) profiling of lead compounds.

Indian CROs are now gearing up for the challenge to establish themselves as providers of in vitro and in vivo preclinical development services. Preclinical services are being considered as the fastest growing outsourced segment of the drug development process. Estimates suggest that there is a gap of approximately 20-30 percent between demand and preclinical capacity globally, more so, in niche areas of genetic toxicology and in vitro alternatives. Preclinical biology outsourcing can be defined and distinguished at two different realms: traditional toxicology profiling and discovery research. Indian CROs have a successful history of providing toxicology support, and this is not expected to diminish in the near future. The second component – discovery research outsourcing – is where the CROs need to build a solid presence, to accommodate its highly flexible requirements. If CROs can deliver high quality data to its discovery customers, then the market will certainly expand

well beyond that for toxicology alone.

Challenges and opportunities

Within the next few years, preclinical services are likely to become a significant component outsourced to India. One of the key challenges will be to have state-of-the-art well-equipped facilities to develop and provide discovery services. Leading Indian CROs have, in recent years, invested in modern facilities that not only provide toxicological services, but also a range of services required for discovery, early and advanced preclinical development required for identification of candidate molecules for clinical development.

Sourcing and retaining of talented researchers is a key determinant for the efficient functioning of a biology-focused CRO. Identifying researchers who work with the discovery mindset, yet adapt to the needs of timely delivery of data, is a huge challenge. Development of specialists for key components in the discovery chain, like those for cell biology, pharmacology, DMPK and toxicology, is a prerequisite for effective operations. Efficient facility management where the CRO is nimble footed, intelligent and sensitive to respond quickly to the changing requirements of discovery-focused projects, are some of the essential requirements.

The animal experimentation is the cornerstone of the preclinical domain. Currently most of the animal facilities are confinedto rodent and dog. There is an urgent need to extend these to primates, but current government regulations do not encourage primate studies by the CROs as a service portfolio. At present, there are only a few animal facilities that have Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) accreditation.

The sourcing of healthy and genetically characterized animals is an absolute necessity for functioning of a CRO handling outsourced biology. Regulations on importing animals have been streamlined. Logistical issue of reaching out to multinational clients need to be addressed by innovative methodologies.

Preclinical research at DRF

Dabur Research Foundation (DRF) turned into a full-fledged contract research organization in the last couple of years, when it started offering services in the niche area of discovery and preclinical development.

The DRF has a young preclinical team which has prior experience of discovery, development and commercialization of its own molecules.

The DRF model hinges on developing and provides high-end services in cell biology and pharmacology, besides the complete battery of toxicology, absorption, distribution, metabolism, elimination, pharmacokinetics (ADME–PK) and analytical services. The services offered are designed to support discovery projects of global clients in several therapeutic areas inclusive of oncology, metabolic diseases, immunomodulation and dermatology.

DRF has built a Central Innovation Research Team (CIRT) which customizes and validates disease models required by clients for their specific projects. These models are transferred to study teams, to take the client projects rapidly through different milestones of their preclinical development. DRF has developed several unique cell biology in vitro- based efficacy models.

These enable critical decisions for clients in early stages of the projects in a cost and time-effective manner. It also has a wide range of in vivo efficacy models and unique toxicity models, for early assessment of clinical safety of molecules. DRF operates in pay-for-service as well as milestone payment models.

Global R&D, outsource and preclinical outsource spend

	Total R&D spend ($bn)	Outsource spend ($ bn)	Preclinical outsource spend ($ bn)
1992	n/a	1	n/a
2000	42	6	n/a
2001	45	7	n/a
2003	52	10	n/a
2005	63	13	2.5
2008	86*	18*	3*
2010	110*	24*	5*

*Source: Kalorama Information ; * – estimated; n/a – not available*