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CRO: Evolution and challenges

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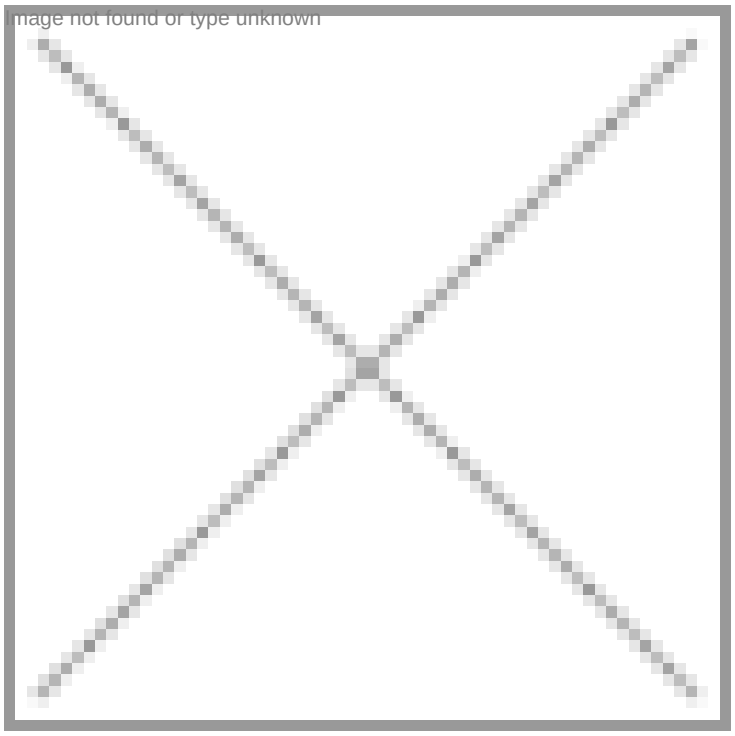

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, chairman and founder, Metropolis Healthcare, Maharashtra

Dr Sushil Shah is the chairman and founder of Metropolis Healthcare. He has served as the director on the board of Dr Reddy's Laboratories, Hyderabad; and as executive director of two of the group companies; Span Diagnostic and Zydus Cadila. His qualifications include a research fellowship from the Cornell Medical Center, New York, US; a MD in pathology; and he is also a guide to PhD students at Bombay University.

Most of today's major pharmaceutical companies with revenues in excess of ₹14,070 crore ($3 billion) and R&D expenditure in excess of ₹2,345 crore ($500 mn), were founded in the late 19th and early 20th centuries. These companies have further consolidated over the years, as a result of mergers and acquisitions between pharmaceutical and biotechnology industries of complementary capabilities. As these companies scan for new growth opportunities over the next decade, they find that some of the most promising areas are found in the world's emerging economies.

The clinical research industry, today, comprises of service providers catering to various needs of pharmaceutical clients. The basket of services offered include: clinical trial and site management, central laboratory, medical writing, data management and statistical analysis; these industries emerged mostly in the 1990s, due to stiff competition amongst manufacturers, to reduce drug development-to-market time in rapidly growing therapeutic areas. Industry analyzers such as IMS Health and BCC Research, estimate the global pharmaceutical market to be worth over ₹4,692,755 crore ($1 trillion) by 2013.

Status of emerging economies

McKinsey's India Pharma 2015 report estimates the Indian pharmaceutical market size at ₹93,853.40 crore ($20 billion) by 2015, as compared to ₹29,566 crore ($6.3 billion) in 2005. Major drivers of such enormous change encompass both economic and service factors. While McKinsey's analysis sees doubling disposable incomes, expansion of medical

infrastructure and greater penetration of health insurance, as reasons for the changing economic scenario, our exposure in the industry as a clinical research service provider, sees the increasing number of trained good clinical practice (GCP) sites, successful completion of US FDA audits, extensive use of English as the medium of communication, and good information technology infrastructure enabling electronic data capture (EDC) and telemedicine studies, as major service factors affecting the above growth.

According to US government's clinical trials registry, out of 93,860 registered clinical trials in the world, in August 2010,South Asian countries have 1566 registered trials â€“ with India alone accounting for 87 percent. Hence it has been predicted that countries like China, Taiwan, South Korea, Singapore, Thailand and India will play a crucial role in determining drug development to market time in the coming decade.

Clinical Research in India

India, in particular, is expected to play a crucial role according to McKinsey, due to the growing prevalence of lifestyle disorders similar to those in developed countries. Statistics reveal that the prevalence of diabetes in India will rise from 2.8 percent in 2005 to 3.7 percent in 2015, cardiac disorders from 3.3 to 4.9 percent, obesity from 1.3 to 2.7 percent, and the hypertensive population to hit five crore over the next decade. This projection correlates with Sanofi-Aventis' initiative to conduct a study, to ascertain the prevalence of diabetes and hypertension, titled 'SITE-Screening India's Twin Epidemics in 2009-10'.

Challenges ahead

With India rapidly acquiring center stage in the clinical research industry, service providers are faced with several challenges. A decade ago these challenges could broadly be classified as regulatory, educational and ethical.

Regulatory issues were mainly due to the lack of provision in drug laws for global studies, high import duty, no data exclusivity and long start-up times. These have been resolved to a certain extent by several initiatives by the Indian government, like not levying import duty on clinical trial supplies, allowing export of biological specimens, subject to protocol approval, abolishing the one-phase lag requirement in India for multi-national trials, and exempting CROs from service tax for trial-related activities. In addition to these, the Patent Act and IPR are also in place, though these still need to be streamlined as they will determine the future of patented products.

Educational challenges are due to the lack of familiarity of the medical community with the concept of clinical trials, absent or low GCP awareness, and limited access to IT infrastructure in medium and small healthcare set-ups. Today, India has its own GCP guidelines for clinical trials that have evolved on the lines of WHO, ICH, US FDA and European GCP. This, along with increasing involvement of private medical practitioners, acting as principal and co-principal investigators, have led to a drastic increase in the number of GCP-trained sites, at least in tier-1 cities, many of which have even successfully completed US FDA audits, with no major non-compliances.

Ethical concerns are mainly related to minimal number of institutional review boards (IRBs), with even fewer being US FDA-compliant, lack of SOPs and poor ICF processes. These too have been overcome today, with the establishment of GCP-compliant IRBs at major centers. However, as cited by the present industry experts' accreditation of ethics committees, training of regulators and EC members, scheduled regulatory inspections; and enhancement of the overall regulatory resource pool, are some areas that are yet to be addressed, and improved on.

If challenges a decade ago were process-related, today they are operations, analytical and revenue centric. These are the core areas that both service providers and policy-makers need to focus on, in the coming decade, to bring about an overall process improvement in clinical research.

Operational challenges are mainly related to site management, where delay in convening IRB meetings, multi-tasking site staff, and overambitious site feasibility response submitted to sponsors delay time lines, leading to huge revenue deficits. This, added to the high attrition of GCP-trained personnel at sites, make timely subject enrollment and site closeouts within predefined budgets, a huge challenge. The way in which these may be addressed are: by forming a consortium of clinical research service providers, regulatory policy-makers and the academia, to debate implementation of penalty clauses for delays at sites, define personnel, is to study ratios and drafting guidelines for verifying site feasibility response, based on past case records. Attrition can be dealt with by creating partnerships with academic institutions for supplying trained resources, and addressing the reasons for attrition, in detail.

Analytical issues have not received much coverage in clinical research forums till date, as these mainly involve central laboratory operations, which is still a niche area, having few service providers. Major concerns are sample logistics across tier-II cities, maintaining specimen integrity and turn around time of lab reports, such that they are well within protocol time lines. Steps have already been initiated towards process improvement with key central labs forming the Indian Association of

Pathology Laboratories (IAPL), that focus on working with regulatory bodies, to bring about legislation covering accuracy, patient care and safety in clinical diagnostics, collaboration with technical institutions to upgrade skilled manpower, harmonizing results, and reference ranges, in case of decentralized testing and benefiting from global outsourcing opportunities.

Revenue-related concerns are currently ambiguity in the service tax act which exempts CROs conducting clinical trials, approved by the Drug Controller General of India (DCGI), and routine diagnostic testing from service tax, but is yet to clarify the status of laboratory medicine services in the ambit of clinical research. This is one area that bodies like the IAPL need to address, in collaboration with our policy-makers.

Conclusion:
To sum it up, the Indian clinical research industry though fraught with challenges, has already overcome many of them, by making positive inroads into those yet to be addressed in the next decade. This pace can be maintained only by sustained collaborative efforts of the pharmaceutical industry, clinical research service providers, policy-makers and academia for as the English proverb goes-smooth sea never made a skilled mariner.

Dr Sushil Shah, chairman, Metropolis Labs, with inputs from Dr Shilpa Puthran