GLOBALIZATION: OUTSOURCING OPPORTUNITIES IN CLINICAL RESEARCH

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Presentation Overview

- Globalization of clinical trials
- Rapid pace of changes
- Clinical Trial Infrastructure in India
- Case studies
- Enablers & Challenges in the current scenario
- The way ahead
Figure 1 | **Density of actively recruiting clinical sites of biopharmaceutical clinical trials worldwide.** Density is in per country inhabitant (in millions; based on 2005 population censuses); darker orange/red denotes a higher density. The trial density and average relative annual growth rate in percent is shown for selected countries. The countries in grey had no actively recruiting biopharmaceutical clinical trial sites as of 12 April 2007.

**Emerging markets : Increasing clinical trial density**
India – a significant market for Phase II/III trials

- The number of industry-sponsored Phase II-III sites in India has grown by sizeable proportion based on the US trial register.
- India has moved from rank 18 to 12 across the 60 most active countries.
- India stands next to Japan in Asia in its number of industry-sponsored Phase II-III clinical trial study sites and accounts for nearly 20% of sites in Asia.

Rapid pace of changes
Large patient pool

Every Year, an estimated 1.15 Bn ailments are reported

[Graph showing percentage contribution of key diseases in total disease burden]

Note: Reported ailments here signifies commencement of new ailments
Source: WHO - 2007

Every Year, an estimated 30 Mn cases of hospitalization are reported

[Graph showing percentage contribution of key diseases in hospitalization cases]

Source: Morbidity, Healthcare and condition of the aged NSSO 60th Round
*Febrile illnesses include malaria, diphtheria etc.; **Others include disabilities, skin and oral diseases, Sexually Transmitted Diseases etc
India’s disease burden and patient mix corresponds to the therapy areas for which global trials are being conducted.

Chronic diseases are expected to grow at a faster rate as compared to acute ailments in alignment with R&D portfolio of large pharma companies.

Total R&D expenditure in 2007 by therapeutic area:

- **Oncology**: 16%
- **Nervous system**: 14%
- **Musculoskeletal**: 7%
- **Respiratory**: 11%
- **Other**: 24%

India has one of the fastest subject recruitment rates globally:

- **Comparison with global averages**
  - Average recruitment rate: Nearly three to five times higher
  - Screen failure and drop out rates: Lower by nearly 40–50%
  - Patient contribution for a global multi-centric study: 15–30%
Public & private medical infrastructure - large pool of potential clinical research sites

Over last six decades India has added significant physical infrastructure and human resources for healthcare...

Currently India has over
- 42,000 Private Hospitals
- 9,000 Government Hospitals
- 9,42,000 Hospital Beds
- 14,000 Diagnostic Labs
- 250 medical colleges
- 6,00,000 English speaking physicians

Source: Fostering Quality Healthcare for All – EY FICCI HEAL 2008
Rapid changing in trial geography

The healthcare infrastructure is largely concentrated in urban areas which is the key catchment area for subject recruitment.

Healthcare distribution across Rural and Urban

- Bangalore, Mumbai, Hyderabad, Chennai, New Delhi, Pune and Ahmedabad have the highest concentration of sites in India.

Companies are beginning to move into Tier 2 cities and towns to access a larger group of patients.

- Trials are increasingly being carried out in towns such as Jaipur, Nagpur, Lucknow, Thiruvananthapuram, Coimbatore, Cochin, Vellore, Ludhiana, Madurai, Vishakhapatnam, Mangalore, etc…
Overall costs competitive compared to developed markets

Significant cost advantage in manpower cost, rental cost, IT cost and operational cost, over most developed nations like the US and most of the European countries.

**Overall Indexed Clinical Trial Costs**

<table>
<thead>
<tr>
<th>Country</th>
<th>Overall Indexed Clinical trial costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>India</td>
<td>0.56</td>
</tr>
<tr>
<td>China</td>
<td>0.52</td>
</tr>
<tr>
<td>Russia</td>
<td>0.4</td>
</tr>
<tr>
<td>Australia</td>
<td>0.73</td>
</tr>
<tr>
<td>US</td>
<td>1</td>
</tr>
<tr>
<td>Spain</td>
<td>0.93</td>
</tr>
<tr>
<td>Germany</td>
<td>1.2</td>
</tr>
<tr>
<td>France</td>
<td>0.71</td>
</tr>
<tr>
<td>UK</td>
<td>1.09</td>
</tr>
<tr>
<td>Poland</td>
<td>0.77</td>
</tr>
</tbody>
</table>

Hourly rate comparison in India & other developed economies

<table>
<thead>
<tr>
<th>USD / Hr</th>
<th>India</th>
<th>US</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRA</td>
<td>40-55</td>
<td>120-150</td>
</tr>
<tr>
<td>Project Manager</td>
<td>50-60</td>
<td>160-180</td>
</tr>
</tbody>
</table>

Source: Industry analysis

Charge-out rate (USD/hr)

<table>
<thead>
<tr>
<th>Job Position</th>
<th>India</th>
<th>Developed economies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Data Entry operator</td>
<td>10-20</td>
<td>30-50</td>
</tr>
<tr>
<td>Bio-Statistician</td>
<td>30-70</td>
<td>100-150</td>
</tr>
<tr>
<td>Pharmacovigilance professional</td>
<td>50-100</td>
<td>140-250</td>
</tr>
</tbody>
</table>

Note: The charge-out rate may also vary based on the qualification and experience of the employee hired for the job.

However, investigator grants, site and ethics committee fees, etc have been gradually increasing over the past few years (especially for experienced sites).
Significant evolution of the regulatory processes in the last few years

Government of India envisions the country’s transformation into a Pharma innovation hub by 2020

► Multi-billion dollar initiative with 50% public funding through a public private partnership model
► Focus on building infrastructure for talent and research and offering financial incentives to encourage and incubate innovation

Steps to improve quality of governance and oversight for clinical trials
► Registration and regular audit of CROs in India
► Registration of trials with the Drugs Controller-General of India (DCGI) mandatory from June 2009
► Potential 10-year imprisonment for violation of ethics or norms in clinical trials

Clinical proposal review timelines by Indian regulators are on the decline and expected to further reduce...

Source: Clinical Trials – New Horizon India, DCGI Presentation, March 2009
### US FDA – NDA
*(Data generated from India)*

<table>
<thead>
<tr>
<th>Drug Company</th>
<th>Molecules / Brands researched</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcon</td>
<td>Vegamox</td>
</tr>
<tr>
<td>AstraZeneca</td>
<td>Meropenem</td>
</tr>
<tr>
<td>Cangene</td>
<td>Hepatitis B Vaccine</td>
</tr>
<tr>
<td>Eli Lilly</td>
<td>Alimta, Gemcitabine</td>
</tr>
<tr>
<td>Glaxo</td>
<td>Lamotrigine</td>
</tr>
<tr>
<td>Janssen</td>
<td>Resperidal</td>
</tr>
<tr>
<td>Novartis</td>
<td>Tegaserod</td>
</tr>
<tr>
<td>Pfizer</td>
<td>Voriconazole</td>
</tr>
<tr>
<td>Roche</td>
<td>PEG-Interferon</td>
</tr>
<tr>
<td>Santen</td>
<td>Quixin</td>
</tr>
<tr>
<td>Wyeth</td>
<td>Influenza A Vaccine</td>
</tr>
</tbody>
</table>

Reference: CDSCO, Mckisney 2008
Exponential increase in Pharma & CROs promoting clinical research

- **Pharma/ Biotech**
  - Eli Lilly & Pfizer (1995)
  - SmithKline Beecham (1998)
  - Aventis (2002)
  - Merck (2005)
  - GSK (2005)
  - Small Biotech companies & Mid Size Pharma (2006)
  - Biogen (2007)
  - Amgen (2007)

- **CROs**
  - DiagnoSearch (1996)
  - Siro Clinpharm (1996)
  - Quintiles (1997)
  - ICON (2000)
  - Neeman (2001)
  - Omnicare (2001)
  - PharmOlam (2003)
  - Reliance (2004)
  - Veeda (2004)
  - Pharmanet (2005)
  - PPD (2005)
  - GVK (late Phase) (2005)
  - Kendle (2005)
  - Parexel (2005)
  - CliniRx (2006)
  - Semler Research centre (2006)

- **Early Movers**
  - 1993
  - CROs

- **Wait and Watch Players**
  - 2005

- **New Entrants**
  - 2009

- **Over 50 CROs present in different regions in India**
- **Primary locations**: Bangalore, Hyderabad, Mumbai, Delhi, Ahmedabad
The Clinical Research Infrastructure
Clinical Research: Service Infrastructure

Sponsors
- Pfizer
- Eli Lilly
- Novartis
- GSK
- AZ

SMOs*
- Max Neeman
- Excel
- Lifesciences
- SMO-India...

Laboratories
- Covance Labs
- Icon Labs
- Metropolis
- SRL
- Quest

Couriers
- World Courier
- DHL
- TNT
- Blue Dart

*Site Management Organization

Clinical Operations
Central Lab Analysis
Pharmacovigilance

Full service providers
Global CROs
- Quintiles
- Icon
- Parexel
- Parexel
- Clinitec
- PPD

Indian CROs
- Siro Clumpharm
- Diagnosearch
- Semler R C
- Veeda CR
- Clinigene

IT / ITES
- Cognizant
- Accenture
- TCS
- Wipro

Niche service providers
- Sciformix
- Symogen
- Indegene
- Sristek

IT Vendors
- Oracle
- PhaseForward
- Argus
- Forte

Other niche services such as cardiac safety testing, imaging, patient recruitment, etc not depicted above

E&Y, 2009
Case Study of a Major Multinational Phase III study
Case Study of a Major Multinational Phase III study
Case Study of a Major Multinational Phase study
Case Study of a Major Multinational Phase study
Enablers & Challenges of the clinical trial ecosystem
Rapidly evolving clinical trial eco-system

- Big Pharma - e.g. Pfizer, GSK, Eli Lilly, Novartis, Sanofi Aventis, Bayer, J&J, etc
- Global CROs with direct and indirect presence
- Indian CROs steadily globalizing reach and scale

- Over 2299 industry-sponsored Phase II-III clinical trial study sites (registered with the US trial register)
- Over 1500 trained investigators (based on 1572s filed with USFDA)
- Trials conducted as per the ‘Ethical Guidelines for Biomedical Research on Human Participants’ issued by ICMR* in 2006
- Regulators increasing focus on training & oversight of ECs

- Twenty CAP-certified central laboratories including international players providing esoteric services
- Entry of international SMOs
- Increasing sponsor interest

- CROs & sponsors
- GCP-compliant sites
- Central labs
- Site management organizations (SMOs)
- Ethics committees (ECs)
- Human resource expertise

*Indian Council of Medical Research
Key Enablers

- Patient pool
- Institutional infrastructure & Investigator resources
- Regulatory/EC
- Other support services (IT, Travel connectivity, Logistics, Courier)
- Public awareness
- Formal – Clinical Research education
- Support from Govt. bodies (funding & active participation)
Challenges

✓ Regulatory: Review Timelines

✓ Institutions: Institutions participating in clinical research – smaller in percentage. 
  Overcrowding of experienced sites

✓ EC: Limited governance mechanism on work processes and compliance of ECs

✓ Medical documentation: Variation in standards of source documentation practices

✓ Lab accreditations: Local labs associated with hospitals non accredited – necessitating involvement of central labs

✓ Training: Variations in degree of training (especially at sites)

✓ Manpower: Availability & retention of manpower

✓ Cost escalation: pricing pressure
Creation of a world class clinical research environment – The way ahead
Creating world class clinical research

- Drug development costs & timelines – key challenges (patient enrollment – rate limiting)
- Accelerated regulatory processes – single window clearance
- Institutions – develop centers of excellence
- Integrated management models – combining creative study approaches, training methodology & technology to address issues related to study planning, site productivity
- End to end approach
- Capacity expansion – infrastructure, human resources
- Evolution of metrics to define and understand improvement parameters at organizational & site levels
- High compliance (inspections and oversight)