Clinical Trials
New Horizon – India

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“So far as I am able to judge, nothing has been left undone, either by man or nature, to make India extraordinary country that the sun visits on his rounds. Nothing seems to have been forgotten, nothing overlooked”.

Mark Twain, from following the Equator
The journey towards becoming an attractive new destination for clinical research


- 61 Companies
- 100 CROs
- 80 Hospitals
- 150 Investigators registered with US FDA
Overall Country attractiveness index: India 2nd most preferred destination

Notes: Higher scores indicate higher levels of attractiveness.
The 15 countries analyzed were selected based on size, diversity & geographical distribution.

Higher scores indicate higher levels of attractiveness.
PRIORITIES

* Establish Single Window clearance for approvals
* Fix timelines for each application (2-6 Weeks)
* New Drug application status on the web - Update fortnightly
* Subject Experts-reviewers - Internal / External
* Staff & Infrastructure at one site
* Training
Clinical Trials in India

“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.”

CenterWatch (Aug 2003)

“India’s business and regulatory climates have undergone dramatic change in the past 18 months through passage of a patent bill, regulations updated to harmonize with TRIPs and international standards, and plans for a more US FDA-like regulatory body.”

CenterWatch (July 2007)
## Indian Clinical Research Market

* The Indian pharmaceutical industry is growing at an annual rate of 11% while the clinical research industry is growing at an annual rate of whopping 84%.

* McKinsey estimated that clinical research in the country would be a $1bn ($1000m or €800,000m) industry by 2010 whereas Ernest & Young indicates around $1.5-2 billion by 2010.

* **Market value for clinical trials outsourced to India is estimated at around $300 million, having increased by 65% in 2006, it is expected to touch $1.5-2 billion by 2010. By 2010, the industry will spend USD 300M+ on clinical trials in India**

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* *Goldman Sachs, Centre watch, Goldman Sachs and McKinsey (2008)*

Growth of Indian Clinical Trial Industry

As per FICCI - Ernst & Young Survey Report 2008, India can attract between 5 - 10% of the global contract research outsourced market (all services including chemistry, toxicology and clinical research) over next 5 years.
Clinical Trials from India
(www.clinicaltrials.gov; 15 Apr08)

<table>
<thead>
<tr>
<th>Phase of trial</th>
<th>No. Trials (Log transformed)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>India</td>
</tr>
<tr>
<td>Phase-1</td>
<td>32</td>
</tr>
<tr>
<td>Phase-2</td>
<td>165</td>
</tr>
<tr>
<td>Phase-3</td>
<td>394</td>
</tr>
<tr>
<td>Phase-4</td>
<td>63</td>
</tr>
</tbody>
</table>

Phase-1 Phase-2 Phase-3 Phase-4
## CLINICAL TRIAL ACTIVITIES IN ASIA
### ALL STUDIES

Countries with more than 100 studies listed

<table>
<thead>
<tr>
<th>Country</th>
<th>All Studies</th>
<th>% Industry Sponsored</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td>1572</td>
<td>62.72</td>
</tr>
<tr>
<td>Chinese Taipei</td>
<td>903</td>
<td>45.29</td>
</tr>
<tr>
<td>Japan</td>
<td>732</td>
<td>67.76</td>
</tr>
<tr>
<td>Korea</td>
<td>674</td>
<td>72.26</td>
</tr>
<tr>
<td>China</td>
<td>643</td>
<td>53.50</td>
</tr>
<tr>
<td><strong>India</strong></td>
<td><strong>582</strong></td>
<td><strong>72.16</strong></td>
</tr>
<tr>
<td>Singapore</td>
<td>335</td>
<td>68.36</td>
</tr>
<tr>
<td>Thailand</td>
<td>327</td>
<td>69.42</td>
</tr>
<tr>
<td>Chinese Hong Kong</td>
<td>250</td>
<td>82.00</td>
</tr>
<tr>
<td>Philippines</td>
<td>206</td>
<td>93.20</td>
</tr>
<tr>
<td>Malaysia</td>
<td>180</td>
<td>93.33</td>
</tr>
</tbody>
</table>
India : Resource advantages

- Large No. of specialists in different therapy segments
- Medical Training In English
- 600,000 Eng. Speaking physicians
- PG training from Europe/US
- Treatment Protocols in line with West
- Large no. of ICH/GCP compliant Investigators / sites

- Large, Diverse, therapy-naïve
- Advantage of having 6 out of 7 genetic varieties
- Large pt. pool in acute/chronic disease segment
- Increasing no. of pts in life style disorders segment, HIV, Oncology
India: Resource advantages

- Over 200 Medical Colleges
- Over 22,000 graduates per year
- 15,622 hosp., 903,952 hosp. beds >75% in urban area
- 14000 diagnostic labs
- 700,000 scientists and engineering graduates / year
- World class medical / lab facilities at secondary / tertiary care centers
- Skilled computer savvy biomedical work force

Clin. Res. Infrastructure

- Highly developed IT / ITES
- Motivated & committed personnel

IT Support

- High quality digital connectivity
- Excellent air/surface transport facilities across country

Connectivity
In conclusion…

<table>
<thead>
<tr>
<th>Patient pool</th>
<th>Scanty</th>
<th>Large</th>
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</thead>
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<tr>
<td></td>
<td></td>
<td>India</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Patient Recruitment rate</th>
<th>Lowest rate</th>
<th>Highest rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>India</td>
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<table>
<thead>
<tr>
<th>Speed</th>
<th>Low</th>
<th>High</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td>India</td>
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</table>

<table>
<thead>
<tr>
<th>Cost</th>
<th>Most expensive</th>
<th>Least expensive</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>India</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Facility &amp; Investigator pool</th>
<th>Smallest pool</th>
<th>Highest pool</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>India</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Industry trial experience</th>
<th>Least experience</th>
<th>Most experience</th>
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<tbody>
<tr>
<td></td>
<td>India</td>
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</table>

<table>
<thead>
<tr>
<th>Regulatory Environment</th>
<th>Least Conducive</th>
<th>Most Conducive</th>
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<tbody>
<tr>
<td></td>
<td>India</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Quality of data</th>
<th>Unacceptable to EU/US</th>
<th>Acceptable to EU/US</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>India</td>
<td></td>
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</tbody>
</table>
**US FDA NEW DRUGS APPLICATION 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>Merenem</td>
</tr>
<tr>
<td>Cangene</td>
<td>Hepatitis B Vaccine</td>
</tr>
<tr>
<td>Eli Lilly</td>
<td>Alimta, Gemcitabine</td>
</tr>
<tr>
<td>Galaxo</td>
<td>Lamotrigine</td>
</tr>
<tr>
<td>Jannsen</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>
Government’s facilitating initiatives
Fiscal Incentives

- No import duty on clinical trial supplies (2003)
- Exemption from registration requirements for clinical trial supplies (2003)
- Export of clinical trial related biological specimens allowed, based on protocol approval (2005)
- Exemption from Service Tax on new Drug testing (2007)
# Timelines for Regulatory Approvals

<table>
<thead>
<tr>
<th>Agency / Institutions</th>
<th>Approval</th>
<th>Time</th>
</tr>
</thead>
</table>
| Drugs Controller General of India (DCGI) | Regulatory approval for study conduct in India | • Category A trial is approved using a fast-track process within 6 weeks after the required documentation  
  • Category B within 8 to 12 weeks |
| Drugs Controller General of India (DCGI) | Test license to import trial supplies | 2 weeks in addition |
| Ethics Committees (Independent body) | Local Ethics committee approval by sites | 6 – 8 weeks (in parallel) |
| | | Total (parallel processing)  
  6-8 weeks – FAST TRACK (Category A)  
  16 weeks (Category B) |
| Directorate General of Foreign Trade (DGFT) | Permission to export Biological samples | Additional 2 to 4 weeks |
Clinical Proposal Review

Timelines

- Multinational trials
- Local Trials
- Query resolution

YEARS

DAYS

2000-06 2006-07 2008 2009-10
# Global Clinical Trials Permitted

<table>
<thead>
<tr>
<th>YEAR</th>
<th>No. of Trials</th>
</tr>
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<tbody>
<tr>
<td>2003</td>
<td>30</td>
</tr>
<tr>
<td>2004</td>
<td>50</td>
</tr>
<tr>
<td>2005</td>
<td>100</td>
</tr>
<tr>
<td>2006</td>
<td>143</td>
</tr>
<tr>
<td>2007</td>
<td>264</td>
</tr>
<tr>
<td>2008 (upto August)</td>
<td>115</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>702</strong></td>
</tr>
</tbody>
</table>
2 meetings of Phase I and Phase 0 (Micro dosing) have been organized on July 16, 2008 and August 12, 2008

Representatives who attended were:

- Academia
- CRO Representatives
- Clinicians
- Pharmacologists
- Social Groups
- NGO’s
- Lawyers Group
- Medicines Sans Frontiers Representatives
MICRO DOSING - ISSUES

* Analysis of molecule by LC MS, Radio Labeling
* Monitoring of clinical trials
* CT registry
* Insurance Coverage
* Fingerprinting of the volunteers
* Sharing of data between various centers
REGISTRATION OF CRO’S

Framing of Guidelines

- A group constituted to lay down requirements standards for approving CROs
- The group will consist of CDSCO officials, industry representatives academicians and experts
- Requirement of approval of CROs will be prepared after consulting internationals guidelines and documents.
- A draft of such requirements will be made public to receive comments
- Final guidelines will be prepared for implementation
GOALS FOR CLINICAL TRIALS REGULATION

Short Term Goals
Year - 2008

* Guidelines for Registration of CROs
* Training for Clinical Trials site inspections
* Robust review process for clinical trial proposals
* Meeting timelines
* Revision of regulatory requirements pertaining to clinical research
Medium Term Goals
Year - 2009

* Registration of CROs
* Inspection of Clinical trial sites in the country and overseas
* Guidelines for Registration of Ethics Committees/IRBs
* Mandatory registration of clinical trials in centralized clinical trial registry
Long Term Goals
Year 2010 - 2015

* Ensuring penal provisions for fraud & misconduct in clinical research

* Allow Phase 0 (micro dosing) studies and phase 1 studies in the country in controlled manner
INTERNATIONAL COLLABORATIONS

- WHO
- USA FDA
- Health Canada
- ANVISA, Brazil
- South Africa
TRAINING

With USFDA:

- Training on GCP and clinical Research Inspection
- workshop on clinical trial oversight for vaccines
- advanced workshop on GCP / Clinical Research Inspection
- workshop on Pharmacovigilance
- workshop on medical devices
- 1 Technical Officer was nominated for training in medical devices at USFDA
- 1 ADC and 1 Technical officer nominated for training at CDER and CBER (USFDA)
With WHO & Health Canada

* 3 ADCs sent for on the job training to WHO headquarters at Geneva and Health Canada, Ottawa
* Training on harmonization of Form 44, with CTD format besides preparation of SOPs, checklist and guidance documents
* Workshop on Vaccines clinical trial oversight / inspections
India: Your Gateway to Clin. Res. and R&D
E-GOVERNANCE-DRUG REGULATORY SYSTEM

* LAN / WAN connectivity of CDSCO campus
* Online submission of all the forms
* Digitalized interactive portal
* Digitalization of records
* Online approvals with Digital signature
* Inbuilt feature would administer spontaneous and random
* Checks to ensure quality ethical standards.

Vision : Paperless CDSCO office
“Let us not follow a path set by others
Let us set a path for others to follow”