

TRADE DEVELOPMENT AUTHORITY OF PAKISTAN

Clinical Research Management in Pakistan

Prepared by the TDAP- WTO CELL

2008

ACKNOWLEDGEMENTS

This report summarizes the activities undertaken by the Trade Development Authority of Pakistan, Ministry of Health and Jinnah Postgraduate Medical Centre, Karachi, for promoting Clinical Research Business in Pakistan. In its second part it provides suggestions, opinions, strategy and a model for promotion and growth of this business in the country.

During all this process and in the preparation of this report we received great support from some kind people.

We are grateful to Mr. Tariq Ikram, Minister of State & Chief Executive, TDAP, for his complete support during all this process.

We are also thankful to Mr. Naved Arif, Secretary TDAP, for his continuous support in all administrative matters throughout the process. The DG Administration, TDAP, Mr. Shahid Latif made the events, meetings and all other related activities possible, by taking personal interest in these activities. Mr. Muhammad Farooq, AD Admn. and Syed Masood Ahmed Zaidi assistant to the AD Admn. were also very helpful in all the administrative matters.

We also feel obliged to thank Prof. Dr. Rashid Jooma, ED JPMC, Karachi, for his energetic and enthusiastic efforts, to make all this come true.

Mr. Tariq Wajid, GM & MD, Sanofi-Aventis Pakistan, Mr. Khurram Zaki Khan, and his team from Metrics Research, Dr. Ghulam Murtaza Qasuri, Director Medical, Eli Lilly Pakistan, Dr. Amanullah Khan Medical Director, Sanofi-Aventis Pakistan, Dr. Yousuf Hasan Khan, CEO IRD, and Dr. Asim Awan, GM Medical Affairs, Clinision, also supported us in making the events successful.

Author's Credentials

Abdul Aleem Khan, Economist, Advisory Unit, WTO Cell, TDAP, an MBA- Finance from Institute of Business Administration (IBA), Karachi, and MS-Economics from SZABIST, Karachi, has 4 years research experience with organizations like TDAP, Social Policy and Development Centre (SPDC), and Asiatic Advertising. He also has 4 years experience of teaching Economy of Pakistan, Micro & Macro Economics, and Financial Management to MBA, BBA, and M.Sc. classes. Mr. Khan has also served as a sales manager for two years in a local manufacturing concern.

Mr. Khan has received training from WTO trainers in Islamabad and ITC trainers in Karachi.

He has delivered lectures to grade 17 & 18 officers at Directorate of Training (Income Tax), Government of Pakistan. He has been invited by the Sindh Education Foundation, Government of Sindh as an external interviewer to assess the candidates of finance related jobs.

Mr. Khan has produced three research papers (two refereed). He has also written various newspaper articles for well-reputed English newspapers. He has worked for many reports on Pakistan's economy produced by SPDC.

State Bank of Pakistan and a well-reputed English newspaper have cited Mr. Khan's research work.

Mr. Khan has appeared in many TV programs to give his opinions, views, and suggestions on the economic policies. His email address is aleem@tdap.gov.pk.

PART I
**REVIEW OF CLINICAL
RESEARCH SEMINAR**

1. THE CLINICAL RESEARCH BUSINESS AND PAKISTAN'S PLACE

Clinical Research also called Clinical Investigation, is the business of testing new drugs/ compounds in human subjects for discovering potential beneficial effects and/or determine its safety and efficacy¹. This business is now increasingly being outsourced by the multinational pharmaceutical industry. The business which was estimated to be a US\$5-6 billion market in 2002, reached around \$10 billion by the end of 2005 and is now estimated to have reached the volume of U.S \$ 60 billion with Asian and Eastern European Contract Research Organisations (CROs) often being the destination of a business expected to reach volumes of \$ 20 billion by 2010.

United States is the leading country in the field of Clinical Research. According to a 2003 study by Connecticut-based Business Communications Co (BCC), US-based spending on clinical trials is growing at 12% per year - and should generate \$26.5 billion by 2007. The reason the business is growing so rapidly is that the pharmaceutical industry is required by government regulations to conduct human trials before marketing new drugs.²

The 2006 report³ by BCC states that the US spending on clinical trials was nearly \$24 billion in 2005. By 2006 this number will rise to \$25.6 billion and then \$32.1 billion in 2011. In 2005, biotechnology and pharmaceutical companies spent approximately \$51 billion on research and development efforts, with \$21 billion (41%) spent on clinical trials. In comparison, government contributions to clinical trials were considerably smaller. The National Institutes of Health spent \$2.9 billion on clinical trials in 2005 and budgeted \$3.0 billion for 2006. Total funding for 2005 was \$24.4 billion. In 2006 this number rose to around \$26 billion and in 2011 it is expected to reach \$32.6 billion. The number of clinical trials performed in 2005 was 8,386. BCC research predicts that this number will reach almost 13,000 by 2011.

Pakistan is the 6th most populous country in the world with its population of around 160 million people. Being a developing country, the patients' population in Pakistan is also very large. 141, 229 cancer patients were reported in 2004 and around 8 million people are diabetic. There are 12,454 hospitals/institutions, 97,945 beds, 96,248 doctors, 4,622 dentists, and 40,019 nurses in Pakistan.

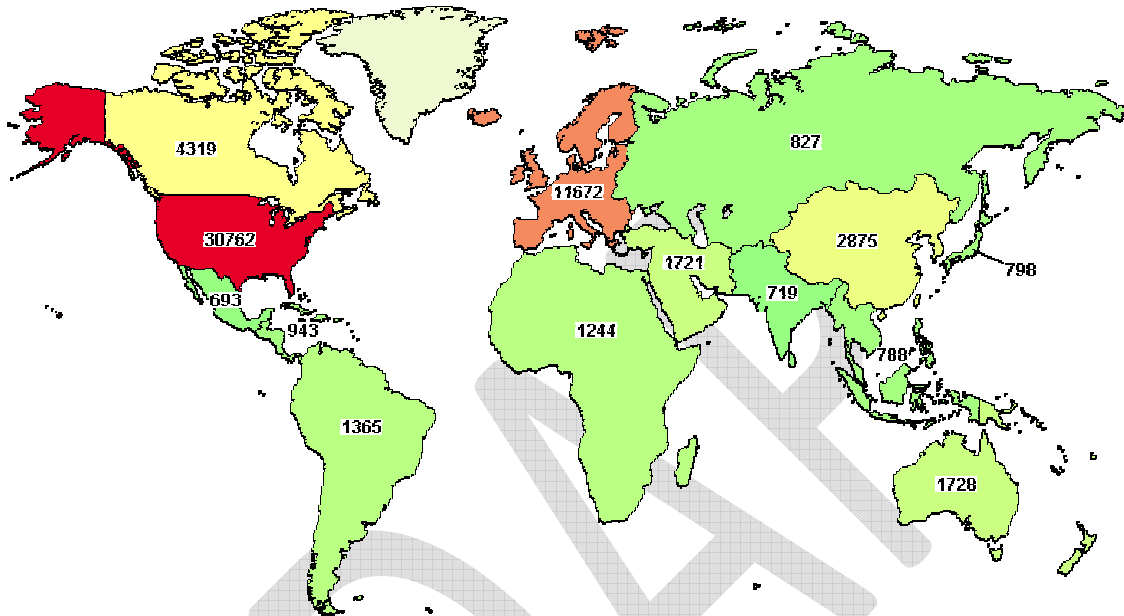
While its neighbour, India, with around 100 government and privately owned Indian hospitals engaged in global and local clinical trials, is increasingly emerging as a preferred destination for the outsourcing of clinical trials, the business is in its infancy in Pakistan despite of having a large pool of patients, a large number of English-speaking physicians, a low value of Rupee, a network of high volume medical centres and a good know how of this business as many physicians have conducted Clinical Trials in other countries.

¹ Definition adopted from www.dcri.duke.edu/patient/glossary.jsp, www.possis.com/patients/glossary.php, and www.wcctrials.com/glossary.HTM

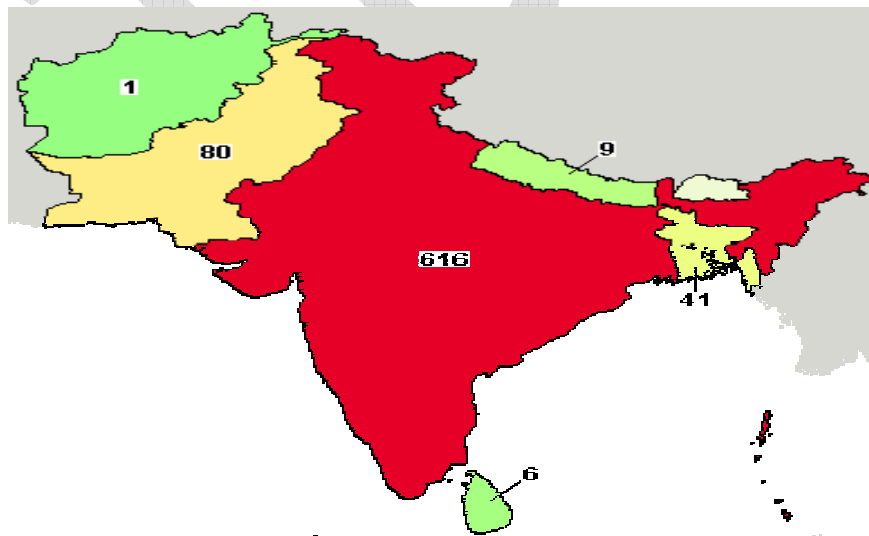
² Source: http://www.atimes.com/atimes/South_Asia/GE12Df04.html

³ The Clinical Trials Business, BCC Research, August 1, 2006, 231 Pages - Pub ID: WA1354481
source: <http://www.bccresearch.com/RepTemplate.cfm?reportID=450&RepDet=HLT&cat=phm&target=repdetail.cfm>

Out of the total of around 60,500 Clinical Trials conducted across the globe, 58 percent are in North America, 19 percent in Europe, 5 percent in Central and South America, 5 percent in China, 3 percent in Arab & Middle East Countries, 2 percent in Africa, a little above 1 percent (616) in India and only 0.1 percent (80) in Pakistan.⁴



Out of the total 80 trials in Pakistan, 39 are recruiting, 12 are active but are not recruiting, while 29 have been completed. 16 trials are related to Oncology, 16 to infections, 13 to Hypertension and ICH, 5 TO Blood Disorders, 4 to CNS & Psychiatry, 3 to Metabolism and Diabetes and remaining to other fields.



⁴ Sincere thanks to Dr Ghulam Murtaza Qasuri, Medical Director, Eli Lilly Pakistan and Dr. Amanullah Khan, Medical Director, Sanofi-Aventis Pakistan, for providing this information. Original Source: www.clinicaltrials.gov.

2. CROs IN CLINICAL RESEARCH

By March 1, 2005, all countries had to adopt patent rules in line with WTO rules. Pharmaceutical companies worldwide have been concentrating on new drug development. It is estimated that the number of drugs developed has gone up from 4,194 in 1997 to 7,067 in 2002, which underlines the necessity for increased demand for Clinical Research Organization/ Contract Research Organization (CRO) services.

An independent CRO provides committed resources for clinical studies. This helps to maintain the high standards set by the industry, such as strict adherence to protocols, excellent clinical practices and complete and accurate documentation. CROs ability to provide timely and proficient trials speed up the process of clinical studies.

CROs offer their clients a wider range of pharmaceutical research services including clinical trial management of a high standard. Thus, CRO activities offer good opportunities for health care facilities, conduct clinical trials and data management in accordance with international standard, and provide new and research based treatments to the patients. The training of health care providers in the management of clinical trials improves overall research environment in the country and allows contributions to the knowledge base of the world.

3. ROLE OF TRADE DEVELOPMENT AUTHORITY OF PAKISTAN (TDAP)

The remit of the TDAP is to enhance the exports of goods and services from Pakistan. Pakistan's Export Development Strategy focuses on 12 sectors, one of which is the services sector. Medical Services, among other services, have a great potential to generate export revenue for the country. Clinical Research Services are important medical services a country can export.

Realizing the potential of the country to be an attractive venue of Contract Research, TDAP in Collaboration with Ministry of Health and Jinnah Postgraduate Medical Centre (JPMC) aims to invite the companies that conduct clinical trials to come to Pakistan and establish their centers in the country. The three government organizations have planned to attract more and more international outsourced clinical trials in the country.

There is a need for developing partnership with the international CROs and other outsourcing providers. Some of the major CROs in the world are interested in working in Pakistan. Such companies need some encouragement from the regulators in Pakistan. They are also concerned about data reliability and management, documentation and Intellectual Property Rights. There is a platform required to not only look at these issues holistically, but also to act as a coordination conduit. TDAP intends to provide such a platform.

In December 2007, TDAP, Ministry of Health and JPMC jointly took the initiative to promote this business in the country. It was considered an imperative that multinational pharmaceutical companies in Pakistan, Local CROs and Relevant Experts from Hospitals should not only be consulted but should also contribute in this initiative, given their already vast international experience in this field.

TDAP convened three meetings of Chief Executives and Medical Directors of selected Pharmaceutical MNCs and CROs in January and February this year. A Steering Committee of 11 members, comprising of some Chief Executives and Medical Directors of Pharmaceutical MNCs and Heads of Local CROs was formed for organizing a seminar on 'Clinical Research Management in Pakistan'. A basic Concept Paper on Clinical Trials Management was prepared and sent to the members of Steering Committee on 15th Jan, 2008.

First outline draft of the program of the seminar, prepared by TDAP's WTO Cell, was sent to the members of the Steering Committee on Thursday, Jan 17th 2008. The programme went through various modifications during the meetings.

The specific objectives of the seminar and the workshop were:

1. Introduce the Clinical Trial Business and to understand the roles, responsibilities, and services of CROs.
2. Understand the characteristics of a country that becomes a preferred destination for outsourced Clinical Trials.
3. Create a national network of health care practitioners, CROs, pharmaceutical industry, Ministry of Health for developing well regulated, ethical and quality contract research activity in Pakistan.
4. Identify other initiatives to facilitate growth of this service industry sector.

Media coverage of the meetings attracted many companies and hospitals. TDAP and JPMC team met many representatives from Local CROs, Pharmaceuticals and Hospitals. Finally, TDAP in collaboration with Ministry of Health & Jinnah Postgraduate Medical Centre (JPMC) organized this seminar on 26th of April 2008. A dinner was also hosted, in the evening of April 26, by the Minister of State and Chief Executive, TDAP in the honor of the Federal Minister of Health, foreign and local speakers and various other guests related to the field of clinical research. A technical workshop was organized on 27th of April 2008.

The TDAP covered all the expenditures of seminar, dinner and the workshop and the travel and accommodation expenses of resource persons from abroad.

4. THE SEMINAR

Representatives from International CROs, Ministry of Health, Local CROs, Pharmaceutical Industry, Regulatory / IPR bodies, Physicians of local Institutions/ Hospitals, and IT Experts related to the field of Clinical Research participated in the seminar.

In his welcome address, Professor Dr. Rashid Jooma, Executive Director, JPMC pointed out that despite of the fact that the country has conducted only 80 clinical trials, the growth in the registration of trials is significant and encouraging.

The Minister of State and Chief Executive of TDAP, Mr. Tariq Ikram discussed the objectives of the seminar and the role of TDAP. Mr. Ikram invited the international CROs and Pharmaceutical MNCs to join hands with Pakistan's government, local CROs and hospitals to promote the business in the country.

The Secretary, Ministry of Health, Mr. K.A. Lashari ensured all kinds of support from his ministry to support the clinical research activity in the country. Mr. Lashari asked TDAP to play a greater role in developing the Clinical Research sector.

After the introductory session, some very informative presentations were given by the foreign and national experts from various organizations.

Brief, relevant, and relatively non-technical summaries of most of these presentations are given in the following sub-sections. Highly technical presentations or part of presentations that were not suitable for this document have not been included.

4.1. Developing Clinical Trials in New Emerging Countries in Asia

Mr. Anand Tharmaratnam, Head of Quintiles Asia Pacific, talked about developing clinical trials in new emerging countries in Asia. Mr. Tharmaratnam said that because of the saturation in the American market the trials are increasingly being outsourced to Asian markets particularly, China, Japan and India. He said that Asia is attracting more business because of its huge (60 % of the world) population. There are 150 cities in Asia, which have a population of over one million. Urban population is expected to double from 2000 by 2030.

Dr. Tharmaratnam said that the Asian economies are also improving and now Asia produces 28 percent of global output, which is expected to reach 36 percent in 2050.

Another encouraging factor is that the middle class in Asian countries is increasing. He added that the growth of Biopharmaceutical Clinical Trials is highest in Asia after Eastern Europe as depicted by the following table.

Table 1: Annual Relative Annual Growth Rate by Regions

Region	Annual Relative Annual Growth Rate
Eastern Europe	+24%
Asia	+20.4%
Latin America	+19.8%
Western Europe	+3.5%
North America	-6.9%

Fabio A. Thiers, Anthony J. Sinskey and Ernst R. Berndt, MIT Center for Biomedical Innovation, Nov 2007

Dr. Tharmaratnam also said that among other factors large number of patients, qualified doctors, good quality of investigations, competitive start-up times, supportive commercial and regulatory considerations in the national laws, intellectual property rights, good infrastructure, and ICH GCP mandate, can attract clinical trials in the country.

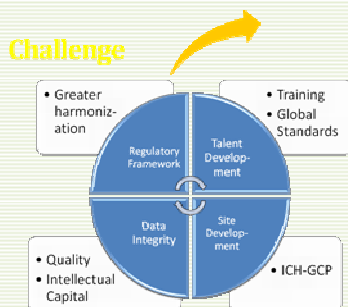
He also presented a SWOT (Strength, Weaknesses, Opportunities and Threats) analysis of the Asian clinical trials market. Because of the usefulness of this analysis we have summarized it in chart 1 below.

Chart 1: SWOT Analysis of Asian Clinical Trials Market					
Singapore & Hong Kong	South Korea & Taiwan	Malaysia, Thailand & Philippines	Indonesia & Vietnam	Mainland China	India
Strengths					
*Fast regulators	*High standard of healthcare	*Significantly large population	*Large population	*1.3 Billion population	*>10 year history of NCE international Drug Development
*High standard institutions	*Significantly large population and marketing potential	*Drug naïve patients	*Govt/ NGO/ PPP/ limited pharma study experience	*Study experience from local registration	*Much longer history of generic Development
*Respected investigators	*Keen investigators	*Large academic / referral centers with high throughput	*Receptive to industry knowledge	*Excellent infrastructure and Expertise	*English is the language of medical education and care
*Transparent		*Many keen investigators			
*High literacy rate					
*High access to healthcare					
*Good command of English					
Weaknesses					
*Small City States – limited population	*Regulatory authorities Timelines	*Smaller hospitals do not have research set-up	*Variable literacy, limited infrastructure beyond major cities	*Start up Timelines longer than the rest of Asia	*Investment in Infrastructure necessary
	*Slower responses from feasibilities			*Shortage of English speaking talent to work on global studies	*High Transportation costs IP and Biologicals
Opportunities					
*Polyclinic Groups (post-tertiary)	*SMO, Network Hospitals	*With support centers of excellence for clinical trials	*Many potential sites	*Untapped potential in most of China	*Huge Potential in investing and opening more sites
		*Large private centers, mid-size government hospital	*Less Competition for sites		
			*Good relationships with sites and regulators		
Threats					
*Cost approaching ‘Western’ standards	*Intense competition for investigator sites	*Competition For Sites at major cities	*Perceived instability, perceived political patronage		*Escalating costs
*Strong competition from other CRO, pharma, biotech with regional HQ base locally	* Cost approaching/exceeding ‘Western’ standards	*Limited Talent Pool to employ			*Saturation of Experienced Sites as more trials are conducted in India
*Investigators becoming selective					

List 1: Key Questions to Address When Evaluating New Geographies

- Access to Patients
- Access to Experienced Investigators
- Access to Sites
- A stable, honest and effective Regulatory Framework
- A Potential Talent Pool from Which to Hire and to Train
- Level of Government Engagement
- Commercial Considerations
- Logistics
- Security Evaluation
- Sustainability and Scalability of Business

Chart 2



Dr. Tharmaratnam then presented country attractiveness (for clinical trials) index, which shows that the most significant factor that attracts the clinical trials in the country is the size and availability of *suitable patient pool*, which carries 30% weight. Cost efficiency, which includes *cost of labour* and *cost of facilities and travel*, is weighted at 20%. Regulatory conditions (*country’s regulatory laws, strength of intellectual property protection, and perspective of FDA*) also carry 20% weight. Relevant expertise and infrastructure and environment, both, are weighted at 15% each. Relevant expertise includes *number of CROs, number of clinical trials, and size and availability of labour force with relevant skills*. While infrastructure and environment includes *protection of IP, level of healthcare infrastructure, level of country infrastructure, country risk factors*.⁵

He also talked about the key issues that are addressed when Pharmaceutical MNCs evaluate new geographies for outsourcing clinical trials. These issues are listed in List 1.

Dr. Tharmaratnam presented a useful diagram (Chart 2) to emphasize the significance of dealing with the challenges such as:

1. Greater harmonization of regulatory framework
2. Trainings for developing talent of international standards
3. Data integrity to the extent that ensures quality and protection of intellectual capital, and
4. Site development in the light of ICH - GCP

⁵ Original Source: AT Kearney www.atkearney.com 2008

4.2. Fundamentals of Site Management

Dr. Cellia Habita, CEO, Arriane Consulting talked about the fundamentals of site management. She said that clinical trials are necessary to ensure human health. They are intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of an investigational product/s and/or identify any adverse reactions to an investigational product/s, and/or study absorption, distribution, metabolism and excretion of an investigational product/s with the object of ascertaining its safety and/or efficacy.

She explained the following components of site management:

- Recognize the regulatory basis for monitoring clinical research activities
- Carry out site management and clinical monitoring responsibilities from study initiation to study completion
- Maintain the integrity of trial data
- Ensure compliance with informed consent procedures

Key elements in site management are:

- Documentation
- Patient Enrollment
 - Patient consenting
- Patient Management during the course of study
- Investigational Product
- Data Management
- Pharmaco-vigilance

She also talked about the major steps in Clinical Trial Management that are investigators and volunteers recruitment and patient consenting. Then she talked about the day to day activities and issues of site management. She said that patients' safety always comes first. There is the need of proper documentation and ensuring quality and integrity of data.

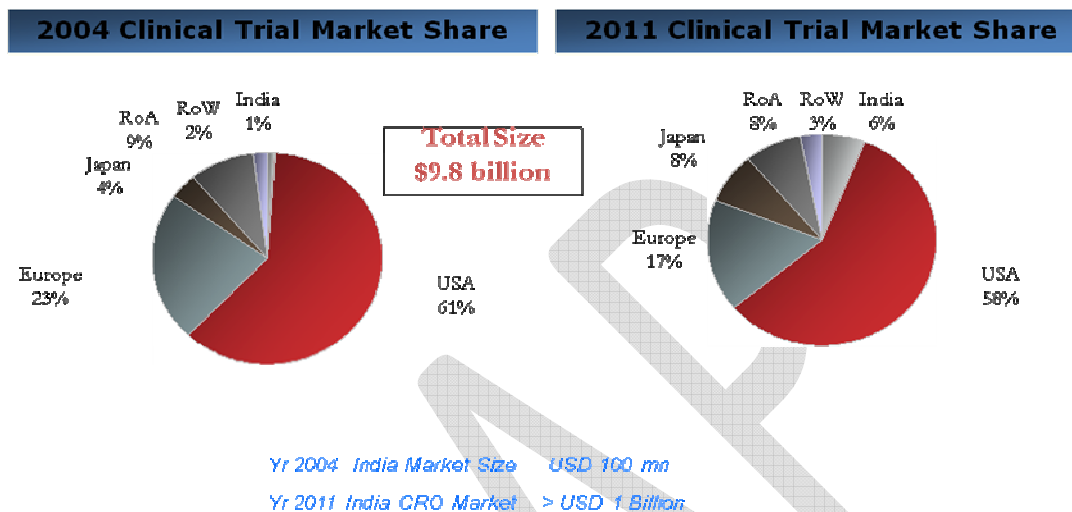
She discussed in detail about the clinical study teams, pre-study visit, investigators meeting, site initiation visit, monitoring visit and the site close out.

4.3. India :Building a Sustainable Clinical Research Industry

Dr. Guljit Chaudhri, Senior Advisor, i3 Research India, discussed the development of clinical research industry in India. While presenting chart 4 she said that India's share in global clinical trials market is projected to grow to 6% in 2011 from 1% in 2004. In 2007

India accounted for only 2% of global clinical trials which is expected to grow to 14% by 2011.

Chart 3: Global CRO Market Trends



Source: William Blair research

Dr. Chaudhri talked about the performance, challenges, problems and limitations of conduct of clinical trials in India. In 2002 it was estimated that there were 150-200 clinical researchers in India, and the industry has now grown to over 7500 in 2007. Mckinsey estimated that India needs 30-50000 professionals to manage clinical trials of USD 1bn by 2011.

The government of India has allowed duty exemption on import of Investigational Products and on Research Services. Registration of clinical trials was made mandatory in 2007. The Clinical Trials Registry- India (CTRI) was set up by the ICMR's National Institute of Medical Statistics (NIMS) and is funded by the Department of Science and Technology (DST) through the Indian Council of Medical Research (ICMR). It also receives financial and technical support through the WHO, WHO-SEARO, and the WHO India Country office.

Regulatory approvals are possible in 6 to 8 weeks in India. Typical time lines for regulatory approvals are given in the following table presented by Dr. Chaudhri.

Regulatory body	Approval	Time
Drugs Controller General of India (DCGI)	Regulatory approval for study conduct in India	<ul style="list-style-type: none"> ▪ 4 weeks – FAST TRACK, US IND / MHRA CTA available ▪ 16 weeks, no documentation to support successful US/EU/CTA
Drugs Controller General of India (DCGI)	Test license to import trial supplies	2 weeks in addition
Ethics Committees	Local Ethics committee approval by sites	6 – 8 weeks (in parallel)
Total (parallel processing)	-	6 – 8 weeks – FAST TRACK 16 weeks (track B)
Directorate General of Foreign Trade (DGFT)	Permission to export blood samples	Additional 2 to 4 weeks

Site Infrastructure in India, according to Dr. Chaudhri’s presentation is as follows:

Capacity

- Over 700,000 speciality hospital beds, 16-18000 hospitals with 221 medical colleges & English speaking medical personnel.
- 750+ Sites located in both large government hospitals and private hospitals.
- Leading Investigators have taken initiatives to setup Clinical Research Units in their hospitals.
- Infrastructure: broad band facilities, fax lines easily available diagnostic facilities: CT scans, MRI etc.

Concerns

- “Investigator shortage the chief Challenges in India” – Bio-ITWorld 8th March 2008.
- Large majority of potential investigators lack knowledge of regulations, ethics and GCP and skills for clinical trial management.
- Investigators have relied on mentors to learn how to conduct clinical trials.
- The institutional policies are not yet geared to support the investigator in managing clinical trials efficiently.
- Variability in Ethical Practices for clinical trial conduct.

Other Concerns in India are:

- Regulatory uncertainties about time to approval,
- Involvement of multiple agencies for approval of biotech products and for processing import/export licenses,

- Middle management /domain leadership lacking; high annual turnover of staff (28-35%)
- The quality of global trials and academic clinical research is not uniform
- Differing medical practices
- Lack of adequate infrastructure for communication, drug / sample storage, archival
- The situation is worse in non-metro cities that have tremendous potential for participation in global trials
- Most medical schools lack a formal course in training for clinical research
- Lack of confidentiality
- Different social systems and cultural differences (behavior, tradition, religion, values etc.)

Dr. Chaudhri discussed four models of operations, governance, oversight and pricing of clinical trials.

Chart 4: Structure of Operations, Governance, Oversight & Pricing Models

<p>Functional Service Provider (FSP) Model</p> <ul style="list-style-type: none"> ▪ Focus on Single Functional Expertise ▪ Utilize Sponsors Systems/Processes ▪ Across all Compounds ▪ Build Cross-Company Teams ▪ Sponsor Manages Interfaces ▪ Vendor provides dedicated resources to sponsor and typically works on several projects simultaneously 	<p>Full Time Equivalent (FTE) Model.</p> <ul style="list-style-type: none"> ▪ CRO provides the client with a project team dedicated to the client's studies for a specified period of time at a fixed rate per FTE unit ▪ Extension to the contract staffing model. ▪ Service provider provides the office and manpower but both sponsor and CRO work jointly to manage the resources relevant to the outsourced work. ▪ Sponsor pays a fixed rate per FTE, independent of the workload. ▪ FTE agreement is more appropriate for a long-term program.
<p>Full Service Provider / Fee for Service</p> <ul style="list-style-type: none"> ▪ CRO Performs full range of services with single point of contact. ▪ CRO uses own systems, SOPs, processes. ▪ This model has been the industry standard. ▪ CRO manages the resources. ▪ This agreement is more appropriate mostly for a short terms and some long-term programs 	<p>Newer Models</p> <ul style="list-style-type: none"> ▪ Program Outsourcing <ul style="list-style-type: none"> – By compound – Single or multiple phase support – Leverage compound expertise ▪ Therapeutic Alignment <ul style="list-style-type: none"> – All compounds in therapeutic area – Fill in GAPs across programs / compounds within a therapeutic area. – Leverage Therapeutic Expertise in CRO.

She said that Multinational-studies are the norm and India is becoming a part of the network. This is a great opportunity for Pakistan.

4.4. Cancer Research Group (CRG) Foundation Pakistan. An Affiliate of Pakistan Society of Clinical Oncology (PSCO)

Professor Dr. Shaharyar, President of Cancer Research Group (CRG), Pakistan, talked about the CRG. He said that the Group was founded on 21st November 1999 during the 7th Biennial National Cancer Conference in Multan. The objectives of the Group are:

- To generate the local data on epidemiology & clinico-pathologic features of cancers & to formulate a central registry.
- To identify the common cancer problems in the community & to conduct research to address these clinical issues.
- To integrate the modern scientific developments in cancer detection, diagnosis & treatment with local cancer care system.
- To promote the postgraduate training in the specialty.

CRG has developed the largest database in the country comprising of 45,883 patients including 20903 females and 24980 males. Dr. Shaharyar said that there are 26 cancer centers in Pakistan and around 50,000 patients are seen yearly.

4.5. Pharma R & D Perspective on GCP Research in Pakistan

Dr. Benedict Blayney, Vice President, Medical Affairs, Asia Pacific, Sanofi Aventis, presented the Pharmaceutical Companies' perspective on possibilities of GCP Research in Pakistan. He said that in western world it takes 10–15 years to develop a drug⁶. Cost of developing a drug increased to \$802 million in 2001 from \$318 million in 1987, and \$138 million in 1975. Cost for developing a biologic was \$1.2 billion in 2006.

Total industry R&D spending in 2006 was \$55.2 billion as compared to \$51.8 billion in 2005 and \$47.6 billion in 2004. Approvals in the US Drugs approved in 2006 were 29 (18 NMEs), only 3 of 10 marketed drugs ever produce revenues that match or exceed R&D costs, and average effective patent life for pharmaceuticals is 11.5 years.⁷

He stated that there is more than 17,000 R&D staff (including: Vaccines, Industrial Development, Medical/Regulatory staff of subsidiaries) in more than 20 research centers in France, Hungary, Italy, Spain, Germany, UK, Japan and the US. Global R&D budget

⁶ Source: *Pharmaceutical Research and Manufacturers of America, Pharmaceutical Industry Profile 2007* (Washington, DC: PhRMA, March 2007)

⁷ *Ibid.*

was estimated at €4 billion. 135 clinical studies (Phase I, II and III) were initiated in 2005, 188 in 2006, and 188 (target) in 2007. Number of subjects included in Oct 2007 was 32,166, and the estimated number of subjects to be included in 2008 is 32,000.

Dr. Blayney said that the growth of outsourced clinical trials has increased over the last few years and Asia has emerged as an attractive destination. This is due to the factors such as:

- Acceleration of R&D in the industry – **QUALITY and SPEED**
- Saturation of US and EU study centers - competition
- Decrease clinical development time while ensuring quality
 - More sites per study
- Access to new resources – large patient populations, ethnic diversity, talent (Investigators, research staff)
- Disease patterns, treatment naïve patients
- Established and developing clinical trial sites in emerging countries supported by experience and quality data
- ICH GCP and /or national GCP adopted widely

Chart 5



Rationale for extending study centres to Asia are:

- Shorten clinical development time – earlier submissions for Regulatory approval
 - Opening more sites worldwide
- Competition for US and European study centres
- Interested and qualified investigators
- ICH GCP and /or national GCPS adopted widely
- Large patient populations, ethnic diversity
- Disease patterns, treatment naïve patients
- Higher costs of studies in US and Europe

3 key areas for successful Clinical trial development are:

1 Medical Considerations

Patient demographics & accessible population

- a. Prevalence/Incidence data e.g. Malaria, Cancer, Diabetes
- b. Awareness of disease
- c. Symptomatic vs. asymptomatic conditions
- d. In primary/secondary/tertiary care
- e. Referral systems in place
- f. Clinical expertise
- g. Standard treatment of care

2 Regulatory Considerations

- Study design
 - Placebo controlled study design?
 - Washout period?
 - Is Comparator licensed for targeted indication/dose?
 - Acceptable procedures, tests and follow-ups?
 - Ethical provision of after study care
 - Use of radiolabelled substance, gene therapy
 - Special requirements for Pediatric trials, specialized patient population
- Health authority regulations (“clinical trial friendly environment”)
- Hospital infrastructure –IEC/IRB set-up conforms to ICH-GCP
- Import/Export License (i.e. Study drug, Study materials, equipment, lab supplies)
- Target markets for registration
 - Local registration studies
 - Reimbursement – payer strategies

3. Operational Considerations

- Adequate patient population – number of subjects/site
- Prior performance (research naïve vs. experienced)
- Access to technology (eCRF), lab tests, equipment and/or staffing
- Interest and commitment of Investigators and site staff – time
- Study competition (internal/external)
- Vendor limitations (i.e. central labs)
- Protocol design matching (align with clinical practice)
- Regulatory and IEC/IRB approval time
- Start-up time – contract turnaround time
- Recruitment reliability – projections & previous achievements

Country Selection criteria mentioned by Dr. Blayney are:

- Health authority regulations (“clinical trial friendly environment”)
- Approval Timelines
- Compliance with ICH Good Clinical Practice
- Import license (study drug, lab supplies)
- Export restrictions (blood, tissue, lab samples)
- Hospital infrastructure – EC/IRB set-up conforms to ICH-GCP
- Adequate patient population
- Trained staff & adequate resource
- Standard of medical care
- Other logistic issues (language, medical notes)
- Copy right protection, IP recognition

Finally said that the ‘X’ factor for success in clinical trials is

- ▶ Well trained, full time, in-hospital ,clinical trial nurses/managers

He concluded that Asia is, and Pakistan can be, an area of focus for R and D clinical development, however, there are 3 main prerequisites:

- i) Availability of patients and quality medical care
- ii) ‘User friendly’ Regulatory and Operational environment for clinical research
- iii) Availability of in-hospital well trained clinical trial nurses/managers

Patients and quality medical care are available in Pakistan. User friendly regulatory and operational environment is developing and fulltime in-hospital clinical trial nurses/managers are also available so there is a bright future.

4.6. CT Management in Pakistan: Local CRO Perspective

Mr. Khurram Zaki Khan, Chief Executive, Metrics Research, presented a local CROs perspective about Clinical Trials Management in Pakistan. Mr. Khan said that there are various myths about Pakistan in the western world and these myths keep some international investors away from investing in Pakistan.

He said that many Americans and Europeans believe that Pakistanis cannot speak English and they do not like talking to foreigners. He said that Americans and Europeans related to the field of clinical research are of the perception that there are no CROs in Pakistan, and if there are any, then they are not managing any international clinical studies. This however, is not true, he added as there are eight CROs working in Pakistan, out of which six are in Karachi such as Metrics Research, which is also the first CRO in Pakistan (established 2003, incorporated 2005), IRD, Clinision, Verum Venture, Medco Group, Universal labs, one, Medessense, in Lahore and Milestone Biostudies Centre is in Islamabad.

Chart 6 shows that these CROs are doing BE/BA Studies, Preclinical Research, Phase II, III, and Phase IV trials, Site Management, and GCP Statistics Trainings. Metrics has the capacity to conduct QA audit.

Chart 6: Pakistan CRO Capabilities

CRO	BE/BA Studies	Preclinical Research	Phase II	Phase III	Phase IV	Site Management	GCP Statistics Trainings	QA Audit Capacity	Pan Pakistan Coverage
Metrics Research		X	X	XX	X	XX	X	X	XX
IRD			X	X	X				
* Clinision			X	X	X		X		X
Verum Venture				X	X				
Medco group				X	X				
Universal Labs	X			X	X				
* Medessense				X	X				
Milestone Biostudies	X			X	X				

Many of these CROs are involved in international clinical trials in therapeutic care fields such as Oncology, Hematology, Osteoporosis, Infectious diseases, Cardiovascular diseases, Ophthalmology, and Diabetes.

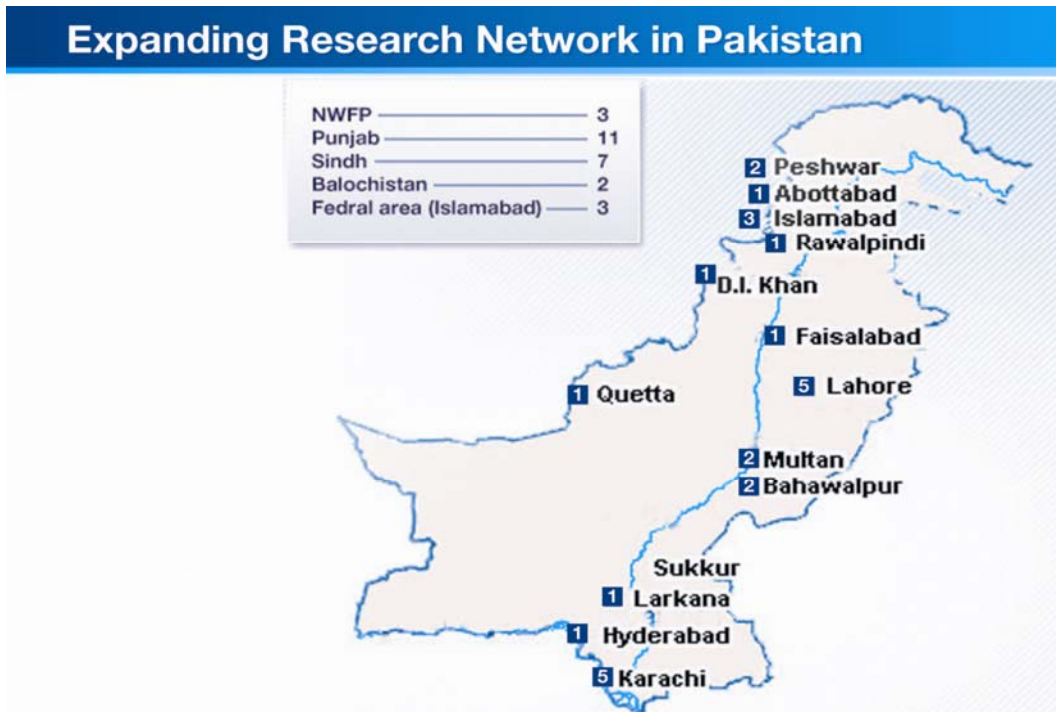
The services offered by the CROs include:

- ✓ Project Management
- ✓ Site feasibility
- ✓ Site selection and Monitoring
- ✓ Site management
- ✓ SOP preparation
- ✓ QA and auditing
- ✓ Pre-audit preparation
- ✓ Regulatory services for local and international customers
- ✓ BE/BA Studies
- ✓ Drug import and registration services (for clinical trials)
- ✓ Medical translation services
- ✓ Clinical trial materials management
- ✓ Statistical Analysis
- ✓ Market research (Pharma)
- ✓ Proteomic and Genomic Research Management
- ✓ Certified Clinical Research training programs (CCRP)

Mr. Khan added that another myth is that there are no or very few GCP trained site personnel in Pakistan, which is not true. He said that Clinision has 1100 Health care professionals, Metrics has 400 Health care professionals mainly doctors, university students and some international students, GSK , Eli Lilly, Pfizer, SanofiAventis etc. have also trained a large number of site personnel, and similarly other CROs also have trained professionals.

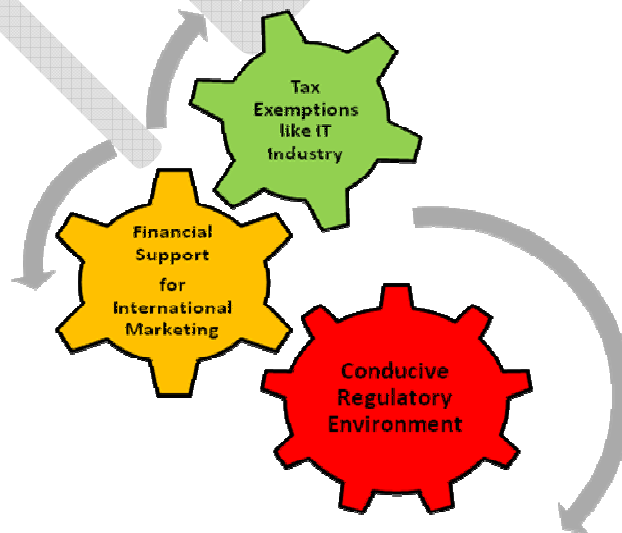
Another myth he said is that there are no research sites in the country, which is again not true as is depicted by the following map. There are 26 research sites in Pakistan out of which 5 are in Karachi, 5 in Lahore and 3 in Islamabad.

Chart 7: Expanding Research Network in Pakistan



Mr. Khan demanded tax exemptions from the government as is provided to the IT sector and financial support for international marketing, he also emphasized on the importance of conducive regulatory environment.

Chart 8: Support Required to Run the CRO Business Engine



4.7. Aga Khan University – Clinical Laboratories

Dr. Farooq Ghani, Associate Professor & Consulting Pathologist, Department of Pathology, Aga Khan University, talked about the role of Aga Khan Laboratories in Clinical Trials. He said that Aga Khan Hospital has a broad national network of Diagnostic Services, which includes:

- 172 Phlebotomy stations
- Stat Labs (Hyderabad, Lahore, Quetta, Peshawar & Multan)
- 3 AKHSP Labs
- Clifton Medical Services
- South City Hospital

There are 39 Faculty, 1172 Staff (718 Off-campus), 6 clinical sections, which include Chemical pathology, Haematology, Blood bank, Histopathology, Microbiology, and Molecular pathology.

Research areas are Infectious diseases, Cancer, Genetic basis of metabolic disorders Cardiovascular. 390 publications have been produced during 2000-2006.

AKU has accreditations from Joint Commission for International Accreditation (JCIA) 2006, and Further Accreditation planned is from College of American Pathologists (CAP)

AKU plans to establish phlebotomy stations at locations with ≥ 0.1 m population (2007-2010), 282 stations in 75-80 cities/towns by 2010, and one stat lab per year.

4.8. Bioequivalence Studies

Prof. Dr. Tasneem Ahmad, Director of Center for Bioequivalence Study & Bioassay Research (CBSBR), Punjwani Centre for Molecular Medicine and Drug Discovery, Karachi University gave a rather technical presentation in which he focused on various aspects of bioequivalence studies.

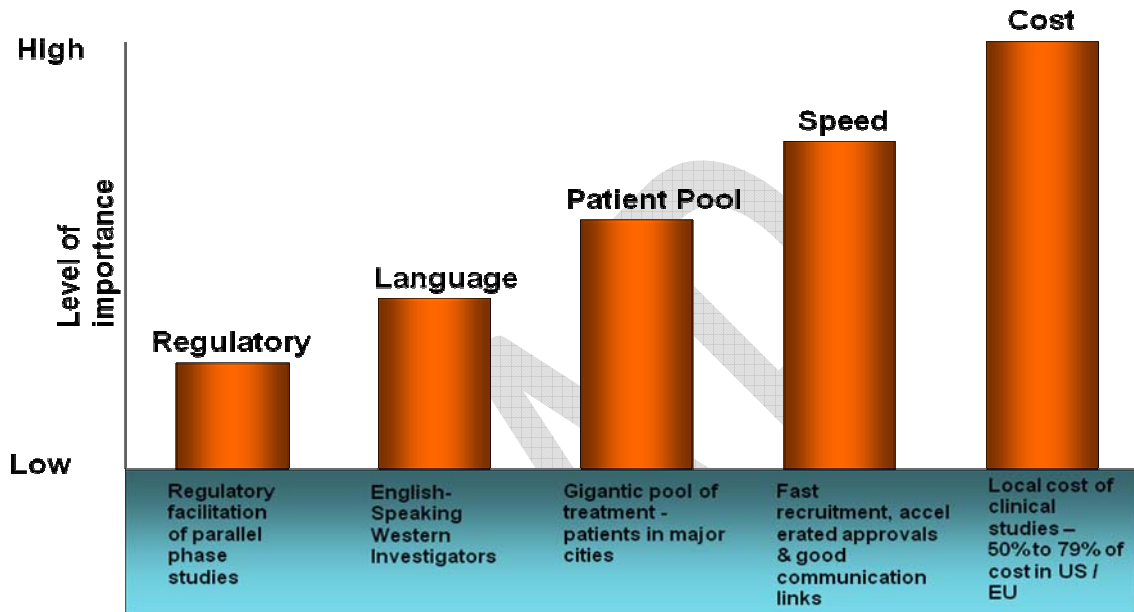
4.9. The Future of CRO in Pakistan Today - A Review of Asia Pac Model

Prof. Iffat Yazdani, Area Director Asia Pac, Glaxo Smith Kline (GSK), discussed the future prospects for CROs in Pakistan while presenting the Asia Pac Model.

She discussed the outsourcing trends in pharmaceutical companies and said that globally, pharmaceutical companies spent 23% (US\$6.5bn) of development costs on outsourcing services in 2006 and most “mega” pharma companies are investigating how to outsource more. Spending on clinical outsourcing is growing faster (16%) than the increase in spending on clinical development overall (11%). Clinical trials outsourced to India are expected to reach \$1000M in

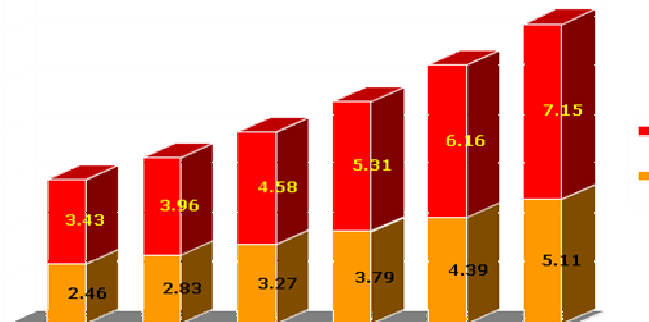
2010. While in China the market is expected to reach \$12.3 bn in 2011 growing from \$ 5.9bn in 2006.

The India Advantage



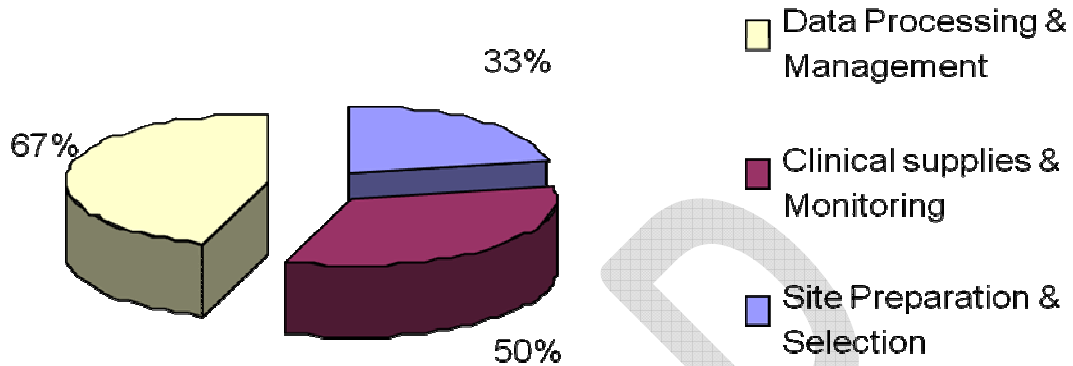
CRO Market in China

- The drug discovery outsourcing market (preclinical and clinical) in China was worth \$5.9bn in 2006, and is projected to reach \$12.3bn in 2011.



Outsourcing Trend in China

◆ CRO Business Distribution.

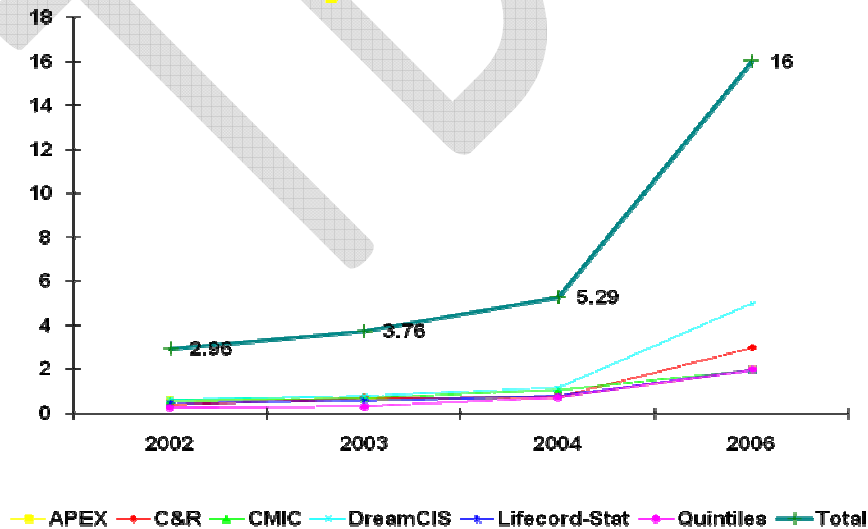


50% of Pharma companies to increase outsourcing

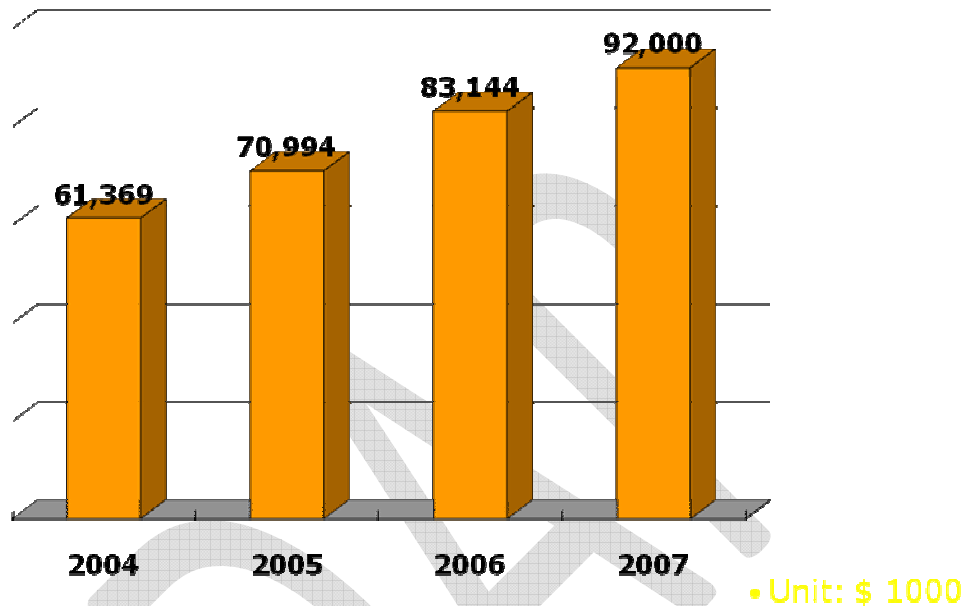
Korean CRO market has witnessed 30% annual growth rate over the last few years.

CRO Market Trend in Korea

◆ 30% annual growth rate in CRO Market



CRO Market Trend in Japan



Similarly the Japanese market has also grown substantially over the years.

Dr. Yazdani also presented the GSK perspective on CRO Hiring & Outcome.

4.10. The Role of Information Technology in Clinical Trials

Mr. Taha Kisat, COO, ECAS, introduced the services related to clinical research that his company can provide. He talked about Pharmacogenics, Electronic Data Capture (EDC) system, and areas where IT can add value.

Mr. Kisat emphasized on raising awareness regarding integrity of clinical trial data. Another emphasis of his presentation was that the IT regulatory framework has to be an integral part of any pharmaceutical regulations and the government inspectors should be equally knowledgeable about not only the clinical trials but also the role of information technology in this business.

4.11. Verum- Ventures

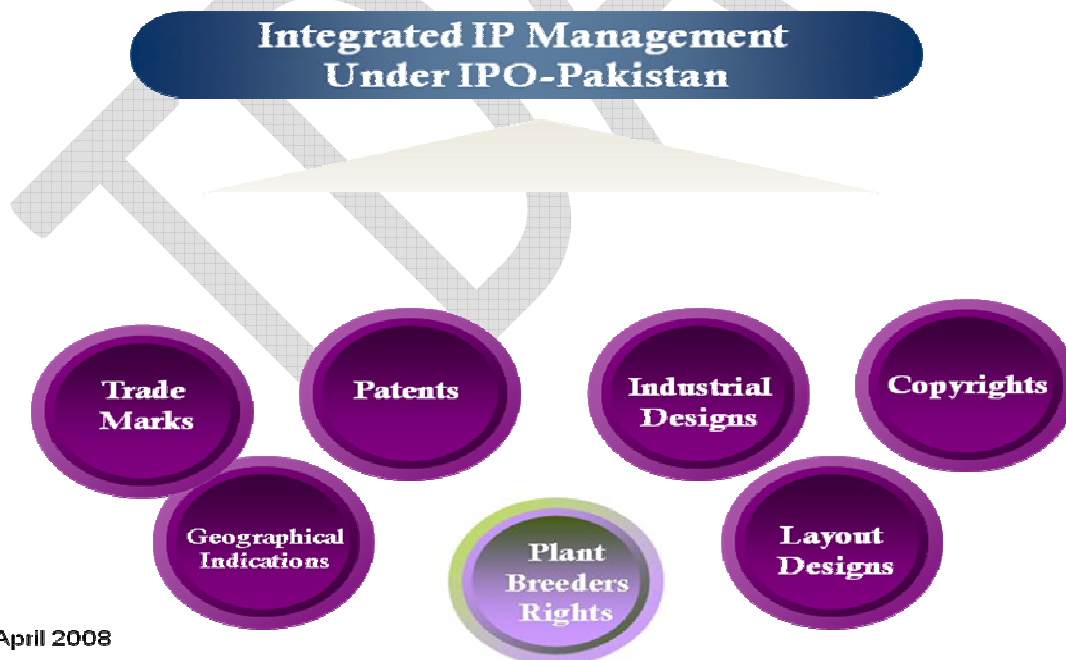
Dr. Zubair Mirza, from Verum-Ventures, a joint venture between, Venture Pharmaceuticals Karachi, Pakistan, and Verum.de GmbH Munich, Germany, presented his company as the first joint venture clinical research company in Pakistan. Dr. Mirza also highlighted the importance of Pakistan as a future destination for international clinical trials.

4.12. Intellectual Property Management in Pakistan

Mr. Muhammad Mohsin, Registrar of Trade Marks, IPO, Pakistan, said that intellectual property covers Trade Secrets (Trade Marks), Service Marks, Patents, Industrial Designs, Layout Designs of Integrated Circuits, Copyrights Geographical Indications, Genetic Resources, Plant Breeders Rights, and Technical Know How.

He added that IPO-Pakistan was created on 8th April 2005 to address the deteriorating situation of IPR protection, integrate the fragmented management of different IP, improve the quality of service of the IP registries, and create awareness regarding the importance of IP in the contemporary era.

IPO manages all the kinds of IPs as is shown by the following chart:



26th April 2008

4.13. Patent Rights in Pakistan

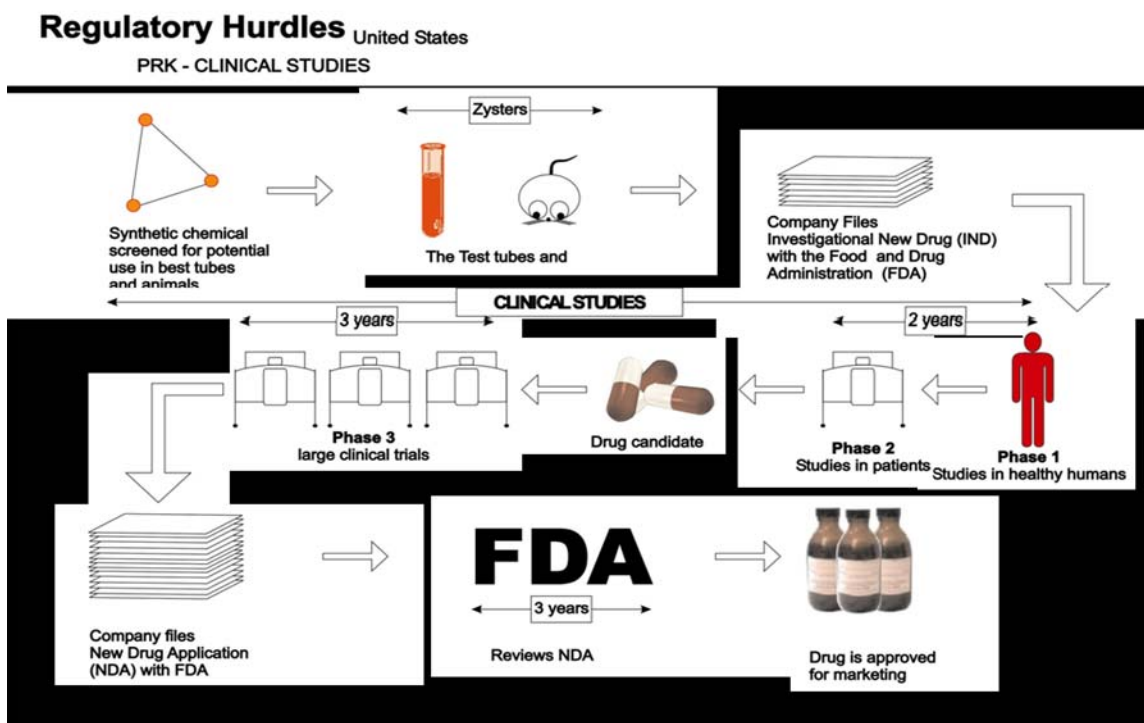
Mr. Hasan Irfan Khan from United Trademark & Patent Services, talked about the patent rights in Pakistan. He said that in Pakistan Patents relating to pharmaceutical field are granted for :-

- Product (new chemical product)
- Process (of new product) or new process of an old product.
- Formulation/composition (of new product) or new formulation/composition of an old product.
- Drug delivery systems
- Medical devices

He added that **Innovations** (Patents) and **Clinical Trial Data** (test or other data) submitted to Government for obtaining marketing authorization are two independent IPs. TRIPs agreement also recognizes this by providing for Data Protection and Patent Protection under separate articles. (Art. 27 & 39.3)

He said that the purpose of clinical research/trials is to generate clinical data for a drug to establish its safety, quality and efficacy, which is required for submission to the Government for obtaining marketing authorization. Clinical trials may be conducted by medical institutions, hospitals and universities for a sponsor. The sponsor of the drug will need to rely on this data to secure the marketing authorization for the drug.

Mr. Khan presented the following chart to discuss the regulatory hurdles in the clinical trials process in US.



He added that Clinical trial/research is a developing field and Pakistan can attract substantial investment in this vast area by making available the necessary platform and improving legal protection of IPRs, in particular providing protection to test data. This is also because companies invest in countries where IPR protection is adequate. Jordan is one example where after 2000 reforms to improve IPR laws, size of pharma market substantially increased, exports have grown from about US \$ 49 million to more than US \$ 280 million. Before IP reforms no international drug innovative company conducted clinical R&D in Jordan. Currently eight American and European Companies are carrying on clinical R&D in Jordan. By 2004, medical tourism in Jordan has grown to about US \$ 650 million. By 2005, medical tourism exceeded US \$ 1.3 billion.

4.14. CREATING A NETWORK OF STAKEHOLDERS FOR THE PURPOSE OF DEVELOPING CLINICAL RESEARCH IN PAKISTAN

Prof. Dr. Rashid Jooma, ED JPMC, conducted an interactive session on networking of stakeholders of Clinical Research, for developing this industry in Pakistan.

This session tried to find answer to the question that what is really required NOW as a follow up of all that has done and said on Clinical research.

The TDAP wants to move Pakistan onto the horizon of clinical research. The ground is clearly fertile, but there are a lot of gaps, so lots of development work is required and there is too much cost involved.

The responses from the participants were,

We should have:

1. A National website devoted to Clinical trials in Pakistan, with portals for Sponsors+ CROs + Clinical sites: having their registry as well as resources.
2. The website should have available links to resource material for clinical trialists, CROs and sponsors.
3. The website could serve as a Registry for trials being conducted in the Country.
4. National Accreditation and Education for clinical trial sites and their staff.
5. PMRC contribution for the site. H.I.M.S. data being collected in Islamabad, by the MOH could be highlighted within the site.
6. National Ethics Committee needed to provide an standard across the country and make approval process more efficient.
7. Commercial knowledge awareness needed.
8. Education, multi faceted drive, involving key staff who can take strategic and tactical strides.

4.15. Provisional Plan for Pakistan to Conduct Research Trials

Dr. Huma Qureshi, Executive Director, Pakistan Medical Research Council, summarized the seminar findings and said that Clinical trials require Patients, Hospital, Staff (investigator, assistants, nurses), Laboratories, NBC or IRB for ethical evaluation, Computerized data management cell, Contract research organization, and Clinical research Units.

She also discussed the requirements stage-wise, some extracts from which have been presented below in the same sequence:

Before the Trial Starts

- Investigator's brochure
- Signed protocol and Case Report Form
- Information for trial subjects (consent)
- Financial aspects/agreement
- IRC/NBC composition and approval
- CV of Investigators
- Normal values of tests

Labs/hospitals

- Certification, accreditation
- Quality assessment (internal/external)
- Other validations
- Procedures for blinding and decoding
- Pre trial monitoring report

During the trial

- Updates in brochures, labs values,
- Any revision
- CV of new members
- Monitoring reports
- Subject identification code list and enrolment log

After completion

- Left over product accountability
- List of investigational product destruction
- List of trial completed subjects
- Audit
- Treatment decoding
- Final report

Dr, Qureshi also summarized the phases of clinical trials, she said that pre-clinical studies involve *in vitro* (test tube or laboratory) studies and trials on animal populations (*in vivo*). Wide-ranging dosages of the drug are given to the animal subjects or to an *in-vitro* substrate to obtain preliminary efficacy, toxicity and pharmacokinetic information. This assists the pharmaceutical companies in deciding whether it is worthwhile to go ahead with further testing.

Phase 0 trial

- Also known as human microdosing studies, are designed to speed up the development of promising drugs by establishing very early on whether the drug or agent behaves in human subjects as was anticipated from preclinical studies.
- Here single sub therapeutic doses of the drug is given to a small number of subjects (10 to 15) to gather preliminary data on the agent's pharmacokinetics (how the body processes the drug) and pharmacodynamics (how the drug works in the body).

Phase 1 Trials

- They are the first stage of testing in human subjects. 20-80 healthy volunteers are paid and studied to assess the safety (pharmacovigilance), tolerability, pharmacokinetics, and pharmacodynamics of a drug.
- These trials are often done in an inpatient clinic, where the subject can be observed by full-time staff until several half-lives of the drug have passed.
- These phase I trials also include dose-ranging, also called dose escalation, so that the appropriate dose for therapeutic use can be found

Phase II trials

- They are performed on larger groups (20-300) and are designed to assess how well the drug works.
- When the development process for a new drug fails, it is usually during Phase II trials when the drug is discovered not to work as planned, or to have toxic effects.
- Some Phase II trials are designed as case series, demonstrating a drug's safety and activity in a selected group of patients.
- Other Phase II trials are designed as randomized clinical trials, where some patients receive the drug and others receive placebo/standard treatment.
- Randomized Phase II trials have far fewer patients than randomized Phase III trials

Phase III studies

- They are randomized controlled multi centre trials on large patient groups (300–3,000 or more depending upon the disease).
- They are aimed at assessing, how effective the drug is, in comparison with current 'gold standard' treatment.

- Because of their size and longer duration, Phase III trials are the most expensive, time-consuming and difficult trials to design and run

After Phase III Trials

- Once a drug has proved to be safe and effective then:
- The results are combined into a large document containing a comprehensive description of the methods and results of human and animal studies
- The manufacturing procedures, formulation details, and shelf life.
- This information is sent for "regulatory submission" for review to the appropriate regulatory authorities.
- They review the submission, and, give the sponsor approval to market the drug.

Phase IV trial

- Also known as **Post Marketing Surveillance Trial**.
- Phase IV trials involve the safety surveillance (pharmacovigilance) and ongoing technical support of a drug after it receives permission to be sold.

Phase III and Phase IV clinical trials of new drugs

- These trials are usually administered by a Contract Research Organization (CRO) hired by the sponsoring company.
- A CRO is a company that is contracted to perform all the administrative work on a clinical trial. It recruits participating researchers, trains them, provides them with supplies, coordinates study administration and data collection, sets up meetings, monitors the sites for compliance with the clinical protocol, and ensures that the sponsor receives 'clean' data from every site.
- Recently, site management organizations have also been hired to coordinate with the CRO to ensure rapid IRB/IEC approval and faster site initiation and patient recruitment.

She said that Large number of patients, Many large and medium sized hospitals, Staff, Laboratories, NBC/IRB, and Data Management cell etc are available in Pakistan, what is required is:

- Staff needs capacity building/training specific to GCP
- Laboratories need up gradation/accreditation/QA
- Data management cell with programmers and analysts
- Clinical Research Units to be established in each potential hospital so that patients and staff are located at specific site and not scattered all over.

She also proposed plans for next 5 years:

Plan for next 5 years

- Strategic Frame work to be developed with partners
- All international clinical trials should be cleared by NBC, registered and monitored
- Establishment of at least 1 clinical research unit per province
- Training of the trainers in GCP and trials on priority.
- Identification of Contract Research Organizations
- Multi centre trials can be done all over the country along with disease specific trials in a province
- With each trial the hospital and its labs get upgraded and personnel get training.

TDAP

PART II
SUMMARY/ CONCLUSION
AND
SUGGESTIONS

5. CONCLUSION

The global business of clinical research projects a tremendous growth for the next decade and offers crucial opportunities for all Asian countries including Pakistan.

Pakistan is the 6th most populous country with 160 million inhabitants and a very large patient population, growing middle class, a large number of trained English-speaking physicians, a low value of Pak Rupee, and a network of high volume medical centres. Many Pakistani physicians have conducted Clinical Trials in other countries also.

Despite of all these advantages the business is in its infancy in Pakistan and only 80 clinical trials have been registered. The growth however is encouraging and Pakistan can now learn from the experiences of US, EU, Latin America, Japan, China, India, South Korea, Taiwan, Hong Kong, Malaysia Philippines and Singapore to increase its share in the global clinical research business, which is currently negligible, 0.1 percent.

Among many reasons that kept Pakistan behind other countries in this area some are: lack of awareness, no government initiatives in the past, lack of coordination between the stakeholders, and misperceptions and little knowledge about Pakistan in the western world.

Some of these misperceptions are that Pakistanis cannot speak English, they do not like talking to foreigners, there are no CROs in Pakistan, and if there are any, then they are not managing any international clinical studies, there are no or very few GCP trained site personnel in Pakistan, and there are no research sites in the country.

The facts however are different. There are eight CROs working in Pakistan, and most of these CROs are involved in international clinical trials in therapeutic care fields such as Oncology, Hematology, Osteoporosis, Infectious diseases, Cardio-vascular diseases, Ophthalmology, and Diabetes. There are many well trained, English speaking health care professionals, mainly doctors, in the country, various multinational Pharmaceuticals regularly train a large number of site personnel, and similarly other CROs also have trained professionals. There are 26 research sites in Pakistan.

There is now a need for developing partnership with the international CROs and other outsourcing providers. Some of the major CROs in the world are interested in working in Pakistan. Such companies need some encouragement from the regulators in Pakistan. Pakistan can be an area of focus for R & D clinical development, however, the field has to be prepared.

The TDAP-MOH Seminar, 'Clinical Research Management in Pakistan', on April 26, 2008, was the first step towards this. The objectives were to introduce the Clinical Trial Business and to understand the roles, responsibilities, and services of CROs, understand the characteristics of a country that becomes a preferred destination for outsourced Clinical Trials, create a national network of health care practitioners, CROs, pharmaceutical industry, Ministry of Health for developing well regulated, ethical and

quality contract research activity in Pakistan, identify other initiatives to facilitate growth of this service industry sector.

The seminar succeeded in creating awareness and understanding the importance of CROs in this business.

An independent CRO provides committed resources for clinical studies. This helps to maintain the high standards set by the industry, such as strict adherence to protocols, excellent clinical practices and complete and accurate documentation. CROs ability to provide timely and proficient trials speed up the process of clinical studies. CROs offer their clients a wider range of pharmaceutical research services including clinical trial management of a high standard. Thus, CRO activities offer good opportunities for health care facilities, conduct clinical trials and data management in accordance with international standard, and provide new and research based treatments to the patients. The training of health care providers in the management of clinical trials improves overall research environment in the country and allows contributions to the knowledge base of the world.

The seminar also provided the insight into the selection criteria on the basis of which a country can attract clinical research business. This includes:

- Adequate patient population, Access to Patients (Number of Subjects) and Patient Demographics
- Number of sites/Access to sites
- Compliance with/Site Development ICH Good Clinical Practice
- A Stable, Honest, Clinical Trial Friendly and Effective Regulatory and Operational framework/environment
- Regulatory and IEC/IRB approval time
- Competitive Start-up time – contract turnaround time
- Import license (study drug, lab supplies)
- Export restrictions (blood, tissue, lab samples)
- Level of Healthcare infrastructure – EC/IRB set-up conforms to ICH-GCP
- Level of Country Infrastructure
- Country Risk Factors
- Standards/Quality of Medical Care
- Other logistic issues (language, medical notes)
- Data Integrity and Copy right protection, IP recognition
- Well trained, experienced, qualified, full time, in-hospital, clinical trial nurses/managers/Doctors
- A potential talent pool from which to hire and to train
- Trainings for developing talent of international standards
- Cost of Labor and size and availability of labor force with relevant skills
- Good quality of investigations
- Level of government engagement
- Commercial considerations
- Security Evaluation

- Sustainability and scalability of business
- Cost of Facilities and Travel
- Perspective of FDA
- Number of CROs
- Number of clinical trials
- Prior performance (research naïve vs. experienced)
- Access to technology (eCRF), lab tests, equipment and/or staffing
- Interest and commitment of Investigators and site staff – time
- Study competition (internal/external)
- Vendor limitations (i.e. central labs)
- Protocol design matching (align with clinical practice)
- Recruitment reliability – projections & previous achievements

Most of the requirements in the above list are available in Pakistan the need is to improve them and create better coordination between the stake holders.

The seminar also brought together the stake holders, the health care practitioners, CROs, representatives from pharmaceutical industry and hospitals, IT people related to the field of clinical research, and Ministry of Health which can be considered as the first step towards creating the national network.

The group emphasized on the importance of conducive regulatory environment, raising awareness regarding integrity of clinical trial data, IT regulatory framework as an integral part of pharmaceutical regulations and the capacity of government inspectors to evaluate not only the clinical trials but also the role of information technology in this business.

The group was of the view that Clinical trial/research is a developing field and Pakistan can attract substantial investment in this vast area by making available the necessary platform and improving legal protection of IPRs, in particular providing protection to test data. This is also because companies invest in countries where IPR protection is adequate. Jordan is one example where improvement and enforcement of IPR laws, resulted in substantial increase in the size of pharma market and exports.

Some of the group members also demanded financial support for international marketing and tax exemptions from the government as is provided to the IT sector and.

It is now required to achieve all the objectives on a broader scale and to identify other initiatives to facilitate growth of this service industry sector.

SUGGESTIONS

Removed from the document and would be included after the review and recommendations from the Minister of State and Secretary TDAP and Secretary Ministry of Health.