

# **Indian Health Scenario**

The infectious diseases are on decline from 56% in 1999 to 25% by 2020, on other hand non-communicable diseases projected to increase from 29% in 1990 to over 57% in 2020.

Affluence, progressive aging of population (more older people), upward socio-economic conditions and changed life styles caused increase in chronic and non-communicable diseases, which is showing an overall upward trend-a typical characteristic of the second phase of epidemiological transition.

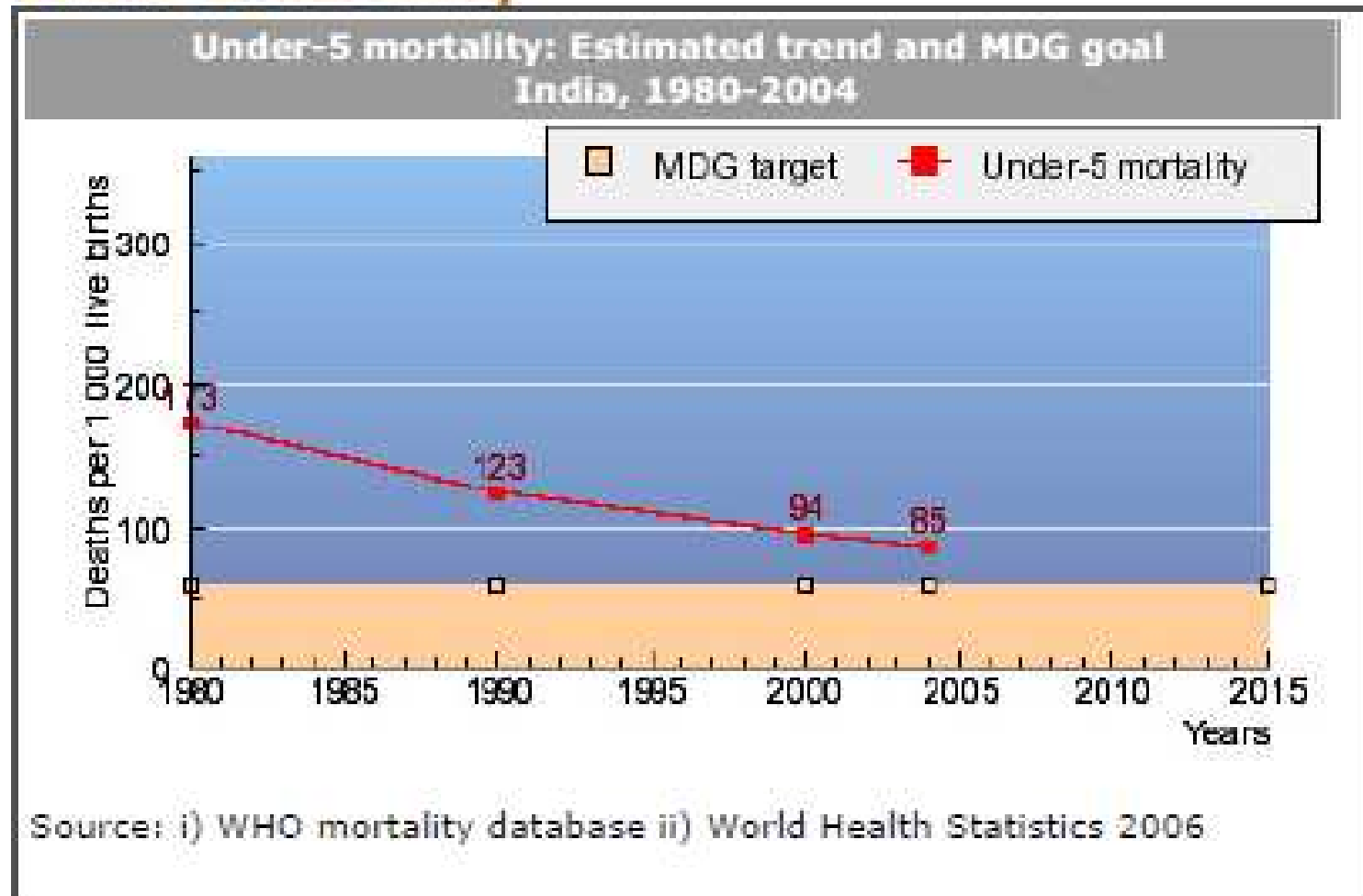
The most remarkable increases among the non-communicable diseases are observed in heart attacks, cancer and paralysis.

Reduction is observed in deaths due to digestive disorders but diarrhoea remains one of the major killers of infants and young children and a formidable challenge to the health system.

Asthma-bronchitis, TB of the lung and pneumonia are accounting heavy toll among the communicable diseases.

Emergence of infectious diseases: AIDS, bird-flu, Dengue, H1N1, resistant strains is also on the rise.

## Under-5 mortality



Among children aged 0 to 4 years, the top 10 causes of death are:

- Diarrhoeal diseases (24%),
- Respiratory infections (23%),
- Other infectious and parasitic diseases (16%),
- Unintentional injuries: other (8%),
- Malaria (7%),
- Nutritional deficiencies (4.8%),
- Symptoms, signs and ill-defined conditions (4.5%),
- Fever of unknown origin (3%),
- Digestive Diseases (1.7% ), and
- Congenital anomalies (1.5%).

Ages 5-14 is generally a period of lower mortality than at ages 0-4 years. The ten leading causes of death at ages 5-14 are:

- Diarrhoeal diseases (17%),
- Unintentional injuries: other (16%),
- Other infectious and parasitic diseases (15%),
- Respiratory infections (10%),
- Malaria (9%),
- Ill-defined conditions (5%),
- Motor vehicle accidents (4%),
- Cancers (2.9%),
- Digestive diseases (2.9%), and
- Fever of unknown origin (2.9%).

The top ten leading causes of death post 25 years of age are:

Cardiovascular diseases (25%), (W: 25.65%)  
COPD, asthma, other respiratory (10.2%), (W: 9.9%)  
Tuberculosis (10.1%),  
Malignant and other neoplasms (9%),  
Symptoms signs and ill-defined conditions (5.3%),  
Digestive diseases (5.1%),  
Diarrhoeal diseases (5%),  
Unintentional injuries: Other (4.6%),  
Intentional self-harm or suicide (3%), and  
Malaria (2.8%), HIV/AIDS 2.4%

Role of Indian pharmaceutical sector towards challenges/threats associated with second phase of epidemiological transition.

## Introduction of Product patent

Post 2005 Indian Patents and TRIPS India stepped into the limelight at a more opportune time while India was experiencing second phase of epidemiological transition. The country became TRIPS compliant and formally recognized product patents and it is now on levels comparable to developed nations.

Thus, for any Intellectual Property (IP) sensitive industry, India is now a destination– not only for R&D but also for contract manufacturing, clinical trials and generic drug research.

## Government to boost pharma sector

It is giving tax exemption for a period of ten years and relieving customs and excise duties of all the drugs and material imported or exported for clinical trials to promote innovative R&D.

### **Deduction for scientific research and development allowance (Under new direct tax code)**

A company shall be allowed a deduction equal to one hundred and fifty per cent. of the expenditure incurred on,-

- (a) creating and maintaining an in-house facility for scientific research and development; and
- (b) carrying out scientific research and development in the in-house facility.

## World ranking of Indian pharma sector

The Indian Pharma industry is now over to Rs 1,00,000 crores (\$ 20 billion) and has shown tremendous progress in terms of infrastructure development, technology base creation and a wide range of products.

It ranks 3rd by volume and 14th by value thereby accounting for around 10% of world's production by volume and 1.5% by value.

Globally it ranks 4th in terms of generic production and 17th in terms of export value of bulk activities and dosage forms.

Consequently, India is becoming the hub for generic drug manufactures providing cost effective drugs to Indian patients as well as other countries (> 200 countries) relatively at a cheaper rates with significant quality.

## Bulk drugs to injectibles

With over 60,000 brands in over 60 therapeutic categories India has world class facilities and expertise in manufacturing with the largest number of US FDA approved manufacturing units in the world outside the US.

From simple headache pills to sophisticated antibiotics and complex cardiac compounds, almost every type of medicine is now made indigenously.

The pharmaceutical industry in India meets around 70% of the country's demand for bulk drugs, drug intermediates, pharmaceutical formulations, chemicals, tablets, capsules, orals and injectibles.

## Status of Indian Pharma sector as on 12. 3. 10

Nearly \$60 billion worth of patents is set to expire in four years

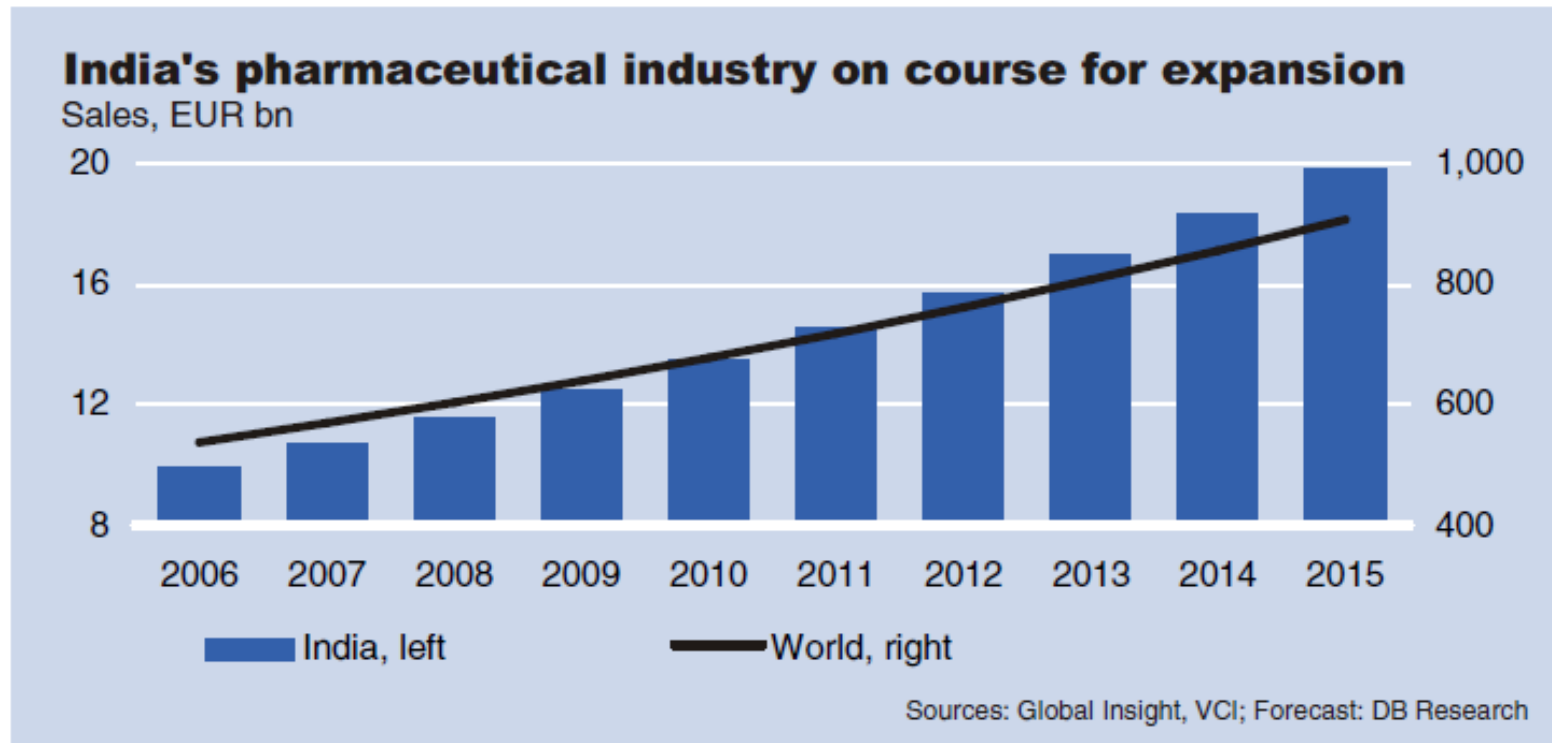
Indian Pharma sector is set to take major share of this pie

Already India is No. 1 exporter of generics with world figure \$8 billion in 2008-09

The Indian Pharma industry is expected to reach \$30 billion by 2020.

## Growth of Indian pharma Market

The Indian pharma market is forecast to grow at three times the pace of growth of the global pharma market during 2006-15. The increasing incidence of chronic diseases and growing accessibility to medical healthcare supported by rising income will help to drive growth.



## Private to multinationals

The Indian pharmaceutical industry directly employs around 500,000 people and is highly fragmented. While there are around 270 large R&D based pharmaceutical companies in India, including multinationals, government-owned and private companies, there are also around 5,600 smaller licensed generics manufacturers, although in reality only around 3,000 companies are involved in pharmaceutical production.

## Top 10 Pharmaceuticals in India, as of 2007

Rank	Company	Revenue 2007 (Rs crore)	Revenue 2007 (USD millions)
1	<a href="#">Ranbaxy Laboratories</a>	4,461	1,026
2	<a href="#">Dr. Reddy's Laboratories</a>	1,933	444
3	<a href="#">Cipla</a>	1,842	423
4	<a href="#">Nicholas Piramal</a>	1,387	319
5	<a href="#">Aurobindo</a>	1,260	290
6	<a href="#">GlaxoSmithKline</a>	1,228	282
7	<a href="#">Lupin</a>	1,180	271
8	<a href="#">Sun Pharmaceutical Industries</a>	1,110	255
9	<a href="#">Cadila Healthcare</a>	1,091	251
10	<a href="#">Wockhardt</a>	980	225

## Top 10 Biotechnology Companies in India, 2007

Rank	Company	Revenue 2007 (Rs crore)	Revenue 2007 (USD millions)
1	<a href="#">Biocon</a>	646	148.6
2	<a href="#">Serum Institute of India</a>	565	129.9
3	<a href="#">Panacea Biotec</a>	217	50.0
4	Venkateshwaria	188	43.2
5	<a href="#">Mahyco Monsanto</a>	166	38.3
6	<a href="#">Novo Nordisk</a>	135	31.0
7	Rasi seeds	87	20.0
8	<a href="#">Aventis Pharma</a>	84	19.4
9	Bharat Biotech	81	18.6
10	<a href="#">Chiron Behring Vaccines</a>	78	17.9

Company	Research areas	Drugs in pipeline	Percent of sales
GSK	Anti-infective, anti-inflammatory, analgesic, gastro-enterological, antiallergic, dermatological.	Otelixizumab anti-CD3 monoclonal antibody type 1 diabetes III <i>Syncria</i> glucagon-like peptide 1 agonist type 2 diabetes III	Generic: 100%
Lupin	Tuberculosis medication, antibiotics, cardiovascular.	LLL-3348 PHASE III Anti-Psoriasis, Herbal(Desoris), LLL 2011 PHASE II anti-migraine(Amigra)	Generic: 100%
Sun Pharma	Neuro-psychiatry, cardiovascular, gastrointestinal, diabetic, gynecological, anti-allergic, antidepressants,	<b>Not available</b>	Bulk: 18% Generic: 82%
Wockhardt	Anti-infectives, anti-biotics, pain management, pulmonary-respiratory, nutraceuticals	WCK 771 commenced Phase II human clinical trials broad-spectrum antibiotic WCK 1152, to treat respiratory tract infections	Bulk: 19% Generic: 81%

Company	Research areas	Drugs in pipeline	Percent of sales
Ranbaxy Labs	Anti-infectives, cardiovascular, gastrointestinal, central nervous system, ophthalmic and ointments, analgesic, anti-asthma, cough and Cold and Vaccines	Phase-III clinical trials Arterolane maleate + Piperaquine phosphate (Anti-malaria combination drug)	Bulk: 22%, Generic: 78%
Dr. Reddy's	Bacterial infections, metabolic disorders, and pain/inflammation.	First Phase III clinical trial of Balaglitazone (DRF 2593) shows significant reduction in HbA1c and improved safety profile	Bulk: 40%,  Generic: 60%
Cipla	Antibiotics, anti-asthmatics, anti-AIDs and TB drugs, anabolic steroids, analgesicsantipyretics, antacids, anti-arthritis, anti-inflammatory, anticancer,	<b>Not available</b>	Bulk: 7%,  Generic:93%
Nicholas Piramal	Analgesics, anti-inflammatory, antibiotics, antifungal, antihistamines, antiseptics, cardiovascular, central nervous system, diabetic,	14 molecules in different phases of development NPS31807	Generic: 100%

## The future of Indian pharmaceutical sector is very bright because of the following factors:

Clinical trials in India cost US\$ 25 million each, whereas in US they cost between US\$ 300-350 million each.

Indian pharmaceutical companies are spending 30-50% less on custom synthesis services as compared to its global costs.

In India investigational new drug stage costs around US\$ 10-15 million, which is almost 1/10th of its cost in US (US\$ 100-150million).

**Role of CSIR Labs in helping Indian Pharma to gain such an enviable position in the area of Generic Drugs and in meeting the new challenge of the product patent regime**

# **Process developed for Generics in CSIR Labs**

# From CDRI - Process Development and Technology Transfer

Disease Area	Generic(s)	Company
Anti-Malarial	Artemether	Themis
Anti-Malarial	Primaquine	Nicholas Piramal
Anti-Malarial	Mefloquine	Wockhardt
Anti-Viral	Acyclovir	Ranbaxy
Anti-Asthmatic	l-Ephedrine	Malladi Drugs & Pharma
Analgesic	d-Propoxyphene	Wockhardt
Analgesic	Paracetamol	Dufor-Interferon + 10 other companies
Anti-Tuberculosis	D-2-Aminobutanol	Themis
Brain-Stroke	Herbal medicament	Themis Medicare
Spermicidal	Isaptent	Hindustan Latex
Hepatoprotective	Picroliv	DIL, Mumbai

## From IICT – Process Development and Technology Transfer

Disease Area	Generic(s)	Company
AIDS (anti viral)	AZT, Acyclovir	Cipla
Anti-Thrombotic	Fondaparinux	Bharath Biotech
Anti-Cancer	Etoposide	Cipla
Anti Inflammatory	RH-8/Enfenamic	Unichem
Cardiac/ cholesterol control	Clofibrate	Ranbaxy
Abortive/oxytocyc ic	Misoprostol/ carboplast Orlistat	AVRA Laboratories
Anti-obesity	Omeprazole	Biocon
Anti Ulcer	Norfloxacin	Cipla
Anti bacterial	Diazepam/Chlordiazepoxi de	Cipla Ranbaxy
Sedative	Eptifibatide	Biocon
Anti-platelet		

# From NCL - Process Development and Technology Transfer

**Anticancer Drugs** - Cytarabine, Etoposide, Vinchrsitine , Camptothecin, Irinotecan, Taxoter , Topotecan

**Cardiovascular Drugs** - Atorvastatin, Rosuvastatin, Simvastatin

**Antidiabetic Drugs** – Miglitol, Repaglinide, Pioglitazone

**Antimalarial Drugs** – Chloroquine, Mefloquine, Artemiscnine

**Antiasthmatic Drugs** – Salbutamol, Ariflo, Azelastin, Montelukast, Zafrilukast, Cisapride

**And many others**

Technologies have been transferred for manufacture and marketing to **Alembic, Cadilla, CIPLA, Dabur, Emcure, Glenmark, Godrej, Agrovvet, Lupin, Orchid Chemicals, Ranbaxy, RPG Life Sciences.**

# **New Drug Development at CSIR**

# Drugs Developed by CSIR

(12 Developed at CDRI, 2 at IICT and 1 at IIM)

Drug	Use	Licensee
● Centimizone (1972)	Antithyroid	*Unichem Labs
● Isaptent	Cervical dilatation (MTP)	*Unichem Labs
● Gugulipid (1986)	Hypolipidemic	*Cipla *Nicholas Piramal Ind. Ltd
● Centbucridine (1987)	Local anaesthetic	*Themis Chemical Ltd.
● Centbutindole (1987)	Neuroleptic	*Chemosyn Pvt. Ltd. *Merind Ltd.
● Centpropazine (1996)	Antidepressant	*Merind Ltd.
● Chandonium iodide (1994)	Neuromuscular blocker	*Ranbaxy Labs Ltd. *Cipla
● Centchroman (1991)	Contraceptive & DUB	*Hindustan Latex Ltd. *Torrent Pharma. Ltd.
● Arteether (1997)	Antimalarial	*Themis Medicare Ltd.
● Elubaquin (2000)	Antirelapse antimalarial	*Nicholas Piramal Ind. Ltd
● <i>Stand. Brahmi</i> extract (2002)	Memory improvement	*Lumen marketing Co.
● Consap Cream (2004)	Spermicidal cream	*Hindustan Latex Ltd.

**(15 out of 18 drugs approved by DCGI in India are from CSIR)**

# CDRI (CSIR) DRUGS IN MARKET

**Ormeloxifene (Female contraceptive)**



**Marketed by Hindustan Latex Ltd.,  
Trivendrum  
in India & Peru**

**Annual turnover 2006-07 Rs. 2450 million**

**Artemether**

**(Antimalarial)**



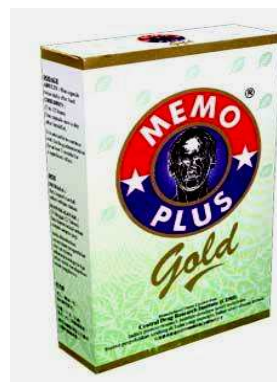
**Marketed By IPCA Labs., Mumbai**  
**Annual turnover 2007-08 Rs. 81 million**

**$\alpha$ - $\beta$  Arteether (Antimalarial)**



**Marketed by Themis Medicare Ltd., Mumbai  
in India & about 30 countries in African  
continent**

**Turnover last 10 yrs Rs. 750 million**  
**CDRI(CSIR)-BESEB (Memory)**



**Marketed by Lumen Marketing Company,  
Chennai**  
**Annual turnover 2007-08 Rs. 6.3 million**



## CDRI – CANDIDATE DRUGS UNDER ADVANCED STAGES OF DEVELOPMENT

Diseases / Disorders	INDs	Efficacy	Clinical status
Liver disorder	Picroliv	Hepatoprotective	Phase III completed
<b>Malaria</b>	<b>Compound 97-78</b>	<b>Antimalarial</b>	<b>Phase I In progress</b>
Diabetes	CDR134D123	Antihyperglycemic	Phase I completed
Osteoporosis	Compound 99-373	Anti-osteoporotic	Phase I to start
Diabetes	CDR134F194	Anti-hyperglycemic & Anti-hyperlipidemic	IND Filed
<b>Malaria</b>	<b>Compound 99-411</b>	<b>Antimalarial</b>	<b>IND to be filed</b>
Cerebrovascular disorders	Herbal Medicament	Anti-stroke	IND to be filed

# New Chemical Entities from CSIR (From IICT, Hyderabad)

Activity	Status	Company
Anti HIV	US Patent 6,191,279	Cytomed
Anti-Asthma	Patent filed	Lupin
Anti Asthma	Patent under preparation	Lupin
Anti-Asthma	Preclinical studies in progress	Lupin
Arterial Thrombosis	Preclinical studies in progress	EVOLVA
Fungal Infections	Preclinical studies in progress	EVOLVA
Influenza	Preclinical studies in progress	Indegene Pharma.
Cancer	Preclinical studies in progress	In house
Gastric Ulcer	Preclinical studies in progress	”
Acetylcholine esterase inhibitors	US Patent No.6649650	”
”	US Patent No. 6855347	”
”	US Patent filed (10/955786)	”

# **Latest Success Story from CSIR**



## Licensed Lead Molecule from IICB, Kolkata

IICB scientists identified an edible herb (Piper betel) commonly known as Paan to have potent anti-Chronic myeloid leukemia (CML) activity and licensed out to Piramal Life Sciences Ltd.

- CML is a kind of blood cancer of myeloid origin and is usually fatal.
- The only available drug costs approximately Rs. 1.5 lakhs for one month treatment.

Phase II human clinical trial with the extract has already been initiated by PLSL & has been referred in Nature Review Drug Discovery (June issue 2009).

## **Licensed Lead Molecule from IMTECH, Chandigarh**

**Nostrum Pharmaceuticals obtained Worldwide Licensing Rights from IMTECH, Chandigarh for Clinical Development of Caerulomycin and its Proprietary Derivatives for their Novel Indication of Immunosuppression.**

## Drug Development – Future

In addition to the various ongoing traditional approaches to drug discovery, several new avenues of drug developments have been initiated at CSIR.

- (a) **BIOLOGICS** – Increased attention is being given to new and upcoming fields to develop ‘biotherapeutics’, ‘**biologics**’ a relatively new class of medicines based on proteins/biomolecules made by living cells.
  
- (b) **SYNTHETIC BIOLOGY** – It aims at design of new and natural biological systems to synthesize small molecules or their precursors in **designer biological systems** for high efficiency and accuracy.
  
- (c) **SYSTEMS BIOLOGY** –The program will also focus on the mechanism of drug combinations, interactions and network perspectives, especially for traditional medicines, plant extracts, etc
  
- (d) **OSDD program** – In the **OSDD** (Open Source Drug Discovery) program, CSIR is providing a global platform where the best minds can collaborate & collectively endeavor to solve the complex problems associated with discovering novel therapies for neglected tropical diseases like malaria, tuberculosis, etc.

## A “Biologic” Licensed from IGIB

A protein with an important therapeutic role, recombinant epidermal growth factor, is being successfully used for treatment of diabetic foot ulcers as well as for burns and skin grafts.

This recombinant protein is being marketed by Bharat Biotech as ‘**REGEN-D**’.

## Recent High Value Technology Licensing

Technology	Company	Revenue (Rs.)
Clot Specific Streptokinase	Nostrum, USA	19.60 Cr. + Royalty 5%
Caerulomycin	Nostrum, USA	14.70 Cr. + Royalty 2%
Fractionation of Sugarcane Bagasse	Godavari Sugar Mills	6.5 Cr. + Royalty 3%
Technology for Carbon Fibre Manufacturing	Kemrock Industries	3.5 Cr. + Royalty 3%
Anti-ulcer drugs	IPCA Labs	2.5 Cr. + Royalty
Epichlorohydrin	Thai Org. Co., Thailand	1.64 Cr.
Head Up Display	BEL	1.6 Cr.
Recombinant Streptokinase	Shasun	1 Cr. + Royalty 3.5%

Rs 1 Cr. = USD 0.2 million

# CONCLUSION

The national laboratories, Pharmas and academic institutions in the country will have to come forward to take new and more aggressive research initiatives and play a major role to usher in the next revolution in the Indian pharmaceutical sector (Similar to INDIAN IT sector) to ensure that affordable healthcare is maintained as a right for all.

# Acknowledgement

**Dr. T. K. Chakraborty,  
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