

**Regulations, IPR protection and Biotech Innovation in
India: Implications of the new Ministry of Health
Guidelines on Biologics**

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Innovations in Developing Countries**

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Outline of Presentation

1. **Biotech industry in India - at a glance**
2. **Regulatory Framework**
3. **Incentives for Innovation**
 - **ABS issues and Biotechnology patents**
 - **Regulatory Data Protection**
 - **Patent Linkage**



The Indian Biotech Industry - At a Glance

- ✓ One of the fastest growing knowledge-based sectors with about 400 biotechnology companies currently operating
- ✓ Biotech industry in India can be divided into five broad categories - bio-pharma, agri-biotech, bioinformatics, bio-industrial and bio-services
- ✓ According to a Association of Biotech Led Enterprises (ABLE) Survey, biotechnology industry in India has notched up a growth of 20 % during 2007 – 08 and the revenues earned were worth USD 2.56 billion. Indian Biotech revenues are projected to reach USD 7.0 billion by 2010
- ✓ Going by the current trend and the new biotech policy of the GOI, the sector is poised to generate USD 13 – 16 billion by 2015 (*India Chronicle, August 2008*)

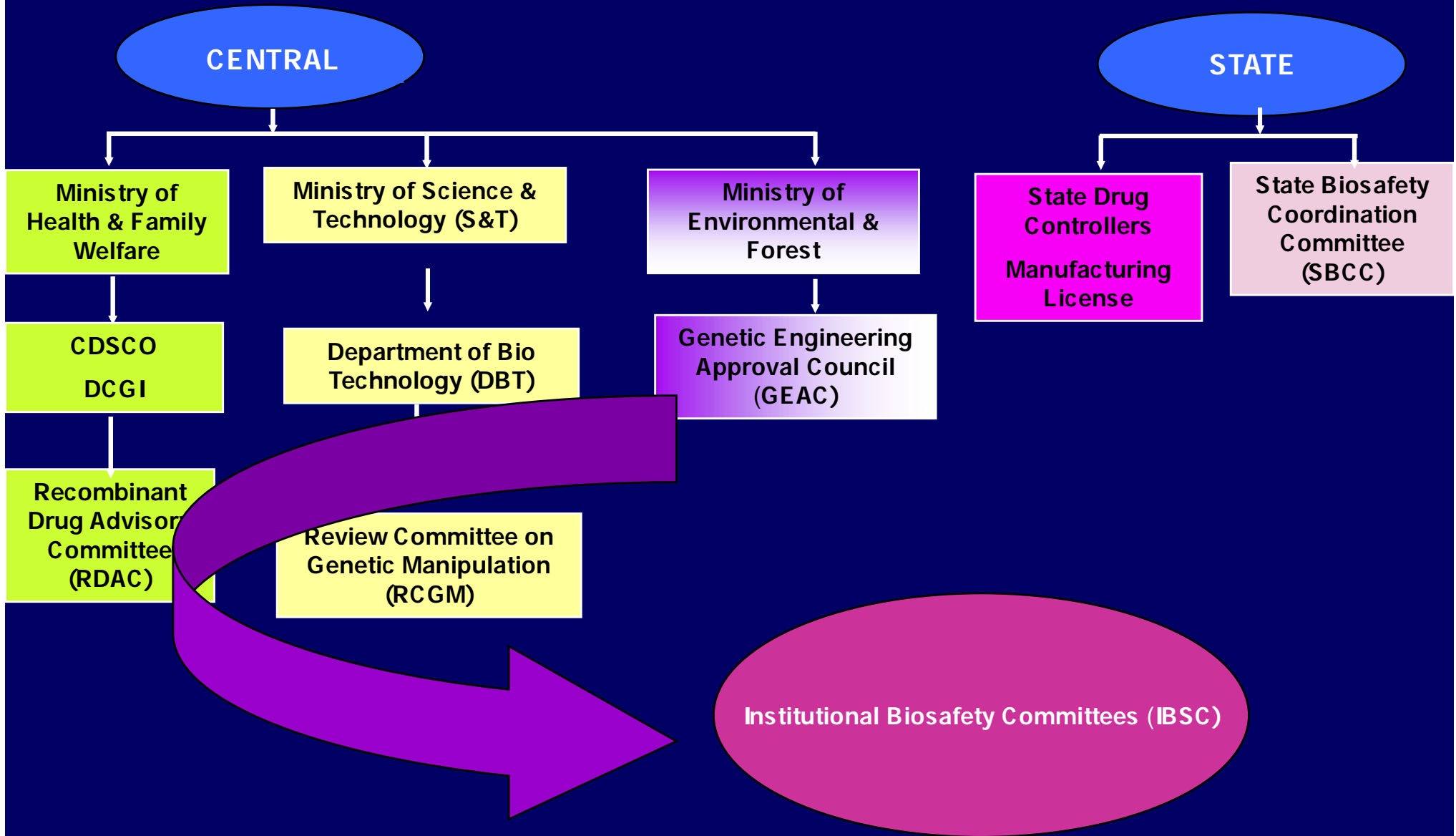
Source: *6th Bio spectrum –ABLE Biotech Industry Survey and India Chronicle, August 2008*



The Indian Biotech Industry - At a Glance

- ✓ Bio-pharma has the largest share. In 2007 – 08, it accounted for 67% of the overall revenues and it is likely to touch USD 4.60 billion by 2012 – 13, (focus on biogenerics and vaccines)
- ✓ 56% is exported of which bio pharma alone accounted for over 70%
- ✓ Over 60% of the total biotech market is shared between 10 companies – Biocon, Dr. Reddy's Lab, Ranbaxy/Zenotech, Shanta Biotech, Wockhardt and so on
- ✓ The Pharma Biotech Industry remains largely generic and export oriented
- ✓ However, Biocon's CEO, Kiran Mazumdar Shaw, told Fortune in 2008, "Unfortunately, [analysts] still tend to categorize us as a generics company...We keep saying, Look, we're not interested in generic companies, because we're trying not to be one." (Source : *Biopharm International, Feb 2008*)

REGULATORY FRAMEWORK





Regulatory Framework

- 1. Proposal made through IBSC - RCGM recommends the application to the DCGI human clinical trials on the basis of pre-clinical data**
- 2. For Submission of Clinical Trial Application for Evaluating safety and efficacy Form 44 of DCA to DCGI and information as per new guidance document - Information to be provided in 4 sections: General Info; Detailed Chemistry Manufacturing and Control as per the format provided ; Non-clinical data and proposed study protocol as per Schedule Y**



Regulatory Framework

**3. For permission of New Drug Approval:
Application in Form 44 and information as
per international CTD format having 5
modules**

Module 1: Administrative/legal info

**Module 2: Summaries of quality and non-
clinical/clinical data**

**Module 3: Quality data (Chemical,
Pharmaceutical and Biological)**

Module 4: Non-clinical data as per Schedule Y

Module 5: Clinical Information as per Sch Y

**Additional Undertaking by applicant, PPD
(Product Permission Document) and
Summary of Product Characteristics to be
submitted as appendices to CTD**



Regulatory Framework

- 4. Application to be made in Form 44, Schedule Y of Drugs & Cosmetics Act Rules to the DCGI**
- 5. RDAC approves the protocol and recommends for conducting human clinical trials**
- 5. IBSC examines the human clinical trial data and sends it to DCGI for commercial release OR recommends to GEAC for environmental release if an LMO**
- 6. Clinical Trials – RCGM decides the scope on a case to case basis: Phase I: 10 - 12 patients; Phase II: 12 - 30 patients; Phase III: 100 - 150 patients**



Regulatory Framework

7. For marketing license, DGCI approval required under the DCA Rules, 1945

- i. Form 41: Registration of production facilities and the drug. If manufactured in India, State Drug controller gives the license**
- ii. Form 10: Import License**
- iii. Form 11: Temporary license for import of drugs for examination, test or analysis – samples sent to CRI, Kasauli or CDL, Kolkata**
- iv. Form 45: License for Marketing**



Regulatory Framework

❑ Post Marketing Approval

- ✓ Schedule Y – requires monitoring for clinical safety and periodic safety update reports (PSURs) – every 6 months for the first two years and for the subsequent 2 years annually
- ✓ It may be a condition of license
- ❑ Currently no clearly defined rules exist for submitting post approval changes. The conditions of Form 45 and Form 41 are taken as the basis for submitting variations mostly as notifications



Regulatory Framework

However, the New Guidance for Industry on Biologics December 30, 2008 uses science-based and risk-based approach for classifying and reporting and/or approving changes after the product has been approved. There are three reporting categories:

Level 1 – Major quality changes – *extensive supporting data* After 30 days of submission if no comments from DC GI – change can be implemented

Level 2 – Moderate quality changes – if within 15 days of submission no comment received from DC GI, the change can be implemented

Level 3 – Minor quality changes – *no prior approval or review needed*. Can be submitted as a annual notification

Examples of different types of changes, the type of reporting category that the change will fall under and the relevant supporting documents for submission is provided

DCGI MoHFW	MoEF	DBT Min. of S&T	ICMR	OTHERS
<p>Drugs and Cosmetics Act 1940 & Rules 1945 thereunder</p>	<ul style="list-style-type: none"> ✓ Environment Protection Act 1986 ✓ Rules for Manufacture, Use, Import and Export and Storage of Hazardous Microorganisms, Genetically Engineered Organisms of Cell, 1989 ✓ Revised Protocols for Recombinant Biopharmaceuticals 2006 ✓ National Environmental Policy, 2006 ✓ Biological Diversity Act, 2002 and Biological Diversity Rules, 	<ul style="list-style-type: none"> ✓ Recombinant DNA Safety Guidelines, 1990 ✓ Revised Guidelines for Safety in biotechnology, 1994 ✓ Guidelines for generating pre-clinical and clinical data for rDNA vaccines, diagnostics and other Biologicals, 1999 ✓ Ethical Policies of the Human Genome, Genetic Research and Services 	<ul style="list-style-type: none"> ✓ Ethical Guidelines For Biomedical Research on Human Participants , 2006 ✓ Guidelines for Good Clinical Laboratory Practice, 2008 ✓ Guidelines for Stem Cells Res and Therapy, 2007 ✓ Ethical Issues & Consent Process Pertaining to Stem Cell Research ✓ Draft Guidelines For Compensation to Participants in Research Related Injury in India(2008) 	<p>DGFT</p> <ul style="list-style-type: none"> ✓ Foreign Trade Policy (2006) <p>Min. of Chem. & Fertilizers</p> <ul style="list-style-type: none"> ✓ Pharma Policy 2002

REGULATORY FRAMEWORK : USE OF LMOs AS DRUGS

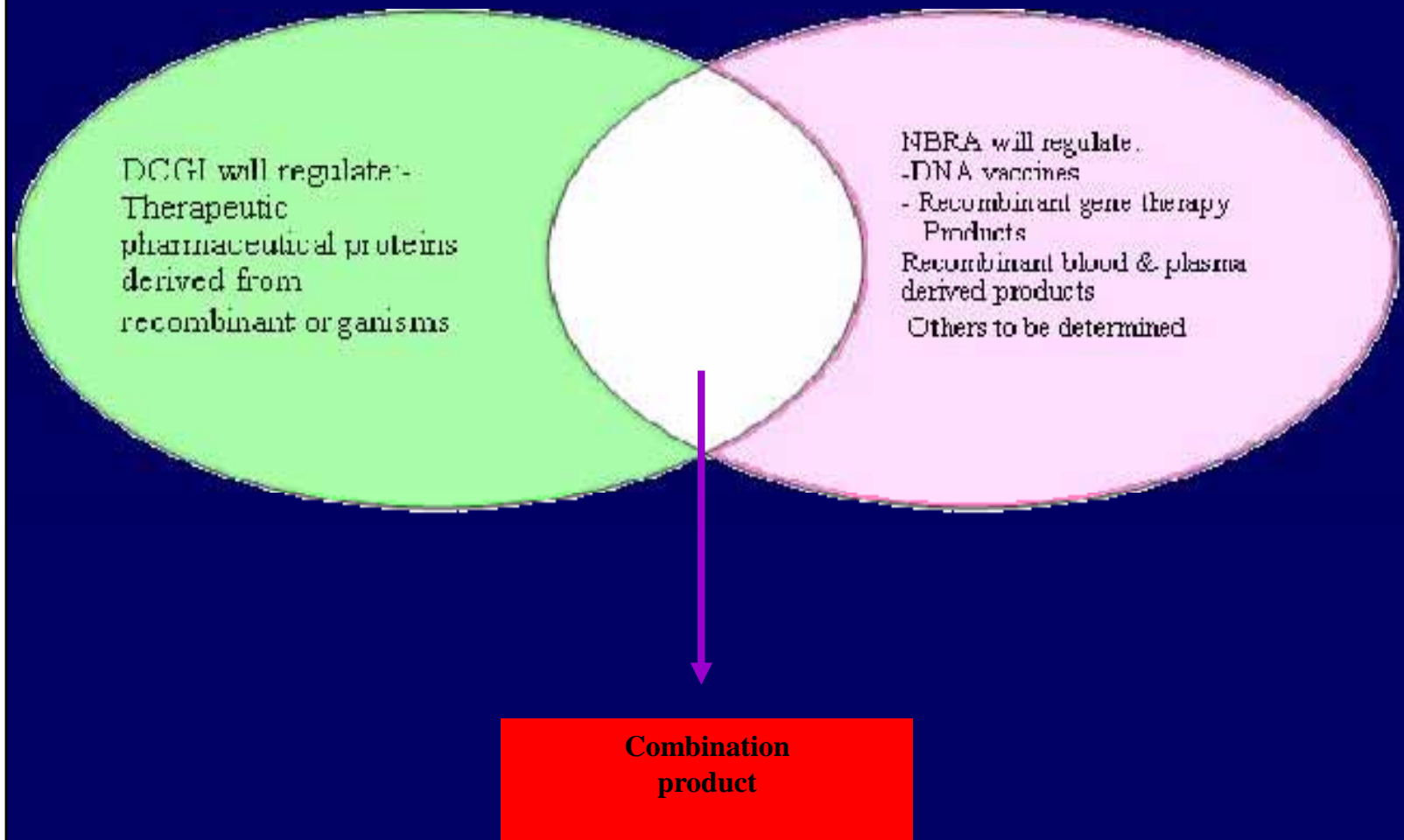
Notification w.e.f. April 1, 2006 created a graded system of scrutiny; detailed assessment being reserved for product categories where the risk concern is higher. It also stipulated fixed timelines for approval at different stages. *LMOs include only those organisms modified by r-DNA techniques through human interventions where the end product is living modified organism*

Protocol I	Indigenous development, manufacture & marketing of pharmaceutical products derived from LMOs but the end product is not a LMO	DCGI (MoH&FW) GEAC (MoE&F) IBSC (DBT,MoS&T) RCGM (MoS&T)
Protocol II	Indigenous development, manufacture & marketing of pharmaceutical products where the end product is a LMO	DCGI (MoH&FW) IBSC (DBT,MoS&T) GEAC (MoE&F) RCGM (MoS&T)
Protocol III	Import & marketing of LMOs as drugs/pharmaceuticals in finished formulations where the end product is a LMO	DCGI (MoH&FW) GEAC (MoE&F)
Protocol IV	Import & marketing of LMOs as drugs/pharmaceuticals in bulk for making finished formulation where the end product is a LMO	DCGI (MoH&FW) GEAC (MoE&F) IBSC (DBT,MoS&T) RCGM (MoS&T)
Protocol V	Import & marketing of products derived from LMOs as drugs/pharmaceuticals in bulk and/or finished formulations where the end product is not a LMO	DCGI (MoH&FW)



Regulatory Framework

A National Biotechnology Regulatory Authority (NBRA) is under consideration.
Stakeholder consultations on.





Regulatory Framework

Separate guidelines for Bio Generics are also being considered

- ✓ India recognizes the need to formulate separate Guidelines for regulating Biogenerics in India
- ✓ DBT has constituted a five member Committee to look into framing of the guidelines to be ready within 2-3 months
- ✓ India is advocating a pathway based on clinical comparability (reduced pathway) at the WHO deliberations for Guideline document on biosimilars – this is likely to feed in to the domestic regulations



Regulatory Framework

Regulatory pathway for new product category should be distinct from generics

- ✓ **Guidance should be category specific**
- ✓ **Reference products should have extensive clinical data and market experience**
- ✓ **Products should have similar molecular structural properties and quality standards as reference product**
- ✓ **Case-by-case approach with non-clinical and clinical requirements to demonstrate safety and efficacy for each indication**
- ✓ **Appropriate risk management and active pharmacovigilance**
- ✓ **Should include a system of distinct names and labeling system clear prescribing, dispensing & surveillance). Science does not support automatic interchangeability/substitution**



Incentives for Innovation

- ✓ **Development of biologics is time-consuming, costly and risky**
- ✓ **Important to encourage innovation in new biological products**
- ✓ **Efforts from innovators need protection: Patents; RDP; patent linkage and Trade Secrets**



Biotech Patents

- ✓ Indian patent practice and jurisprudence with respect to the patenting of biological materials are relatively new and thus not so well settled and/or uniform.
- ✓ The Indian Patents Act does not describe, in an inclusive manner, what is patentable. Rather, Section 3 includes a list of inventions considered not patentable
- ✓ Some of these exceptions reflect ones found in TRIPS Article 27.2 and 27.3 –
 - (i) ordre public and morality exception - Sec 3 (b)
 - (ii) discovery of living things or non living substances in nature - Sec 3 (c)
 - (ii) plants and animals and parts thereof other than micro-organisms - Sec 3 (j)
 - (iii) essentially biological processes for the production of plants or animals other than non-biological and microbiological processes – Sec 3 (j)
 - (iv) methods used for the surgical, diagnostic or therapeutic treatment of humans or animals – Sec 3(i)



Biotech Patents

- micro-organisms and other living organisms other than plants or animals, are patentable provided the organism is novel, involves an inventive step, and is industrially applicable
- Submission and/or deposition of biological material to an International Depository Authority (IDA) is **required if adequate disclosure is not possible - Sec.10(4)(ii)**
- Enforcement of patents continues to be a challenge – several cases are before high Courts in Chennai, Mumbai and Delhi



ABS Issues & Biotechnology Patents

- ✓ **Mandatory disclosure in patent application of source and geographical origin of biological material and traditional knowledge used in invention - Sec.10(4)(d) of Indian Patents Act, 2005**
- ✓ **The law also provides for pre-grant opposition and revocation of granted patents of grounds of non-disclosure or wrongful disclosure of source or geographical origin of biological resources and traditional knowledge - Sec. 25(1) & Sec. 64**
- ✓ **National Biodiversity Authority's prior approval is required for accessing biological material by foreigners/NRIs (Sec. 3) as well as before seeking patent based on biological material and TK obtained from India Sec 6(1) of Biodiversity Act 2002**
- ✓ **ABS provisions in Biodiversity Act, 2002**



Regulatory Data Protection (RDP)

- ✓ No RDP for bio pharma products – Rule 122A of Drugs and Cosmetics Rules 1945
- ✓ Presently, the DCGI approves a new drug
 - 1) if the drug is in use in another country
 - 2) on submission of a limited Phase III confirmatory study on 100 patients
- ✓ The current thinking on RDP is that non-disclosure may be provided for but non-reliance aspect is “TRIPS- Plus”



Patent Linkage

- ✓ Under the current Indian regulatory system - no patent linkage
- ✓ Despite a valid and subsisting patent covering a product, the DCGI is free to grant marketing approvals to subsequent applicants for the same product covered by the patent – making mockery of the grant

THANK YOU



Ms. Krishna Sarma

Managing Partner

CORPORATE LAW GROUP

1106-1107, Kailash Building,

26, Kasturba Gandhi Marg,

New Delhi-110001

Tel : 91-11-43621000 (100 Lines)

Mob : 91-9811734567

Fax : 91-11-23357721

Email: krishnasarma@clgindia.com

www.clgindia.com