CBCC GLOBAL RESEARCH

REGULATORY SCENARIO IN INDIA AND CBCC OFFERINGS

REGULATORY CONSULTANCY SERVICES

The Central Drugs Standard Control Organization (CDSCO), under the Directorate General of Health Services (DGHS), Ministry of Health & Family Welfare (MoHFW) and Government of India (GoI), is the national regulatory authority of India.

India's regulatory regime for pharmaceuticals and medical devices has undergone many changes in the recent past, and is moving towards a mature and competitive level as that of the United States Food and Drug Administration (USFDA) & European Medicines Agency (EMA). Though India has emerged as hub for clinical trials, it's evolving regulations might pose challenges for foreign pharmaceutical, medical device and biotech companies.

CBCC offers highly professional and effective regulatory strategies for obtaining clinical trial permission and product registrations. Our experts are adept in handling end-to-end regulatory assignments for obtaining clinical trial permissions, market authorizations and product life-cycle management.

CBCC Global Research acts as your Indian agent & regulatory partner and helps you get through all regulatory applications and approvals, and is not limited to drug, cosmetic or medical devices with the CDSCO and DCGI offices.

WHAT DO WE DO?

We provide a wide range of regulatory consultancy services to pharmaceutical, medical device and biotech sector companies that are required for obtaining permission for clinical trials and product registrations.

Some services that we offer include:

- Designing regulatory strategy
- Gap analysis
- Pre-screening of dossier
- Indian agent services
- Global clinical trial
- Clinical trial waivers
- Bioavailability and Bioequivalence for export purposes
- New drug approvals
- Import registrations
- Medical device CT
- Medical device import registrations
- Key opinion leaders (KOL) engagement
- Subject Expert Committee (SEC) meetings
- Post approval changes
- CTRI registration and updates

DESIGNING REGULATORY STRATEGY

We, at CBCC, believe that regulatory strategy is very critical to obtain timely approvals for clinical trials and marketing authorizations. Backed by significant experience, having performed several types of successful regulatory approvals, CBCC provides clients with the best-suited regulatory strategy for effective and timely approvals.

We help companies in designing right regulatory strategies for:

- Establishing best possible regulatory approval pathways
- Ascertaining regulatory risks involved, and predicted success rates
- Obtaining clinical trial permission for various phases of trials
- Obtaining permission of clinical endpoint bioequivalence studies
- Phase 3 clinical trial waiver application
- Engaging KOL to develop study protocol, clinical development plan and SEC meetings
- Strategizing for positive SEC meetings
- New Drugs (ND)
- Subsequent New Drug (SND)
- Fixed Dose Combinations (FDC)
- Investigational New Drug (IND)

GAP ANALYSIS & PRE-SCREENING OF DOSSIER

Implementing e-Governance at CDSCO through the SUGAM portal has brought simplicity, transparency, reliability, accountability, timeliness and has simplified the ease of business. It is the project of national importance that directly reflects the government's DIGITAL INDIA initiative, and is a major influence in bringing reforms in the Indian pharma industry.

SUGAM enables online submission of applications requesting for permissions related to drugs, clinical trials, ethics committee, medical devices, vaccines and cosmetics. It builds a database of approved drugs, manufacturers & formulations, retailers & wholesalers in India. The portal also consolidates & publishes data about various RCs/licenses issued by various states FDA offices in India.

Prime objectives of the project are:

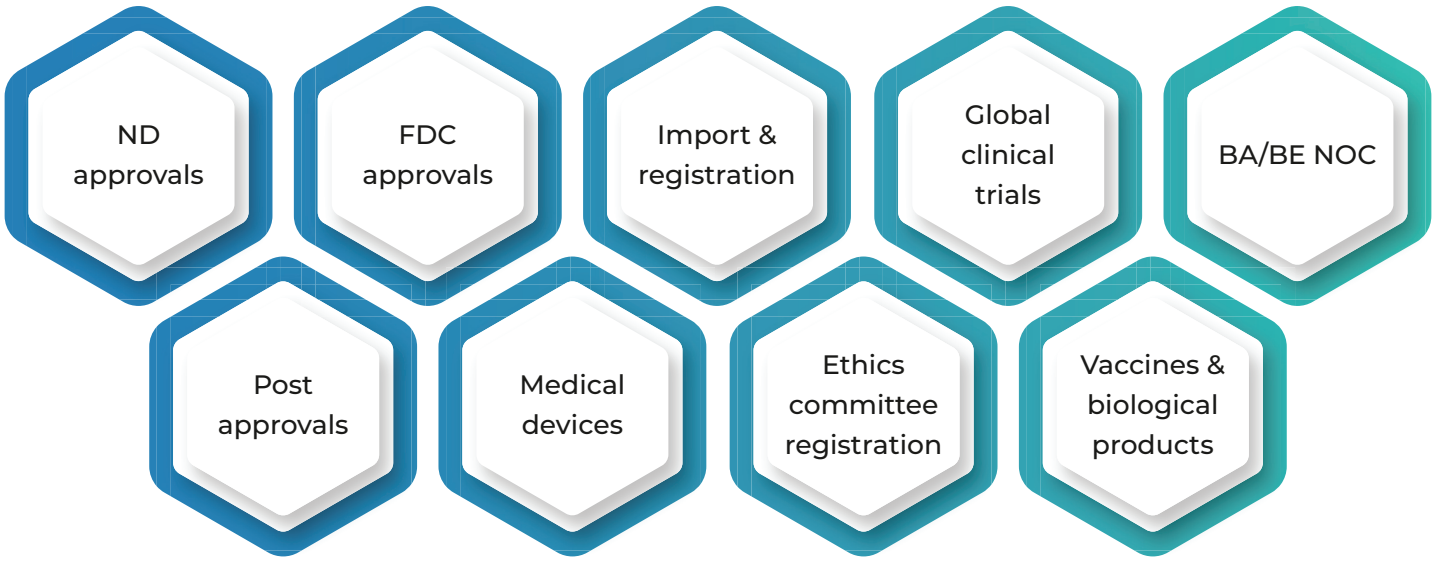
- To establish a single window for multiple stakeholders involved in the processes of CDSCO
- To consolidate the Indian Drug Regulatory Framework by streamlining CDSCO processes
- To enable paperless grant of various clearances by CDSCO
- To enable higher level of transparency in drug regulatory processes
- To enable ease of business for pharmaceutical & regulatory agencies
- To enable greater outreach of citizen centric & consumer centric information related to quality and standard of drugs in India

We do a thorough product analysis and analyze categories for filing the product as per the SUGAM checklist on behalf of the client. The application checklist for different products is different as per the guidelines, and is mandatory to be filled for successful submissions. We help in compiling all necessary documents as per the current guidelines. Any deficiencies in gap analysis are communicated with the sponsor. The strategies are mutually discussed and agreed upon before filing the application.

Queries are generated in SUGAM portal and are communicated with sponsor on almost real-time bases. We liaison with the CDSCO office to better understand the queries before submitting a response thus, it helps reduce review cycles and multiple queries in the application.

INDIAN AGENT SERVICES

As per the Indian regulations, applications can be filed only by an Indian or and Indian company. For our foreign clients, we act as the Indian agent and regulatory partner to provide support for CT & registration of drugs, cosmetics, medical devices & biologics.



We help our clients throughout the process of regulatory procedures by providing step-by-step support for successful submission.

- Analysing approval requirements
- Coordinating & compiling dossier
- Pre-screening technical documents for errors
- Performing submissions (online & offline, as applicable)
- Assisting replying to queries
- Taking physical follow-ups at related government departments
- Presenting SEC on behalf of the sponsor
- On-time approval

GLOBAL CLINICAL TRIAL

With the 2nd largest population in the world and abundant resources like qualified trained and experienced investigator and support staff, India is a hub for large numbers of global clinical trials for registering with international regulatory agencies. However, getting GCTs cleared from CDSCO and SEC is a challenge for international clients.

Application for a GCT approval includes careful planning and flawless execution. It involves 3 sets of documents listed below:

1. **Essential study documents:** protocol, ICF, dummy CRF, IB, IMPD, IRB and regulatory approval of other countries
2. **Documents required from Sponsor:** clinical and non-clinical data, affidavits & declarations, rational for conducting the study in India, clinical development plan, draft label and cGMP certificate of manufacturing site
3. **Documents from sites:** CV & MRC of PI, Investigator Undertaking (IU), Protocol Signature Page (PSP)
4. **Documents prepared by CBCC:** executive summary, challan, declarations, CTA, budget and insurance certificate

CBCC helps the sponsor in receiving, processing and responding to any queries received from the CDSCO office on the SUGAM portal.

GCT applications are referred to SEC review for the respective therapeutic area. CBCC with help of in-house experts, KOLs, potential investigators and sponsor attends the meeting and defends the case in front of CDSCO & SEC. Usually it takes about 1-3 meetings to get the proposal cleared from SEC. CBCC's vast experience of attending SECs and network of KOLs helps the sponsors to get the approval sooner than expected timelines.

CLINICAL TRIAL WAIVERS

As per the CDSCO, local clinical trial waiver for approval of a new drug, which has already been approved in other countries, can be considered under following conditions:

A. The new drug is approved and marketed in countries specified by the CLA under rule 101 and if no major unexpected serious adverse events are reported and there is no probability or evidence, on the basis of existing knowledge, of difference in Indian population of the enzymes or gene involved in the metabolism of the new drug or any factor affecting pharmacokinetics and pharmacodynamics, safety and efficacy of the new drug, and the applicant has given an undertaking in writing to conduct Phase IV clinical trial to establish safety and effectiveness of such new drug as per design approved by the CLA

B. For import of a new drug for which the CLA had already granted permission to conduct a global clinical trial which is ongoing in India and in the meantime such new drug has been approved for marketing in a country specified under rule 101, and there is no probability or evidence, on the basis of existing knowledge, of difference in Indian population of the enzymes or gene involved in the metabolism of the new drug or any factor affecting pharmacokinetics and pharmacodynamics, safety and efficacy of the new drug, and the applicant has given an undertaking in writing to conduct Phase IV clinical trial to establish safety and effectiveness of such new drug as per design approved by the CLA.

C. Further, in general, the requirements of non-clinical and clinical data may be relaxed, abbreviated, omitted or deferred under life threatening or serious disease conditions or rare diseases and for drugs intended to be used in the diseases of special relevance to Indian scenario or unmet medical need in India, disaster or special defense use e.g. haemostatic and quick wound healing, enhancing oxygen carrying capacity, radiation safety, drugs for combating chemical, nuclear, biological infliction etc. However, such relaxation, abbreviations, omission or deferment of data will be evaluated on case-by-case basis depending on the nature of the new drugs, proposed indication, etc.

With the aid of our extensive network of KOLs in various therapeutic areas, we help assesses the possibility of getting a waiver for Phase 3 clinical trial for registration of new drugs in India. This not only helps companies to launch their products early but also helps patients to gain early access to medication. CBCC experts and KOLs help companies in designing their strategies and defending the request in SEC meetings.

BIOAVAILABILITY AND BIOEQUIVALENCE FOR EXPORT PURPOSES

India is the hub for generic medicines and clinical bioequivalence studies required for registering generic products compared to Europe, the USA and other regulatory agencies. Looking at higher number of applications in this category, the CDSCO office had setup a dedicated division to take care of such applications of BE studies for export purpose.

CBCC has vast experience in conducting patient-based BE studies for export purposes. Our regulatory experts help the sponsors in getting the expedited and favorable opinions for complex generic drug BE study application. We have also successfully attended the SEC meetings for such applications in the past.

KOL ENGAGEMENT

KOLs help shape your product and help it to reach its target market. Importance of leveraging KOLs in the healthcare industry has not changed but accessing and engaging with these experts has become increasingly difficult over the years.

Our deep roots in the healthcare industry has helped us connect and form working relationships with KOLs from a wide range of therapeutic areas.

KOL engagement involves forming relationships with expert clinicians and healthcare professionals of the target market or amongst key stakeholders to gain their input and other valuable insights to help strengthen the company's competitive edge. Engaging with them is similar to forming a relationship with a trusted advisor/mentor and is mutually beneficial.

Our network of KOLs in India and USA not only helps us but also our sponsors in various stages of product development. Our KOLs provide valuable inputs in the following aspects:

1. Product development
2. Disease understanding and epidemiology
3. Standard of care and areas of research
4. Designing clinical studies to demonstrate safety and efficacy
5. Review and opinion on clinical study protocol
6. Sponsor meetings
7. Meetings with regulatory agencies like the USFDA, EMA, and CDSCO
8. SEC meetings
9. Providing therapeutic trainings to trail staff
10. Medical advisory board
11. DSMB
12. Investigator identification

SEC MEETINGS

CBCC has immense experience and expertise in handling SEC meetings in India. Our scientific and medical teams attend these meetings on behalf of the sponsor and help them in defending these meetings for successful outcomes.

Our experience in attending SEC meetings:

COVID-19: 8 meetings	Dermatology: 3 meetings
Oncology: 12 meetings	Ophthalmology: 8 meeting
Neurology: 5 meetings	Analgesia: 2 meeting
Gastroenterology: 4 meetings	Reproductive and urology: 2 meetings

Based on our experience with multiple applications, our regulatory team prepares a detailed checklist of the required documents and coordinates with the regulatory agency to get regular updates on SEC meeting schedules for the appropriate therapeutic area.

A detailed presentation is prepared by the CBCC team, which includes protocol details, rationale for conducting the trial in India, risk versus benefit assessment and other aspects related to the trial. This presentation is reviewed by the sponsor for their inputs.

CBCC invites SMEs of the applicable therapeutic area to participate in the SEC meeting.

Based on the suggestions received during the SEC meeting, our team drafts a response and consults with the sponsor before submitting the responses to the DCGI office.

Owing to our detailed dossier analysis, preparing for SEC meetings and handling questions during the meeting, we have successfully defended 90% of SEC meetings so far.

POST-APPROVAL CHANGES

In addition to receiving permission, our team also assists customers to get post-approval changes approved in the shortest time possible.

Post-approval changes typically include:

- Addition/deletion of sites
- Addition/deletion of investigators
- Protocol amendments
- Notification of minor changes
- Notification of EC approvals
- Submission of periodic reports
- Application of additional test licenses for investigational products
- Application for lab kits required for clinical studies

CTRI REGISTRATION AND UPDATES

CTRI is equivalent to the www.clinicaltrials.gov in the USA. CTRI registration is taken care of by ICMR's National Institute of Medical Statistics. It offers a free, online public record system for registering clinical trials conducted in India in addition to multi-national trials where India is participating. Although it was initiated as a voluntary measure, trial registration in the CTRI is an important mandatory step now. For publications, it is compulsory to provide a registration number for each trial conducted in India.

CTRI datasets include Indian investigator details, trial sites, Indian target sample size and date of enrollment. Once a trial is registered, updating the trial status including changes is mandatory.

CBCC helps the sponsor to register their trial on the CTRI website. We prepare draft datasets and get them reviewed by the sponsor before publishing details on the CTRI website. We also periodically update CTRI datasets. It usually takes 2-4 weeks to get a trial registered on CTRI.

www.ctri.nic.in

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