An update on **Regulatory Scenario in India**

cliantha
Science Integrity

Introduction:

India being one of the most populated countries with 1.3 billion people and a premier emerging economy is key market for multinational pharmaceutical and biotech companies to launch their drug products. As a growing market, innovator drug and biotech companies are required by the drug regulatory authority of India to conduct clinical studies involving the local population to prove safety and efficacy of the drug product.

The Drug Controller General of India (DCGI) is the key Indian regulatory that grants approvals based on two factors: a review of clinical data and a determination of manufacturing quality. The Central Drug Standard Control Organization (CDSCO) office handles this process. Note, occasionally in addition to the CDSCO approval, the state drug control authority's approval may be required.

Independent of the fact that clinical trials are a mandate as per Indian regulatory requirements; India has been one of the favored destinations for pharmaceutical and biotech companies to conduct clinical trials. They perform the research in India due to the availability of vast and varied pool of patients plus a maturing contract research sector with the required experience and developed infrastructure.

In 2012 to 2014 there were challenges when applying to perform research in India, it was a period where the government was establishing protections for the Indian population and developed the initial procedures. Today, it can be confidently stated that, the regulatory authority have issued clear rules and guidelines. The current rules have made applications clear and routine. This new process has standardized the applications to the regulatory body and timelines for approvals. Now, India is once again, an advantageous location to conduct clinical trials.

Regulatory Authorities in India; Roles & Responsibilities:

The Central Drug Standard Control Organization (CDSCO) is the key authority for new drug approvals in India, which is headed by the Drug Controller General of India (DCGI). CDSCO is responsible for drug approval and overseeing clinical trials, good manufacturing practice (GMP) monitoring, and other related functions as specified by the central government. The CDSCO is a subordinate office of the Director General of Health Services (DGHS) in the Ministry of Health and Family Welfare (MHFW).

Authority	Main Function	Description/Responsibility
Ministry of Health & Family Welfare	Policy making body	Overall Policy and Planning authority
Director General of Health Services	Advisory & oversight	Technical advisor on all medical & public health matters. Oversight of CDSCO
Central Drugs Standard Control Organization (CDSCO) headed by the Drug Controller General of India (DCGI)	Regulatory Body	Market authorization of new drugs, clinical trials approvals, approval & monitoring of drugs manufacturing

Figure 1: ***India – key regulatory authorities and their responsibilities***

Bottle Neck did occur:

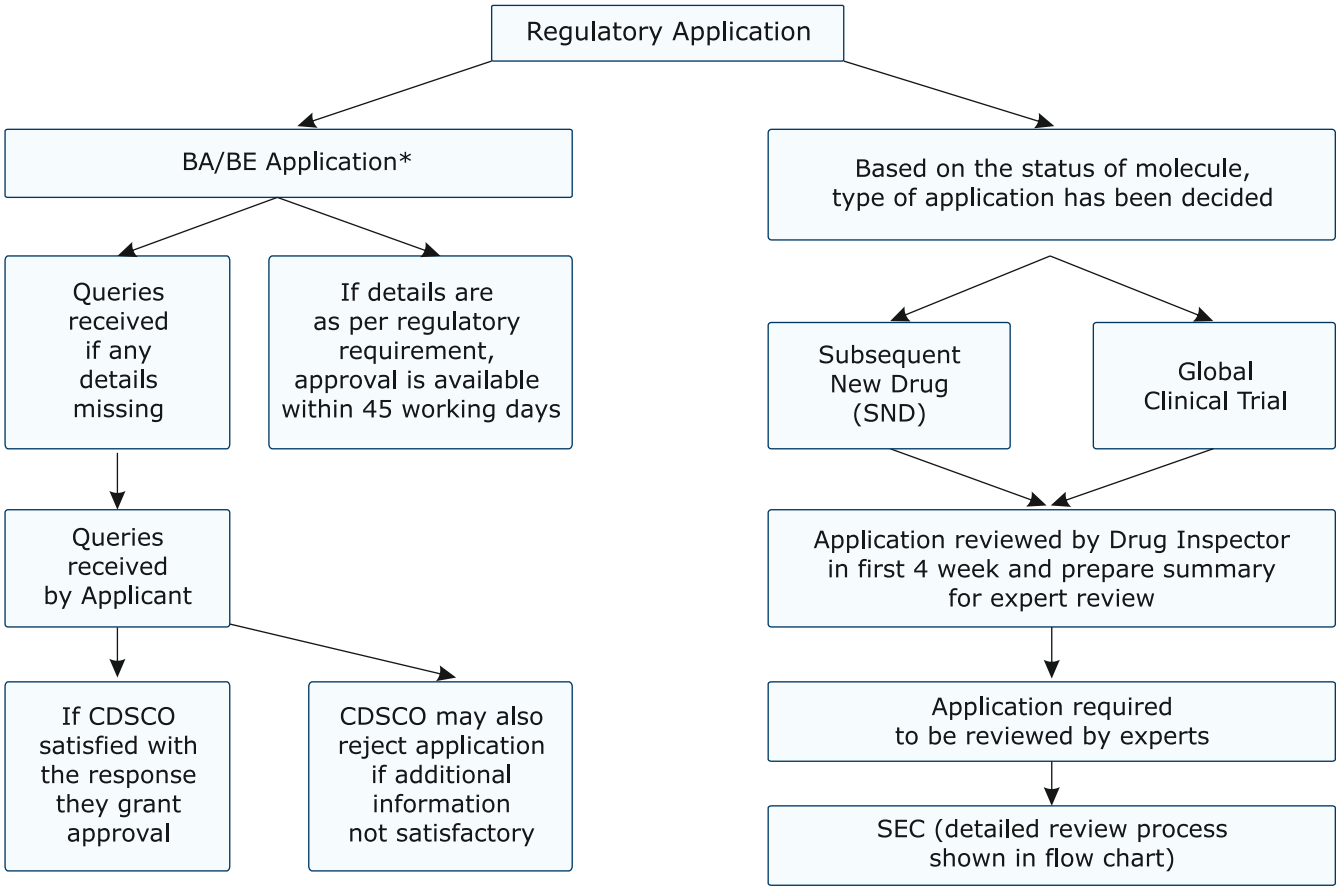
There was a lag period between 2012 to 2014, where approvals were not granted, dossiers were rejected and drastic changes were suggested by the regulators on the study designs and protocols. At this time pharmaceuticals companies reduced their clinical research in India. When amendments to the clinical trial regulations were introduced in India in February 2013 to improve patient safety, this situation began to improve.

One of the changes created difficulties for researchers willing to conduct clinical trials. The amendments included procedures for reporting serious adverse events including deaths during clinical trials and the payment of compensation to patients. Researchers and Contract Research Organizations (CRO) raised issues with the provision in the guidelines. The provision stated that free medical treatment has to be provided to the patient irrespective of whether the impairment was due to a clinical trial or not.

The government heard the objections raised by Industry. In fact, the Health Ministry on consultation with the Drug Technical Advisory Board (DTAB) and suggestions from the Industry Experts introduced an amendment in The Drugs and Cosmetics (Sixth Amendment) Rules in December 2014 and effective starting June 2015. The amendment stated that "In case of injury occurring to the subject during the clinical trial, free medical management shall be given as long as required or till such time it is established that the injury is not related to the clinical trial, whichever is earlier" and additional also stated "In case, there is no permanent injury, the quantum of compensation shall be commensurate with the nature of the non-permanent injury and loss of wages of the subjects".

The introduction of several proactive amendments subsequently by the Ministry of Health (MOH), Govt. of India brought back the certainty of the protection and the matter of compensation for SAEs. Today, the pharmaceutical companies, once again, consider India as a favored destination to conduct their clinical studies. As a result of that the collective regulatory changes, the clinical trial approval process is revised and on par with many other global regulatory agencies.

Clinical Trial Approval Process of New Drugs in India:

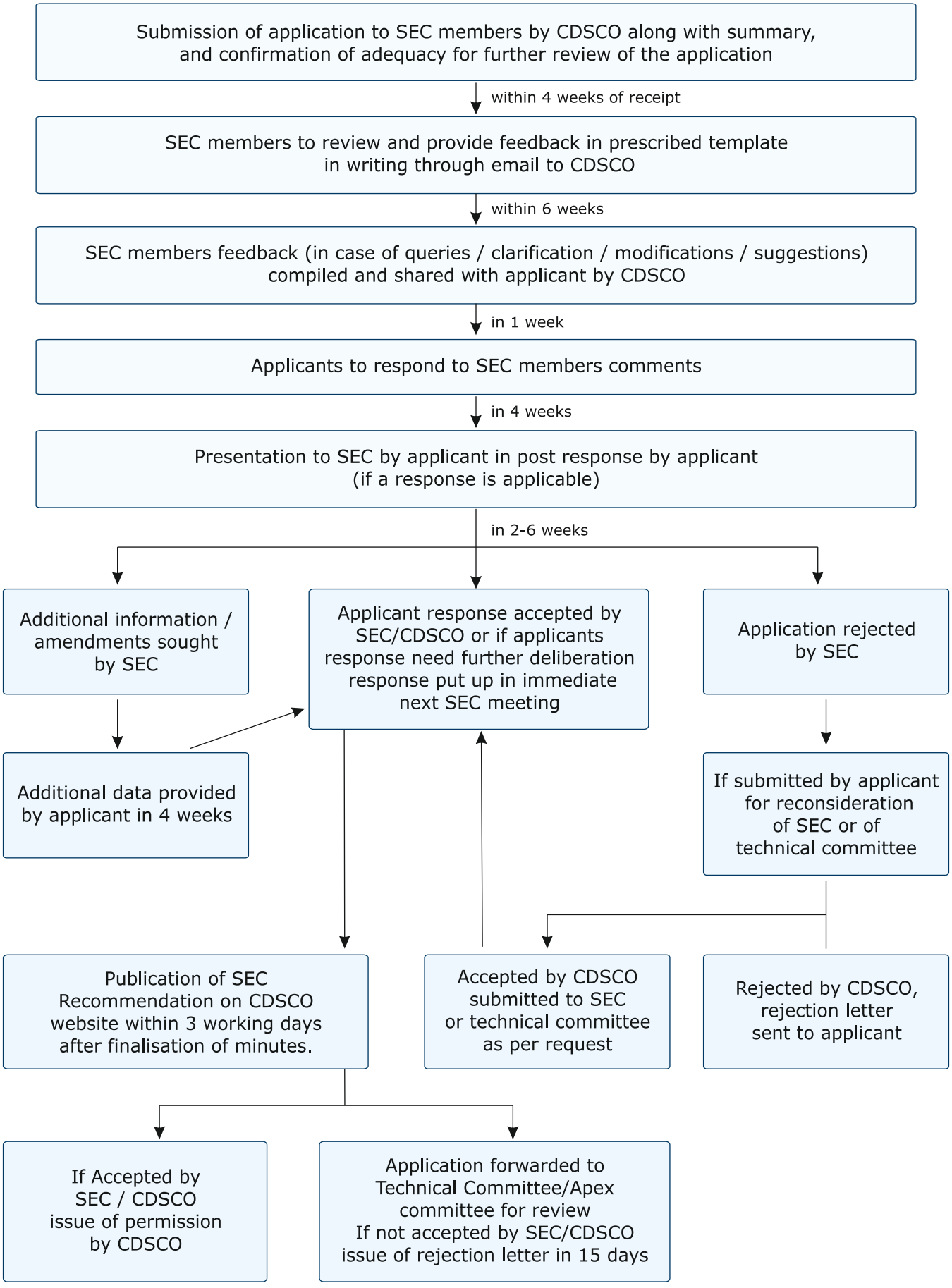


*Some bioequivalence trials in patients for Oncology, Psychiatry and Antiretroviral drugs are submitted under BA/BE division.

SEC: Subject Expert Committee
CDSCO: Central Drugs Standard Control Organization

Figure 2: ***Regulatory application process***

Review by CDSCO officials



***In the month of June 2017,**
CDSCO officials have decided that Clinical Trials approval will be done by SEC only.
i.e. It will be one tier review only, replacing three tier; Technical and Apex Committee.

Figure 3: ***Regulatory review process***

The chart below illustrates the number of Subject Expert Committee (SEC) meetings by therapeutic area and year. The trend is positive.

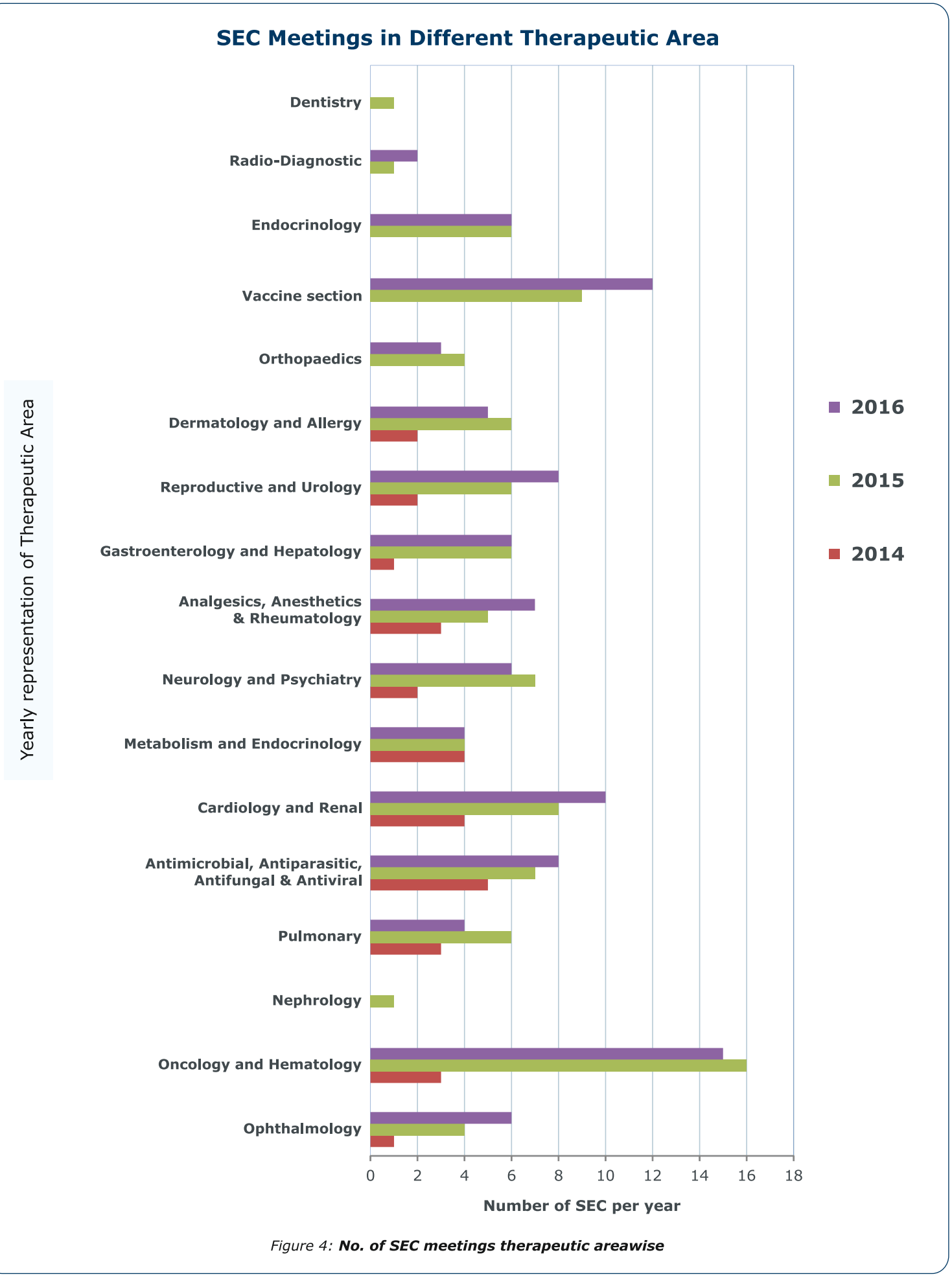


Figure 4: ***No. of SEC meetings therapeutic areawise***

The graph below highlights by year clinical trial approvals by DCGI.

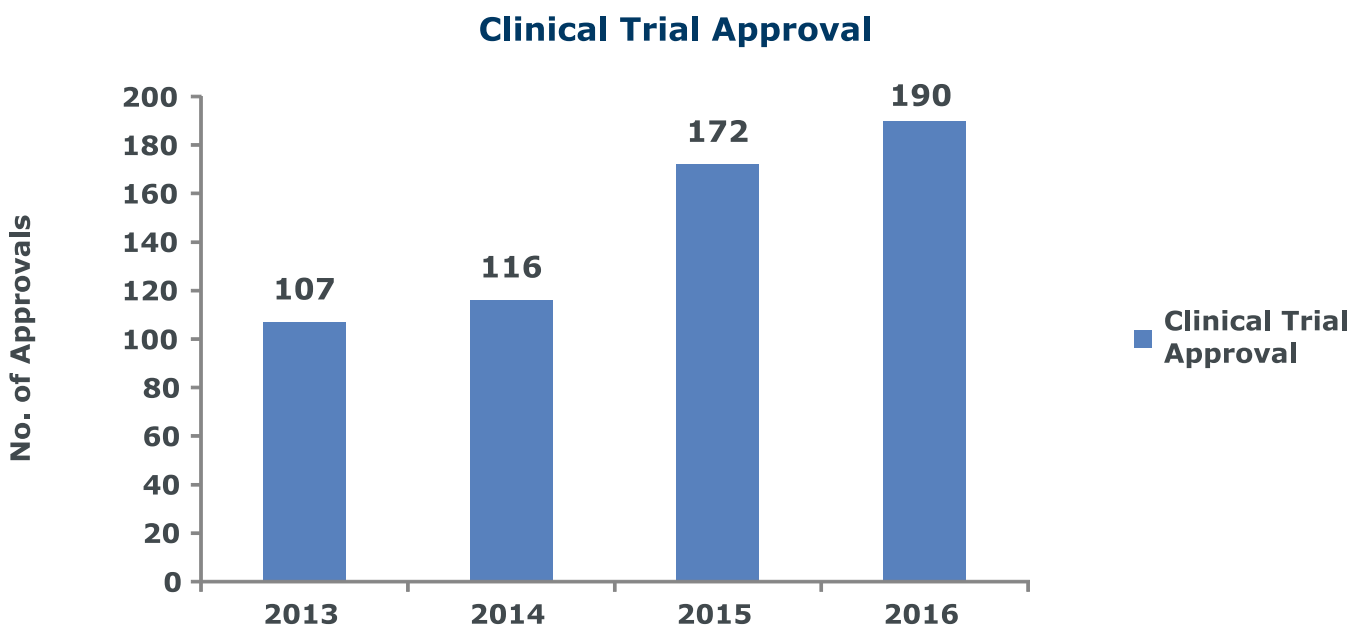


Figure 5: ***Number of Clinical trial approval***

There is a general consensus that the CRO sector is strengthening. This is shown through the number applications reviewed and the subsequent inspections by many regulatory authorities. The standards are global in nature.

To facilitate that the number of applications reviewed The DCGI has a regular schedule of meetings and has limited the number of applications to eight (8) per meeting. The meeting frequency is decided based on the number of proposal to be reviewed. For example, the highest number of applications is in Oncology and hence, there are 2 meetings per month. The majority of the other therapeutic areas are once a month and few meet once every 2 months.

Additional major changes include the removal of the following requirements to streamline the process: 50 beds per hospital, 3 studies per Principal Investigator and Audio Video (AV) recording of ICFs. Beginning in October 2016, the Clinical trial Application is made online through the "SUSGAM Portal". The registration document review, submission and tracking have become much simpler, efficient and transparent with the SUGAM portal. It also helps track all past, current, and future applications in one portal. The DCGI office is proactive in providing its backlog status and asking the applicant to respond quickly otherwise the case will be considered closed.

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ICMR and CDSCO have jointly published the "Handbook for Applicants & Reviewers of Clinical Trials of New Drugs in India" in January 2017, which gives more clarity and guiding principles for all phases of clinical trial conduct.

Guidelines for Sponsors:

The policy changes and efforts put by Government of India in last two years, clearly highlights the seriousness of government about the focus on clinical trials. They specifically focus on the rational approach, in line with global regulatory standards, to leverage India advantage on all fronts. Clinical trial administrators should give a fresh consideration about involving India by conducting detailed feasibility about the conduct of particular study.

For current information please visit the CDSCO website regularly at www.cdsco.nic.in

Conclusion:

Steps taken by the Health Ministry through a number of amendments have definitely given a clear message that the regulators have a mind-set to address the industry perspective and open India for Clinical Trials. The amendments provide rules and regulations that are rational and objective to ensure safety and rights of the trial participants. New clinical research will lead to newer drugs being launched in India for benefits of the patients.

About Cliantha

Cliantha Research is a global Contract Research Organization (CRO) providing integrated clinical offerings in Early Phase (Phase I/IIa), Late Phase (Phase II-IV), Bioequivalence (BA/BE), Clinical Endpoint Trials, Bioanalytical, Biosimilars, Dermatology, Respiratory, Oncology, Allergy, Biometrics, Regulatory Services and Consumer Research services. Our services have science at its foundation that is developed through regular and systematic training of the Cliantha Team.