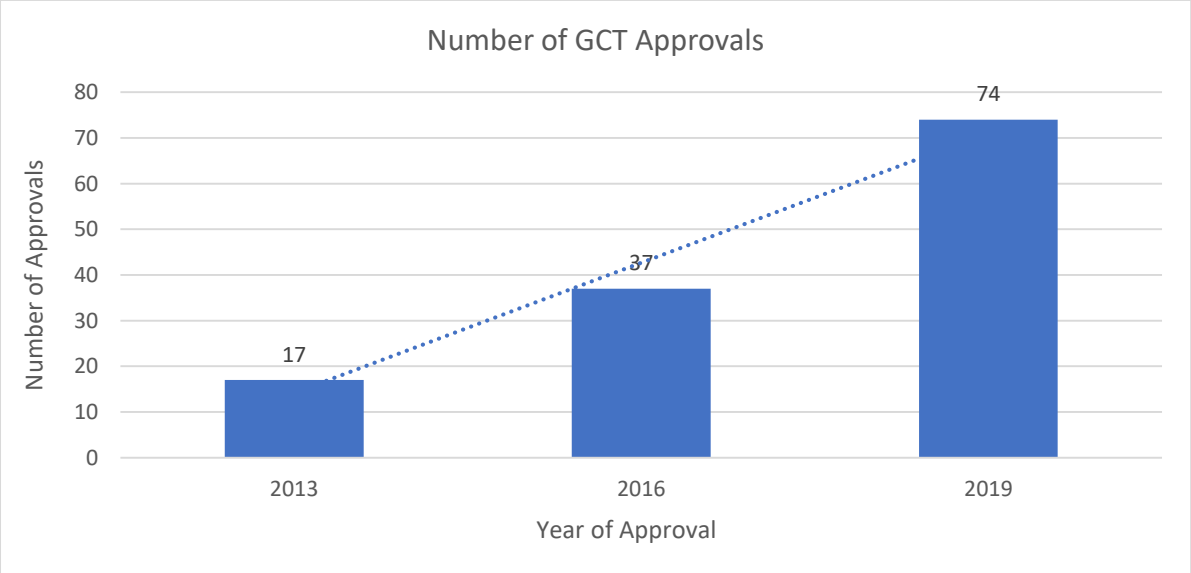
Does new Indian clinical trial regulations bring a pragmatic shift quantitatively and qualitatively with a change in perception within the general population…a question to be asked?

Indian clinical trial industry has seen both the flourishing days and abrupt downfall. Prior to 2013 India was worldwide referred as a preferred destination for clinical trials. The status changed suddenly in 2013, when a litigation filed in Honourable Supreme Court gained prominence and the government was in extreme pressure to pass regulations (e.g. financial compensation, audio video recording of consent process, registration of ethics committees without any formal guidelines and timeline for adaptation) which were considered repressive towards the industry. The problem of sudden change in regulations was fuelled-up when the clinical trial approvals were put on hold and global sponsors were left with no other choice than to terminate or withdraw their studies from India.

Today, looking back at these regulations, we can infer these to be "noble rock" on which the current regulatory paradigm has been laid on. Shaping of the current regulations started in 2015 when the regulators amended some of the stringent regulations framed in 2013, focusing changes in compensation rule, issuing detailed guidelines on AV consenting etc. This move from the regulatory agency and ministry brought back the optimism, enthusiasm and confidence among the stakeholders, which is a required concoction for growth of any Industry.

Since 2015, Industry has gained momentum. In comparison to 2013, the number of global clinical trial approvals have increased (as shown in the figure-1) and it is expected to grow in line to the projection that the clinical trial market in India would reach US $ 3.15 billion by 2025 and would register a CAGR of 8.7% over the forecast period of 2019 to 2025. [1]

Figure-1: Number of GCT Approvals (*source www. cdsco.gov.in*)



The optimism towards the growth of Indian clinical trial market can be sourced towards the following developments since 2013:

1. **Publication of new drugs and clinical trials rules 2019 vide GSR 227 (E):** The publication of new drugs and clinical trials rules 2019 on 19th March 2019 has marked a new and glorifying chapter in the history of clinical trial regulations as this is the Indianized version of regulation

[1] *http://www.pharmabiz.com/ArticleDetails.aspx?aid=119471&sid=9*

which is harmonized with the regulations in the well regulated countries. Some of the key highlights of this regulation are:

i. Ethics Committees have been categorized into two:

   a) Ethics committee approving clinical trial or BA/BE studies

   b) Ethics committee approving biomedical health research.

   Greater emphasis on quality functioning of these ethics committees, as these need to be registered with regulatory bodies as specified in the regulations. Registration validity has been extended from 03 to 05 years. Requirement of extensive documentation for re-registration has been abbreviated. Categorization of ethics committee will bring more transparency, certainty and accountability.

ii. Details related to regulations for permission to conduct clinical trial or BA/BE studies of new drugs and investigational new drugs has been included. This provides clarity to the stakeholders on the requirements and timelines for conducting clinical trial in India.

iii. If clinical trials are being conducted as part of discovery, research and manufacturing in India, then permission to conduct clinical trial becomes effective within 30 working days of filing of application, unless CDSCO notifies deficiencies in the application to the applicant. This step will boost clinical trial conduct in India by considerably reducing the clinical development timeline(s) and thus reduce the dependency on imports and will help to realize the concept of "Atmanirbhar Bharat".[2]

iv. The timelines for permission to conduct a global clinical trial have been reduced considerably from 180 days to 120 days.

v. Introduction of distinctive application forms brings more clarity on requirements. Earlier Form 44 was used for all the applications pertaining to manufacturing, import and clinical trials.

vi. Introduction of the concept of Academic Studies will boost research and development activities at the institutional/university level which will reduce the dependence on imports and will help to realize the concept of Atmanirbhar Bharat.

vii. Chapter IV of the regulation defines the requirement for financial compensation in case of injury or death in clinical trial or BA/BE studies of new drug or investigational new drug – in short the financial compensation to be provided only for related events and that to after the detailed investigation by the expert committee which takes into consideration of the reports from Sponsor, Investigator and ethics committee.

[2]*Atmanirbhar Bharat is a mission with a vision to make India 'Self-reliant India' or 'Self-sufficient India'. This is to make India a bigger and more important part of the global economy.*

viii. BA/BE centers have to be registered with the licensing authority before undertaking any BA/BE studies. This will ensure standardization, quality and accountability.

ix. Detailed labelling requirement for investigational products introduced.

x. SAE reporting timelines made consistent with the global requirements.

xi. More clarity added on the post market assessment with all types of post marketing studies with new drug will need regulatory approval.

xii. Clear specification regarding post marketing surveillance studies or observational studies or non-interventional studies for active surveillance which are conducted under approved conditions of its use does not warrant regulatory provisions applicable for clinical trial of new drug.

xiii. Increase in application fees will help to improve regulatory capabilities in terms of infrastructure, facilities and resources.

xiv. Concept of pre-and post-submission meetings introduced.

xv. Single tier review by SEC or IND committee (based on the application type) will ensure timely approval. Earlier there was three tier review which caused delays in approval.

xvi. Phytopharmaceuticals brought under the gambit of Central Licensing Authority. The requirement for conducting clinical trial of phytopharmaceuticals specified.[3]

2. **Registration of Ethics Committee Reviewing Biomedical & Health Research with Department of Health Research (DHR) on naitik.gov.in:** The biomedical & health research involving human participants has to be conducted in accordance with the ICMR National Ethical Guidelines for Biomedical and Health Research Involving Human Participants, 2017. According to the New Drugs and Clinical Trial Rules, 2019, Chapter IV, ethics committees which will review the biomedical and health research should be registered with the authority designated by the Central Government in the Ministry of Health and Family Welfare, Department of Health Research. This will bring the much-needed transparency, accountability and structure to regulate and monitor biomedical & health research in India. Till date 278 Ethics Committees has been registered with DHR.

3. **Harmonized Regulations for Medical Devices and In-vitro Diagnostics:** In 2017, the much-awaited medical device rules 2017 was published vide GSR 78(E) dated 31st January 2017. This regulation came into force from 01st January 2018. Major highlights of the regulations in terms of clinical investigation and performance evaluation are:

[3]*Phytopharmaceuticals drug means a drug of purified and standardised fraction, assessed qualitatively and quantitatively with defined minimum four bio- active or phytochemical compounds of an extract of a medicinal plant or its part, for internal or external use on human beings or animals, for diagnosis, treatment, mitigation or prevention of any disease or disorder but does not include drug administered through parenteral route.*

i. Medical devices/In-vitro diagnostics classified into four categories A, B, C & D based on risk characterization.

ii. Pilot and pivotal clinical investigation required for investigational medical devices.

iii. No permission from the regulatory agency to conduct academic clinical study on medical devices.

iv. Clinical performance evaluation required for new in-vitro diagnostic medical devices.

v. Prior to clinical performance revaluation permission, report on clinical performance evaluation from the lab designated by central government has to be furnished.

4. **Introduction of Online Application Portal SUGAM:** SUGAM is an e-Governance Solution for the drug regulatory agency in India. All the applications (e.g. registration of ethics committee or permission to conduct clinical trial) has to be submitted online through SUGAM portal. This portal provides unique features of application submission, query resolution, status and approval tracking, post approval applications and notifications. With the advent of this portal the approval timelines have reduced considerably as it brings transparency, accountability and uniformity in the regulatory functioning.

In summary, the developments clearly will bring standardization, transparency and accountability amongst different stakeholders and will certainly pave the way for the growth of clinical trial industry in India. These changes are likely to have positive influence on general population's perception towards clinical trials and will also ensure that the unmet medical need of the country is met. If the trials are being conducted with the assurance of meeting the utmost ethical standards and are approved by quality and process orientated regulatory agency and ethics committee then certainly the perception of general public towards the clinical trials will be progressive and more and more clinical trials to meet the demands in India will be conducted.