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Regulatory intervention in India is more rigorous than ever before

18.03.2024

Tags:

India, CDSCO, Regulator, Regulation

Dr Santosh Indraksha serves as Deputy Drugs Controller (India) for the Central Drugs Standard Control Organisation (CDSCO) under the Indian Ministry of Health and Family Welfare. As a representative of Indiaâ??s main regulatory body for pharmaceuticals, tasked with overseeing the organisationâ??s international cell, Dr Indraksha outlines the key upgrades in Indian regulation in recent years, how the CDSCO is adapting to meet the pace of innovation within pharma, and the ways in which it is adopting digital technologies in its work.

What is the scope and focus of your role as a Deputy Drugs Controller at the CDSCO?

Deputy Drugs Controllers are senior officials within the CDSCO, which is Indiaâ??s National Drugs Regulatory Authority, under the Ministry of Health and Family Welfare, Govt. of India. CDSCO regulates the Quality, Safety and Efficacy of Drugs, Cosmetics, Vaccines, Medical Devices and In-vitro diagnostics in the country. My remit is to oversee the functions of CDSCOâ??s International Cell, engaged in collaborative work with various international organisations like the WHO as well as other national regulatory authorities (NRAs) around the world. We have signed bilateral agreements with NRAs in 16 countries, including the US, UK, Sweden, Russia, Germany, Brazil, Argentina, Denmark, Ecuador, the Netherlands, and Japan etc. Recently, the CDSCO signed a multilateral agreement with the Drug Regulatory Authorities of the BRICS member states (Brazil, Russia, India,

China and South Africa). We are negotiating bilateral collaborative arrangements with more than 30 other countries.

The international cell also acts as a focal point within the CDSCO for issues related to narcotic drugs and psychotropic substances. Also, the international complaints/investigations related to product quality exported by Indian firms are routed through our division for appropriate investigations and return communications. This division also issues Written Confirmation Certificates (WCC) as per Article 46 b (2)(b) of EU Directive 2001/83/EC for the export of API to the European Union.

The International Cell also organizes various International Seminars, Conferences, and Meetings etc. with various other drug regulatory authorities like USFDA, PMDA-Japan, UK-MHRA, DKMA-Denmark, Authorities of the Netherlands, and WHO etc. under various capacity-building programs and initiatives.

Has the work of the CDSCO developed in line with the Indian pharma industryâ??s own evolution?

Yes, my organization has grown in line with the growth of the Indian industry and also in accordance with Global Regulatory Dynamics. The Drugs and Cosmetics Act, 1940 is a pre-independent Act to regulate the import, manufacture, sale and distribution of Drugs, Vaccines, Cosmetics, Medical Devices/IVDs, Veterinary Medicines, Traditional medicines etc. in the country, including approval of New Drugs and Clinical Trials. The CDSCO mainly regulates the import and approval of New Drugs, Clinical Trials, Class C and D (Moderate high to High-risk category) medical devices. There are also provincial agencies (State/UT Drugs Control Authorities) across the country which regulate mainly the manufacture, sale & distribution of Drugs and Cosmetics, Class A and B medical devices (Low to moderate low-risk category). Additionally, there are some joint activities by CDSCO and provincial authorities like inspections of the manufacturing premises, blood banks, LVPs, wherein our regional CDSCO officials usually participate. The provisions of the Drugs and Cosmetics Act, 1940 and Drugs Rules, 1945 are regularly amended to keep abreast of the global regulatory environment.

A big milestone came in 2017, when India introduced the Medical Devices Rules (MDR, 2017). These rules marked a significant shift towards a more organized and comprehensive regulatory framework for medical devices in the country. Before these Rules, only 37 Medical Devices were largely regulated under the Drugs and Cosmetics Rules, 1945, and many other devices did not require any form of pre-market approval. The MDR, 2017 aimed to establish a comprehensive and predictable regulatory pathway, categorizing devices based on their risk associated and streamlining the approval process to enhance safety, quality, and performance standards.

Similarly, in 2019, we brought in the New Drugs and Clinical Trials Rules (NDCTR, 2019). These Rules significantly revamped the regulatory landscape for the approval of new drugs and the conduct of clinical trials in the country and brought India in line with global regulatory dynamics. NDCTR, 2019 is not only in line with Global Regulations but also has unique national features like Compensation, Medical Management, and Post Trial Access to ascertain the subject safety and well-being. This unique compensation mechanism is applicable for serious adverse events happen during clinical trials for drugs or Clinical investigations/performances of medical devices. Additionally, in 2020 we enacted new Cosmetics Rules to regulate the import, manufacture, sale and distribution of cosmetics, including approval of New Cosmetics in the Country.

Lately, we have amended the Schedule-M of the Drugs Rules, 1945 which talks about Good Manufacturing Principles (GMP) in line with WHO guidelines, mandated submission of stability data for all products, and Bioequivalence data for certain categories of products before the grant of

manufacturing licences.

Finally, regulatory intervention in India is more rigorous than ever before. For example, we are conducting joint inspections before the grant of manufacturing licences including periodic joint inspections of manufacturing premises. Also, we conduct Risk Based Inspections (RBI) of Manufacturing premises and Testing Laboratories, to verify the required compliances and any non-compliances are dealt with as per applicable laws.

In what ways have the CDSCOâ??s consultation mechanisms with the private industry changed in recent years?

CDSCO has a very structured consultation mechanism with the Pharmaceutical, Cosmetics, and Medical Devices Industry. This consultation happens at 3 different levels, first before publishing any Regulations, second, during the implementation of such revised regulations and third, for any issues/concerns that arise in further course of action. These consultations happen using inviting written suggestions/comments/objections, physical or virtual meetings, Video or teleconferences etc.

All Regulatory amendments have to travel a structured path. E.g. when an issue is identified, we consult with the Drugs Consultative Committee (DCC) which is a legislative body comprising Drugs Controllers from all the State/UT and Drugs Controller General (India) who discuss the matters arise out of uniform administration of the Drugs and Cosmetics Act, 1940. They advise the State Govt., Central Govt., and Drugs Technical Advisory Board (DTAB). Further, after DCC recommendations, the matter gets deliberated in DTAB, which is another apex legislative body under the said Act, under the Chairmanship of Director General of Health Services (DGHS), and comprising various elected and nominated members from Industry, associations, research institutions, laboratories, academia, invited subject matter experts from Industry or regulatory body etc. The DTAB advises the Central Govt. with its recommendations and accordingly Central Government publishes the draft regulations in the Gazette of India, which is publicly available in e-Gazette, for inviting suggestions/objections/comments on the proposed draft. Any person (including foreign nationals) that is likely to be affected by the proposed regulations may send their written comments/objections to the CDSCO and MoHFW for examination with 45 or 60 days of its publication. CDSCO usually also conducts stakeholder meetings to understand the industry concerns and considers the amendments accordingly, the stakeholders also involve patient groups, NGOs, and various national and international bodies engaged in healthcare. This process is repeated until a satisfactory outcome is reached and if required, it sometimes carries out various trainings, and workshops for the industry to make them aware of new requirements of compliance.

As an example, in October 2018, we have published revised Schedule-M (GMP) requirements however, after rigorous discussion, consultations, workshops, trainings etc. the regulations were finalized in December 2023.

There is a very developed mechanism which allows us to better understand the perceptions and concerns of the industry.

How are digital technologies being integrated into the CDSCOâ??s regulatory processes to enhance efficiency and transparency?

This topic is close to the heart of our honourable Prime Minister. In his first term, starting in 2014, he really foregrounded the concept of ease of doing business. This led to online systems being

introduced across all government organisations, including CDSCO, which has taken a very proactive stance on digitalisation.

CDSCOâ??s digital portal is called â??SUGAMâ?•. We currently have a 100 percent online system for all processes relating to drugs, devices, cosmetics, and imports, meaning that applications can be made from anywhere in the world. If deficiencies are found, they are communicated online, and approvals are also given online.

Further, individual states within India have also had digitized processes but they were not unified across the country, each State/UT used to utilise convenient software/licensing platforms, but sometimes non-uniformity of the formats could lead to a longer review of the applications owing to its verification of authenticity and interoperability issues. CDSCO has taken the initiative to develop and deploy a unified Online Drugs Licensing System (ONDLS) to all the State/UT Drug Control Authorities and many States have already on-boarded this platform, alleviating this issue. Within a couple of years, it is anticipated that all provincial authorities shall also be completely online for issuing unified licences.

To ensure supply chain security of all Active Pharmaceutical Ingredient (API), Govt. of India, vide G.S.R. 20 (E) dated 18.01.2022 has mandated that, every active pharmaceutical ingredient (bulk drug) manufactured or imported in India shall bear Quick Response code on its label at each level packaging that stores data or information readable with a software application to facilitate tracking and tracing. These Rules have been made effective from 01.01.2023 and are applicable for imported/ manufactured/exported APIs.

Similarly, to ensure the supply chain security of finished pharmaceuticals, Govt. of India, vide G.S.R. 823 (E) dated 17.11.2022 has mandated that, the manufacturers of drug formulation products as specified in Schedule H2 (top 300 identified drugs/brands) shall print or affix Bar Code or Quick Response Code on its primary packaging label or, in case of inadequate space in primary package label, on the secondary package label that store data or information legible with a software application to facilitate authentication. These Rules have been made effective from 01.08.2023 and applicable for 300 identified drug products only.

At the 90th meeting of DTAB, the Board recommended that â??the proposal to affix Bar Code or Quick Response Code may be extended to all antimicrobials, narcotic & psychotropic substances in a phase-wise mannerâ?•. The same will be implemented in due course of time and in near future, similar requirements may also be extended to other formulations.

As the complexity of new drugs being launched increases, how is the CDSCO increasing its capacity and capability to cope?

Areas like cell and gene therapy are certainly new frontiers for the CDSCO. However, we are adapting well and recently approved the second CAR-T cell therapy within the country. To adjust to this new reality, we are building out our regulatory expertise across three main pillars. The first is to train our people internally, we do this via our dedicated training division, conducting mass training workshops for all our CDSCO/provincial officials at the rate of about two per month. In 2023 we held 22 such workshops, wherein experts from CDSCO, State Authorities, Industry, Academia, Foreign Drugs Regulatory Authorities etc. have imparted training.

Secondly, we are utilising international collaborative platforms. For example, we are engaging with the Japanese PMDA, the US FDA, and various other European authorities to better understand their regulatory practices and how they review medicines. We recently collaborated with the USFDA and

PMDA Japan on CAR-T, and have more collaborations planned with UK, Danish and Dutch authorities.

The third pillar is to identify the right people within our organisation and send them to on-job training at foreign institutions e.g. ATC Seminars in Japan, WHO conferences, various institutions of excellence in Regulatory Review etc.

As the countryâ??s national agenda shifts from â??Make in Indiaâ?? to â??Develop in Indiaâ?? what will be the role of the nationâ??s regulatory body in supporting the local ecosystem and assisting the ascension of India up the value chain?

As I mentioned previously, ease of doing business is one of Prime Minister Modiâ??s main mottos. To assist the growth of Indian innovation, we have enacted very aggressive timelines for clinical trial applications. For example, if an applicant does not get a reply from us within 90 days, the Clinical Trial application is considered as deemed approved. Moreover, this 90-day standard timeline is still reduced to just 30 days in the case of applications from domestic companies. Further, Indian MSMEs receive a 50 percent concession on fees related to CT and New Drugs approvals. Finally, local clinical trials for academic purposes no longer require CDSCO approval, they just have to register with DHR and Ethics Committee.

We also now have accelerated and expedited approvals for drugs to meet an urgent unmet need. Further, all CDSCO offices have innovation support cell and dedicated helpline to guide the start-ups and innovators to comply with regulatory requirements. The digitized processes help these companies to perform the innovation, scale-up and technology transfer within a reasonable time with the help of Govt. support/incentives and schemes. All these initiatives serve as regulatory enablers for Indian innovation, promoting earlier access to medicine both in India and worldwide.

Has the CDSCO had to hire more people or change its ways of working to meet these tighter deadlines and accelerated speed of operation?

Yes, CDSCO has expanded its regular technical manpower to a great extent to cope with growing regulatory demands using new recruitments, deputations etc. Apart from regular manpower (quality and regulatory), CDSCO uses the expertise of Subject Expert Committees (SECs) for the review of Clinical Safety and Efficacy Study aspects of Clinical Trials protocols or New Drugs approvals. These are panels of doctors from government hospitals specialised in specific areas of medicine, who review applications for safety and efficacy in parallel with our work at the CDSCO. The fact that this work is going on at the same time speeds up the overall process considerably.

Additionally, we are also utilising contractual manpower (Technical Data Associates, Scientists) to support the technical reviews and they assist regular technical staff. Urgently hiring full-time employees is sometimes not feasible due to its recruitment process intricacies, so the CDSCO now has an almost equal number of contractual staff. Utilising the experience of contractual microbiologists, toxicologists, pharmacists, biotechnologists, toxicologists, biomedical engineers, biostatisticians etc. helps speed up the regulatory process and allows us to provide a better and faster service overall.

You have been with the CDSCO for over seven years, having previously spent most of your career in private industry. What do you find engaging and exciting about working for a regulatory body?

I consider my current role to be truly empowering. My previous work in product R&D with J&J certainly impacted peopleâ??s lives in terms of providing novel compounds as new therapies, but this role has an even greater and wider impact on individualsâ?? and patientsâ?? lives by ensuring quality, safe and efficacious medicines available for our population. The regulatorâ??s role was crucial in handling the Covid-19 pandemic situation and I feel a great deal of pride and contentment in serving both my country and the entire globe.

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