THE PHARMACY OF THE WORLD: PILLS AND PITFALLS

Geethu V.A, The National University of Advanced Legal Studies, Kochi

ABSTRACT

The world of pharmacy has come away long way from the midst rat tail concoctions and bloodletting to the modern pharmaceutical medicines that we know of, and at the forefront of this is India, one of the biggest manufacturers of pharmaceuticals, yet grossly unregulated and often times fatal. Authorities the likes of WHO and CDC have linked over 300 deaths to that of Indian-made pharmaceutical products, especially cough syrups containing high DEG concentration, which is a solvent harmful to humans and are explicitly barred from being used in medicines. Even though there has been multiple public regarding the regulations or the lack thereof, this as more or less fallen on deaf ears allowing these perpetrators to go scot-free. The CDSCO, which is the equivalent of the CDC in India, functions on a very unique model; unlike other regulatory bodies, it lacks the enforcement mechanism and relies on other states establishments to carry out the enforcement part, which often flatters and falls behind there can be variations in the interpretation and implementation of regulations by different state-level authorities, leading to inconsistencies in regulatory enforcement. Furthermore, the CDSCO, as such, is low in peaking order and functions under the Ministry of Health; this organization lacks the expertise and therefore relies on CDSCO for the same this leads to the CDSCO often struggling with limited resources, both in terms of funding and infrastructure, which can hamper its ability to carry out its regulatory responsibilities effectively. The organization also lacks in a pharmacy vigilance system for monitoring and addressing adverse drug reactions. So essentially, the watchdog that we do have merely remains a silent spectator as the gruesome spectators unfurl around it.

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India, is the largest democratic republic, home to more than 1.4 billion people, the land of saffron spices and everything nice. Along with numerous titles that adorn the crown of the country, stands tall the title of "the pharmacy of the world", boasting a production of a whopping 60 per cent of the global vaccine production. The country's pharmaceutical market, which has been playing a key role in the global pharmaceuticals industry, with an estimated turnover of $42 billion domestically in 2021 and is expected to grow further in the coming years. India ranks third worldwide for pharmaceutical production by volume and exports pharmaceuticals to more than 200 countries and territories. [1]But these achievements fade in comparison to the fact that the industry that caters to the world is grossly unregulated and completely out of control.

An alarming proof of this statement is the recent death of over 70 children in the country of Gambia due to the consumption of Indian-made cough syrups; the reports from the offices of CDC as well as the WHO states "that medications contaminated with Diethylene Glycol [DEG] or Ethylene Glycol [EG] imported into Gambia led to this Acute Kidney Injury (AKI) cluster among children"[2] this unfortunate event is not a stand-alone incident but rather a part of a series that dons a question mark on the control imposed or the lack of thereof when it comes to the pharmacy industry of India.

There have been recordings of similar events throughout India, the sensational Jammu case in 2020 wherein several children died, all form part of this chain and a probe into these incidents reveals a common component: an industrial-grade solvent named diethylene glycol. This is an organic compound with the formula (HOCH2CH2)2O, It is a colourless, practically odourless, and hygroscopic liquid with a sweetish taste. Diethylene glycol is used in the manufacture of saturated and unsaturated polyester resins, polyurethanes, and plasticizers. This solvent is not to be used for drug-making and is toxic to humans.[3]

Investigation from the part of the WHO into a Haryana-based Maiden Pharmaceuticals has revealed an alarming level of DEG and ethylene glycol in cough syrup. These are toxic to

[1] India living upto it's title of "the pharmacy of the world",*available at: https://www.aa.com.tr/en/asia-pacific/india-living-up-to-its-title-of-pharmacy-of-the-world-/2534294 (Last visited on June 20,2023)*.
[2] Centres for disease control and Prevention "Morbidity and Mortality Weekly Report"217-222 (2023).
[3]*Unregulated, out of Control: Drug Manufacturing in India* (2022) *Deccan Herald,a*vailable at: https://www.deccanherald.com/specials/insight/unregulated-out-of-control-drug-manufacturing-in-india-1155970.html (*Last visited on* January 21, 2023).

humans and are explicitly barred from being used in the manufacture of medicines furthermore, the WHO has now linked 300 such deaths to cough syrups being manufactured in India. All these blood trail leads to a gigantic issue that we have conveniently swept under the rug, which is the lack of regulations over the pharmaceutical industry of India.[4]

The Central Drug Standard Control Organization (CDSCO) under the Directorate General of Health Services, Ministry of Health & Family Welfare, Government of India, is the National Regulatory Authority (NRA) of India. It draws its power from the Drugs & Cosmetics Act,1940[5] and Rules 1945[6], this particular act envisages an array of central and state regulators that ensure the safety rights and well-being of the patients by regulating the drugs and cosmetics. Under the Drugs and Cosmetics Act, CDSCO is responsible for the approval of Drugs, Conduct of Clinical Trials, laying down the standards for Drugs, control over the quality of imported Drugs in the country and coordination of the activities of State Drug Control Organizations by providing expert advice with a view of bring about the uniformity in the enforcement of the Drugs and Cosmetics Act.

Even though the CDSCO prides itself in being the sole organization when it comes to regulating drugs and cosmetics in India, it is at the end of the day, a toothless watchdog on vigil; the CDSCO, unfortunately, lacks the power or the resources to take an action as it is devoid of statutory backing, unlike the other regulatory authorities such as Telecom Regulatory Authority of India and Food Safety and Standards Authority of India.

The CDSCO relies on state authorities to check on the licensing, and even though a complex procedure involving three-part clinical trials and other such measures has been instituted, the actual process mirroring this is more or less very rare. The process of attaining the license is a joint venture between the state and the central authority; the process starts with the manufacturer filing an application with the state regulatory authority upon receipt of the said application; the state authority then forwards this to the central authority. [7]The CDSCO reviews the application to ensure it meets the necessary requirements. These include clinical trails, site

[4] "WHO flags 7 India-made syrups in its probe on contaminated medicine causing 300 deaths globally" Live mint, available at :https://www.livemint.com/news/india/who-flags-7-india-made-cough-syrups-in-its-probe-on-contaminated-medicine-causing-300-deaths-globally-11687246609552.html (*Last visited on*:July 11, 2023)
[5] The Drugs and Cosmetics Act, 1940.
[6] The Drugs and Cosmetics Rules, 1945.
[7] §68A,The Drugs and Cosmetics Rule, 1945.

inspection, CDSCO review and other such measures, and the authority may mandate from time to time.

The clinical trials mandated are to be conducted in three phases to evaluate the safety and effectiveness of the vaccine on human subjects. The trials should follow strict ethical guidelines and Good Clinical Practice (GCP) standards. Phase 1 involves a small group of healthy volunteers, Phase 2 expands to a larger sample size, and Phase 3 includes a larger population to gather sufficient data on safety and efficacy. After successfully completing the clinical trials, the manufacture is to submit an NDA or New Drug Application to the CDSCO. The NDA should include comprehensive data on the vaccine's safety, efficacy, manufacturing details, quality control measures, and labelling information.

Following this, the CDSCO examines the NDA and assesses the data provided. They evaluate the vaccine's safety, efficacy, manufacturing processes, quality control measures, and compliance with regulatory guidelines. The CDSCO may request additional information or clarification during the review process. This is continued by a site inspection where in the CDSCO conducts inspections of the manufacturing facilities to ensure they meet the required standards and regulations for vaccine production, storage, and distribution. They assess factors such as infrastructure, quality control processes, documentation, and personnel training.

All the data collected from these trials, reviews and site visits are then presented before an expert committee for evaluation; they review the submitted data, trial results, and inspection reports. The committee evaluates the vaccine's safety, efficacy, and overall benefit-risk profile. They provide recommendations and advice to the CDSCO based on their assessment.

Based on the recommendations of the Expert Committee and the CDSCO's own evaluation, the organization makes a decision on whether to grant the license for the vaccine. If approved, the CDSCO issues a license for the vaccine, allowing its marketing, distribution, and sale in India. The rules also mandate that the license is to be renewed every five years, and this renewal follows the same process that has been listed above. furthermore, the in-order to assure compliance with the WHO’s pre-qualification programme, the CDSCO implemented what is referred to as lot release, wherein each batch is tested to ensure that the quality is maintained.

Primafacie, the aforementioned process may look like a detailed and well-thought-out one, but the fact is that this remains on paper alone; the state of Karnataka has borne witness to such a

pitfall in the recent past. The KFD (Kaysunar Forest Disease) vaccine manufactured by IAHVB (Institute of Animal Health and Veterinary Biologicals), being marketed in the country since the year 2000, has not had a valid licence since the year 2006 and the same has only been flagged in the year 2021 which effectively means that the vaccine the institute has been manufacturing for the past 15 years has not gone through scrutiny and the same has also resulted in several adverse reactions in patients post the administration of the vaccine. Furthermore a parliamentary committee reviewed the approval process for 42 randomly selected drugs, most of which were awarded licenses between 2004 and 2010. And this brought quite a few dusty skeletons out of the closet, the report stated how the documentation for three of the drugs — which the report describes as "controversial" because they are not licensed for use in most Western nations — was missing, and 11 of the remaining 39 had been licensed without undergoing phase III clinical trials.[8]

As evident from the aforementioned instances, CDSCO as the structure has been inherently flawed; the lack of transparency in CDSCO's decision-making processes and regulatory procedures leads to concerns about undue influence and favouritism; furthermore, the organization faces a shortage of qualified and experienced personnel, especially in specialized areas such as medical devices and the equipment needed for testing efficacy of drugs.

It's imperative to note that the CDSCO often struggles with limited resources, both in terms of funding and infrastructure, which can hamper its ability to carry out its regulatory responsibilities effectively. The organization's also lacks in a pharmacy vigilance system for monitoring and addressing adverse drug reactions. Furthermore, there can be variations in the interpretation and implementation of regulations by different state-level authorities, leading to inconsistencies in regulatory enforcement an addition of the lack of a centralized database into this list makes way for a concoction that allows the manufacturers to grow uncontrolled and unchecked.

This lack of centralized data and variations in implementation allows for manufacturers to produce drugs which are not safe for consumption or, in other words, drugs labelled Not of Standard Quality (NSQ) to be sold. Allow me to elucidate; say a drug manufactured by company A in state B has been labelled as being NSQ; this means the said data would be entered in the state database alone, and this allows company A to shift their manufacture

[8]Gayathri Vaidyanathan, Failings exposed at India's drug regulator, available at https://www.nature.com/articles/nature.2012.10668 (last visited on 18th July 2023).

production and sale to different state thus allowing the companies to continue exploiting the unassuming citizenry.

Even though there have been multiple attempts to call attention to this antiquated and draconian system of drug control but the same has been brutally suppressed and deflected by the government; an example of the same would be the case of the Indian Brand Equity Foundation(IBEF) threatening to sue the group of academics who published a paper claiming that the Indian pharmaceutical industry selling sub-standard drugs in poorly regulated countries. [9]Furthermore, the authors of The Truth Pill, a book containing an in-depth analysis of the current state of drug control, filed an RTI voicing their concerns on the standards of the pharmaceuticals vaccine and medicines produced; this was labelled as uncalled for since the drugs in question were not manufactured in India and where counterfeit though the details of who conducted the said investigations or how they came to this conclusion are not provided anywhere.

If we take a close look at the two cases, a pattern emerges, a pattern of nonchalance, ignorance and utter disregard. Officials that should ideally be concerned regarding this seem to be, or in other words, willingly chooses to be blissfully unaware of lax regulations.

The need of the hour is a centralized system with the CDSCO at its helm and other a network of checks and balances that spans the entirety of India. This particular system can be based on the current model but with more transparency and a definite hierarchy as of now, the CDSCO functions under the Directorate General of Health Services, Ministry of Health & Family Welfare, Government of India, even though the aforementioned lacks the technical expertise and has to rely on the CDSCO for the same effectively preventing the CDSCO from being the watchdog that it was envisaged to be. Furthermore, there needs to be one drug inspector for every 50 manufacturing units and one per 200 distribution.[10] Along with a central database where in the publication of new licenses is announced periodically, and a digital copy of the same is to be maintained be made accessible to the general public akin to that of the trademark registry. Furthermore, if a particular company were to fail in the lot system or were to default in any of the mandates put forth by the authorities from time to time, the same is to be brought

[9]Dinesh S Thakur & Prashant Reddy T "India's pharma industry's problems needs to be fixed, now", *Money Control,*07th October 2022, available at https://www.moneycontrol.com/news/opinion/indias-pharma-industrys-problems-need-to-be-fixed-now-9292881.html (last visited on 18th July 2023)
[10] Department of Pharamacueticals,"Expert Committee Report"(January 2021).

to the notice of the public via publication in Newspapers. Along with the aforementioned changes, there needs to be more stringent laws and repercussions, the likes of compensation, put in place as a deterrent. This would ensure that the pharmacy of the world is not built on the blood of innocents.