Citizens for Affordable,
Safe & Effective Medicine
CASEM

To:

August 20, 2022

Bikash R Mahato
Under Secretary (Drug Regulation)
Minister for Health & Family Welfare,
Government of India,
Room 434, C-Wing,
Nirman Bhawan, Maulana Azad Road,
New Delhi – 110 011.
Email: drugsdiv-mohfw@gov.in

Dear Mr Mahato,

Sub: Comments on Draft of New Drugs, Medical Devices and Cosmetics Bill, 2022

By way of introduction, I am a public health activist and the Founder of Citizens for Affordable, Safe & Effective Medicine (CASEM) which aims to be a collective of like-minded individuals working towards ensuring that the medicines supplied to India and other countries are affordable, safe and effective. I have formerly worked in the Indian pharmaceutical industry and was responsible for exposing the regulatory violations at Ranbaxy Laboratories after which the company was prosecuted and fined $500 million dollars by the United States Food and Drug Administration (USFDA).

Since the end of my whistle-blower lawsuit against Ranbaxy in 2013, I have been engaged in advocacy aimed at strengthening the drug regulatory framework in India. This includes multiple petitions and reports that I have submitted to your Ministry with various recommendations to improve drug regulation in India.

I am writing to you to provide our comments to the New Drugs, Medical Devices and Cosmetics Bill, 2022. This was a much-needed initiative and I am glad that the Ministry finally took this important step to replace the now antiquated Drugs & Cosmetics Act, 1940.

Sincerely,

Dinesh Thakur
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A. Federalism & Drug Regulation

1. One of the burning issues in the debates around reforming drug regulation in India is the issue of federalism. Simply put, the question is whether India should have a single regulator responsible for drug regulation across the country or should it continue with the current system where each state and union territory in the country has its own state drug controller responsible for licensing manufacturing units and pharmacies while the central regulator – the CDSCO – is responsible for regulating only imports, granting approvals to new drugs and the manufacturing licences for limited number of drugs mentioned in Schedule C and C1. The power to test drug samples and prosecute erring companies exists with both the state and central drug inspectors.

2. The above-described setup has led to complicated administrative problems. For example, if a drug inspector in Maharashtra detects a Not of Standard Quality (NSQ) drug manufactured by a facility licensed by the drug controller in Himachal Pradesh, the Maharashtrian drug inspector can at most file a criminal complaint against the manufacturer and wait for the court to hear the case. In the meantime, the drug inspector from Maharashtra cannot exercise any action to protect the citizens of the state. For example, the drug inspector in Maharashtra cannot conduct a 'raid' on the manufacturer's facility in Himachal Pradesh because of a lack of territorial jurisdiction; she cannot cancel the manufacturing license of the erring company or stop the drugs manufactured by this facility from entering the state of Maharashtra. Only the drug controller in Himachal Pradesh can 'raid' the manufacturer to seize evidence or cancel/suspend their manufacturing license. The recent case from January, 2020 when 12 children from Jammu died after allegedly consuming adulterated cough syrup is an unfortunate example of how poor-coordination between different state drug controllers can lead to manufacturers with a poor record of manufacturing NSQ drugs to continue transact business in India. The manufacturer of the allegedly adulterated cough syrup– Digital Vision– was reportedly found to have manufactured and sold NSQ drugs on 19 different occasions by different state drug controllers across the country and also the central drug laboratories prior to the tragedy in Jammu.[1] Yet the drug controller in Himachal Pradesh did not take appropriate action against the company and the consequences were borne by citizens of Jammu.

[1] https://www.livemint.com/politics/policy/how-weak-drug-laws-are-costing-lives-11632761831130.html

3. The back drop to many of these problems is competition between different state governments to attract investment from the pharmaceutical industry. While state governments are known to provide various incentives to the industry while competing for their investment, it should not be at the expense of lax administration of regulation as a means to attract investment. Such a policy is disastrous from a public health perspective.

4. In 2003, a committee constituted by the Health Ministry and headed by Dr. Mashelkar recommended the centralization of all licensing powers with the central government.[2] No action was taken in this regard until 2013 when the Government introduced the Drugs & Cosmetics (Amendment) Bill, 2013 centralising the licensing function.[3] The bill was never debated in Parliament and was ultimately withdrawn.[4]

5. The New Drugs, Cosmetics & Medical Devices Bill, 2022 continues with the existing status quo. In our opinion, this is an incorrect approach. As long as India remains a common market wherein drugs manufactured in one state can be sold in another state, it must have one regulator responsible for granting manufacturing licences across the country. Such an approach is constitutionally feasible given that "Drugs" is a subject in the Concurrent List in Schedule VII to the Constitution. At most, state drug controllers may be given powers to licence pharmacies and distributors in their respective states. We are however in favour of the state drug controllers being allowed to retain powers to test drugs sold in their states and prosecute the offending drug manufacturers immaterial of where they are located in the country. They should continue to exercise such powers alongside the central regulator. Such an arrangement will act as an external check on the central regulator, which has a very poor record of protecting public health. If the central regulator fails to enforce GMP compliance, then the resulting NSQ drugs will be detected by state drug controllers during their testing and sampling. In addition, we recommend creating state level feedback loops so that the central regulator is constantly provided with inputs from different states on the challenges being faced by them due to drug quality issues. If the Health Ministry is unwilling to adopt the above suggestions to centralise the regulation of drug manufacturing, it must at the very least give

[2] Report of the Expert Committee on a Comprehensive Examination of Drug Regulatory Issues, including the Problem of Spurious Drugs, Ministry of Health & Family Welfare (2003) available at https://pharmaceuticals.gov.in/sites/default/files/MashelkarCommitteeReport.pdf
[3] PRS resource page: https://prsindia.org/billtrack/the-drugs-and-cosmetics-amendment-bill-2013
[4] PIB Press Release, Withdrawal of the Drugs & Cosmetics (Amendment), 2013 (June 23, 2016): https://pib.gov.in/newsite/PrintRelease.aspx?relid=146413

state drug controllers powers to prohibit or ban the entry of drugs manufactured by certain companies who have a track record of making drugs that are not of standard quality. For instance, if drugs of a certain company fail testing on multiple occasions and the state drug controller with jurisdiction over that manufacturing plant takes no action, other states should not be forced to allow the sale of the drugs from such a manufacturer within their respective jurisdictions. Instead, states should be given the power to prohibit the entry of such drugs into their territories by prohibiting pharmacies from selling drugs made by such companies.

B. Proposed Structure, Powers & Accountability Measures for a New Drug Regulator

6. The New Drugs, Cosmetics and Medical Devices Bill, 2022 is entirely silent on overhauling the legal structure of the Central Drugs Standard Control Organisation (CDSCO). This is a serious lapse on part of the drafting committee.

7. As of today, the CDSCO has no statutory backing by any law of Parliament. We presume it was created through an executive order (the Public Information Officer at the CDSCO, in response to a RTI application was unable to identify the legal instrument that created it). It currently operates as a subordinate office to the Directorate General of Health Services (DGHS) which itself is a department within the Ministry of Health & Family Welfare. Headed by the Drugs Controller General of India (DCGI), the CDSCO is located quite distant from the Minister of Health in the administrative hierarchy since the Director General-DGHS and the Health Secretary are administratively superior to the DCGI. This distance between the DCGI and Minister likely increases red-tape and reduces democratic accountability.

8. At the level of state government, the drug control departments are generally located within the health department of the states. In some states like Andhra Pradesh and Telangana, IAS, IPS and IRS officers have been appointed as drug controllers despite having no qualifications or experience in drug regulation. Decisions by the drug controllers can be appealed to the non-specialist bureaucrats in the health department who can then over-rule the drug controllers. Similar powers exist with the Union Health Ministry which can hear appeals against the decisions of the DCGI.

9. Separate and apart from the CDSCO is the Drug Regulation Section of the Ministry of Health and Family Welfare which is responsible for policy related decisions to

the Drugs & Cosmetics Act 1940. It is this "Section" which discharges all the functions delegated to the "central government" in the Drugs & Cosmetics Act 1940. This includes making amendments to the Drugs & Cosmetics Rules 1945; drafting amendments to the Drugs & Cosmetics Act 1940 and prohibiting or regulating the manufacture and sale of drugs under Sections 26A & 26B of the Act. Given that this "Section" lacks any specialist officers, it usually depends entirely on the CDSCO for its technical expertise.

10. The above administrative setup is completely antiquated and is not keeping with modern regulatory structures that have evolved post liberalisation. Post 1990, Parliament created a number of statutory regulators such as the Securities & Exchange Board of India (SEBI), Telecom Regulatory Authority of India (TRAI), Food Safety & Standards Authority of India (FSSAI) and Unique Identification Authority of India (UIDAI). Each of these regulators have their own corporate existence; meaning that they exist outside the legal entity that is the Government of India and hence are exempt from the usual regulations that apply to the Government of India. These regulators have also been given some rule making powers. As a result, these statutory regulators can formulate their own recruitment, financial and administrative rules. They do not necessarily have to conduct recruitment through the Union Public Service Commission (UPSC) and can instead formulate their own employment rules. Such regulatory structure can make it easier to recruit talent from the private sector. This is absolutely essential for regulators dealing with cutting-edge technology since the private sector generally has better technical expertise.

11. Nine years ago, the government had introduced the Drugs & Cosmetics (Amendment) Bill, 2013 to give a proposed Central Drugs Authority an independent corporate identity. As explained earlier, this bill was withdrawn from Parliament.

12. We strongly recommend that the government consider creating a statutory drug regulator, called the National Drug Regulatory Authority (NDRA), with an independent corporate existence and rule-making powers. We propose that such a regulator have four specific divisions: **the first dealing with the creation of technical standards & policy issues; the second dealing with clinical trials & new drug approvals and drug related advertisements; the third dealing with manufacturing licensing, inspections and compliance and a fourth dealing with legal affairs including prosecutions**. Each division should be headed by a Director General, who reports to the Director General of Drug Regulation (DGDR),

the executive head of the regulator equivalent to the rank of Secretary within the Government of India structure.

13. The appointment of the DGDR and the four Director Generals should be made by the President of India on the recommendation of the Council of Ministers. In keeping with norms of democratic accountability, the President should also have the power to remove the DGDR and the four Director General provided such a recommendation has been made by the Council of Ministers.

14. The DGDR should be vested with the power to make rules for recruitment, discharge of financial powers, the creation of posts within the regulator and any technical rules required for the purpose of administering the law.

15. The DGDR should be answerable to **National Drug Regulatory Oversight Board (NDROB) headed by a Cabinet ranked Union Minister and whose membership should consist of two representatives of the Indian Medical Association, two representatives of the Pharmacy Council of India, the Health Secretary and two external experts with experience in drug development and public health and no demonstrable conflicts of interest with the bio-pharma industry.** The NDROB should be required to mandatorily meet twice a year to review the functioning of the regulator and sign off on the Annual Report, Audit Report and accounts of the NDRA which should be tabled before both Houses of Parliament before April 30 following the end of a financial year.

16. In addition to the oversight provided by the DAOB, the law should mandatorily require that **the NDRA to be subject to a detailed evaluation once in four years by a panel of experts nominated by the Union Minister of Health, the Leader of Opposition and the Comptroller & Auditor General of India.** The evaluation report should be tabled before Parliament within 90 days of being submitted to the Union Minister of Health.

17. An important issue that must be clarified in the law, are the qualification requirements for the post of DGDR and the four Director Generals heading each division. So far, the post of the DCGI has primarily been captured by a lobby of pharmacists who lack broad exposure to public health. Despite the 59th report of the Department Related Parliamentary Standing Committee on Health & Family Welfare raising this issue and urging the government to appoint doctors with experience in public health to the post of the DCGI, the Ministry has taken no step

to change the qualification requirement.[5] This despite an expert committee setup by the Ministry and comprising Satyananda Misra, M.K. Bhan and Dr. Ranjit Roy Choudhury agreeing with the Parliamentary Committee's recommendation on this issue.[6] This is because of deep seated opposition by the lobby of pharmacists in control of the CDSCO. **The Ministry would be well advised to consider the issue of drug regulation through a public health perspective rather than continue to look at it as a purely a manufacturing issue**. Typical training imparted to pharmacists is limited to manufacturing and they usually have little exposure to broader public health concerns. **Ideally, a medical doctor with considerable training or experience in public health should be appointed to the post of DGDR.** Similarly, the law must provide for the qualification criteria of each of the four Director Generals to ensure specialists and not IAS officers are appointed to these positions.

C. Reforming the regulatory process for clinical trials

18. Clinical trials have had a short and controversial history in India. The Indian Parliament has historically never formulated any policy on the regulation of clinical trials. The Health Ministry has always regulated clinical trials through its rule making powers. The most recent effort was the New Drugs & Clinical Trial Rules, 2019.

19. The New Drugs, Cosmetics and Medical Devices Bill, 2022 presents the first opportunity for Parliament to create a sound regulatory structure for regulating clinical trials. Unfortunately, the government's proposals in this Bill creates only a skeletal regulatory structure for clinical trials, which is inadequate and completely insufficient to ensure public health and enable the industry to upskill itself.

20. The proposed Bill covers only the basic requirements, i.e., clinical trials must be approved by both the regulator and an ethics committee, that records pertaining to the clinical trials must be maintained, that compensation shall be payable to those who volunteer for a clinical trial if they suffer adverse events causally related to the trial and finally penalties for violating either the aforementioned

[5] 59th Report of the Parliamentary Standing Committee on Health & Family Welfare on 'The Functioning of the Central Drugs Standard Control Organisation' at para 3.6 to 3.8 available at http://164.100.47.5/newcommittee/reports/englishcommittees/committee%20on%20health%20and%20family%20welfare/59.pdf.
[6] Report of the 'Expert Committee setup to suggest recruitment rules/job description for senior level posts in Central Drug Standard Control Organisation' available at https://dineshthakur.com/wp-content/uploads/2016/03/2016.03.11-PIL-1-Annexure-C-24.pdf.

mandatory requirements of prior permission or the terms and conditions of approval. In our opinion this regulatory structure is very basic, fails comprehensively in guaranteeing transparency and concentrates too much power in the hands of a "central licensing authority". We propose a few recommendations below to create a more robust process.

21. **Giving the Clinical Trial Registry a legal backing:** We strongly recommend that the government give legal backing to the Clinical Trial Registry of India (http://www.ctri.nic.in) which is an online database maintained by the National Institute for Medical Statistics, which operates under the umbrella of the Indian Council of Medical Research (ICMR). The CTRI has existed since 15th June, 2009 as a voluntary measure. The New Drugs & Clinical Trial Rules, 2019 made it mandatory for all clinical trials to be registered on the CTRI despite the CTRI itself not having any legal recognition. The new Bill must provide legal recognition to the CTRI and place it under the administration of a Registrar of Clinical Trials, who should be responsible for maintaining the authenticity and integrity of the data contained in the CTRI. The Registrar of Clinical Trials should be given the power to formulate rules regarding the functioning of the Registry including the hiring of appropriate resources.

22. **Mandating the disclosure and publication of clinical trial results on the CTRI:** While the nuts and bolts of the CTRI's functioning can be left to the Registrar, we do strongly recommend that certain requirements be spelt out clearly in the law. **In the interests of furthering transparency, the new law must mandatorily require the CTRI to host on its website, not just the minutes of all ethics committees but also the results of the approved clinical trials.** By "results of the clinical trials", we mean the primary data collected during clinical trials as well as the pre-prints of studies intended to be published in peer-reviewed journals. This is an absolute necessity from a public health perspective; especially in a country like India where large-scale data fabrication is a common phenomenon at clinical research organisations conducting these clinical trials. Even in countries like the United States, the Food and Drug Administration Amendments Act enacted in 2007, mandatorily requires sponsors of clinical trials to disclose all results of the clinical trials. The United States Congress specifically enacted this law in order to make it impossible for pharmaceutical companies to hide inconvenient results during clinical trials.[7] There is no reason for India to not enact a similar requirement in

[7] *Seife & Lurie v. U.S. Department of Health and Human Services et al.*, No. 1:18-cv-11462, 2020 WL 883478 (S.D.N.Y. Feb. 24, 2020) available at https://law.yale.edu/mfia/projects/open-data/seife-v-hhs

its law given the number of poorly designed studies that have been registered and approved by the regulator currently in the CTRI.

23. Further, given the controversial history of clinical trials in India, the law must also mandatorily impose a duty on the ethics committee to investigate and submit reports to the Registrar of the CTRI in the case of any deaths or serious adverse events during the conduct of clinical trials within a time period of 30 days. Such reports, upon review, must be publicly disclosed so as to build public confidence in the regulator.

24. **The approval of clinical trials:** The process of approving a clinical trial under the current law is left to the "Central Licensing Authority". In our opinion, it would be a serious mistake to vest this important responsibility in the hands of one person. **The law should mandate the creation of a multi-disciplinary "Clinical Trial Advisory Committee" that draws from a roster of independent experts with experience in the conduct of clinical trials for the specific therapeutic area under review and qualified biostatisticians who can review the trial design.** These experts should be required to assess and approve the clinical trial protocol and make their recommendations to the "Central Licensing Authority" who should be required to provide reasons in writing if they disagree with the recommendation of the advisory committee. The minutes of the meetings of the advisory committee and the final decision of the Central Licensing Authority should mandatorily be made publicly available within 7 days.

25. **Require mandatory registrations and data integrity measures for CROs:** Over the last two decades, there have been multiple data integrity scandals at Indian Clinical Research Organisations (CROs) across the country. Each and every one of these scandals has been discovered by foreign regulatory agencies from the United States or Europe. In many of these instances, foreign regulatory agencies have cancelled approvals of all drugs whose market authorization was based on data that was generated in these CROs primarily due to data integrity. Fabrication of data or failure to maintain data integrity is harmful not just to trial participants but also to the general public who will be administered these drugs. Yet the New Drugs, Clinical Trials and Medical Devices Bill, 2022 does little to address this issue. At most, Section 158(w) gives the Central Government the power to make rules on the manner in which data, records, registers and other documents are to be maintained by CROs. In our opinion this is wholly insufficient.

26. We strongly recommend that CROs be subject to registration requirements with the law clearly laying down some minimum requirements that need to be fulfilled by CROs prior to registration. **These requirements should include the employment of personnel who have the necessary qualifications and training to conduct clinical trials; informed consent, management of clinical supplies, blinding and unblinding procedures, the use of software programs that record an audit trail in order to protect against data fabrication.** Further CROs must be subject to yearly cGCP inspections. **All inspection reports must be made publicly available in a searchable digital database maintained in an open data format. Lastly, we believe that the law must make it an offence for CROs to manipulate raw data generated during the conduct of clinical trials.** This is necessary because there has not been a single prosecution of a CRO in India despite numerous reports by foreign regulators of data manipulation and fabrication. This may be due to the fact that such an offence is not clearly articulated in the law. Clear articulation in the law of penalties for data fabrication will hopefully act as a deterrent and ensure greater data integrity during the conduct of clinical studies in India.

27. **Requiring CROs to vet trial participants through Aadhaar based biometric authentication:** One of the serious problems with the conduct of clinical trials in India is the fact that study volunteers are not vetted properly. Multiple reports in the press have documented the phenomenon of volunteers enrolling themselves in more than one clinical trial simultaneously or with no interval between two successive clinical trials.[8] They do so because they get paid to participate in each of the clinical trials. Participating in multiple clinical trials at the same time is dangerous for the volunteers and may also lead to distortion of the final results of the clinical trial data. One way to avoid this problem is for all CROs to mandatorily carry out Aadhaar based biometric authentication of volunteers after which their details may be vetted against a centrally maintained database operated by the CTRI. The database should be designed in a manner to automatically flag volunteers who are currently or recently enrolled in a clinical trial.

28. **The creation of such a database will obviously have privacy ramifications and it is important that the CTRI adopt both security measures and a data**

[8] Zeba Siddiqui, 'Serial testers and cursory checks – India's flawed generic drugs trials business', *Reuters* (December 28, 2016) available at https://www.reuters.com/article/uk-india-drug-testing-insight-idUKKBN14G1UO; Priyanka Pulla, 'Lured by blood money: Serial Volunteers set a disturbing trend', available at https://www.thehindu.com/opinion/op-ed/lured-by-blood-money-clinical-trials/article61841026.ece.

protection framework aimed at reducing the possibility of leaks of personal health data of clinical trial volunteers.

D. Reforming the new drug approval process:

29. One of the most controversial areas of drug regulation in India is the issue of approval of new drugs. In 2012, the 59th report of the Parliamentary Standing Committee had made scathing observations regarding the manner in which new drugs were being approved by the CDSCO. The committee accused the CDSCO of colluding with the pharmaceutical industry in order to approve drugs that had not been approved in better regulated markets of the West.[9] The committee diagnosed the following as the main problem[10]:

> "On a more fundamental issue the Committee has come to the conclusion that when it comes to approving new drugs, too much is left to the absolute discretion of the CDSCO officials. There are no well laid down guidelines for determining whether consultation with experts is required. Thus the decision to seek or not to seek expert opinion on new drugs lies exclusively with the non-medical functionaries of CDSCO leaving the doors wide open to the risk of irrational and incorrect decisions with potential to harm public health apart from the possibility of abuse of arbitrary discretionary powers"

30. A subsequent enquiry by a committee constituted by the DCGI to investigate the issues raised by the parliamentary committee concluded that many of the approvals by the DCGI were "arbitrary, whimsical and inconsistent" with the law.[11]

31. In the months following the tabling of the parliamentary committee, the CDSCO did take corrective actions to address some of the findings of the Parliamentary Committee. For instance, the DCGI created Subject Expert Committees (SECs) consisting of external experts to advise the DCGI on approval of each new drug application. However as demonstrated during the COVID pandemic, this new system did not result in a more rigorous system of drug approvals. This was evidenced most prominently by the fact that many of the new drugs approved by

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[9] 59th Report of the Parliamentary Standing Committee on Health & Family Welfare on 'The Functioning of the Central Drugs Standard Control Organisation' at para 7.42 available at http://164.100.47.5/newcommittee/reports/englishcommittees/committee%20on%20health%20and%20family%20welfare/59.pdf at

[10] Ibid at para 7.37.

[11] T.M. Mohapatra, Report of the Committee constituted to review the procedures and practices followed by CDSCO for granting approval and clinical trials on certain drugs *available at* https://dineshthakur.com/wp-content/uploads/2020/07/Mohapatra-Committee-Report-Official-Copy.pdf.

the DCGI on the recommendation of the SECs were not included by the government's national taskforce in its treatment guidelines. The exclusion of these drugs approved by the DCGI from the national treatment guidelines was most likely because they were approved on the basis of poorly designed clinical trials or before clinical trials even concluded. To make matters worse, the government refused to disclose the membership of the SEC until a parliamentary question forced its hand.

32. Any new law must necessarily consider revamping the process by which new drugs are approved. Regrettably, the new bill is entirely silent in this regard. It delegates the power to determine the entire process by which new drugs are approved to the "central licensing authority". It also vests in this authority, the power to abbreviate or do away with the need for pre-clinical or clinical data in public interest. Vesting such vast discretion in the hands of a few unelected bureaucrats represents a continuation of the status quo and will guarantee controversial approvals in the future.

33. In our opinion, any new law must reform the drug approval process by specifying the scientific standards which need to be met and creating a transparent and accountable system of drug approvals.

34. To begin with, the law must specify that the default mode of gathering proof for granting approvals to new drugs is a double-blind, randomised clinical trial that establishes both safety and efficacy of the new drug in question. The law must however also be flexible to allow for deviations from this standard provided of course that the scientific rationale for such deviations is recorded in writing and made available to the general public in a time bound manner.

35. It is also important that the law clearly specify that **a new drug can be approved for marketing only and only if the clinical trial clearly generates adequate proof of safety and efficacy of the drug.** In order to verify the veracity of information submitted by a pharmaceutical company along with an application to approve a new drug, the law must mandate that the application and the accompanying data be subject to a review by a committee of multi-disciplinary scientists with experts in different areas of chemistry, biology, pharmacology, biotechnology, microbiology, statistics and regulatory sciences etc. as may be pertinent for that particular drug. **This committee should be required to prepare a "Drug Assessment Report" and publish the same for public comments and feedback prior to the final approval of the drug.**

36. This "Drug Assessment Report" should then form the basis of deliberations of a "Subject Expert Committee" (SECs) consisting of external doctors and scientists with expertise in the area of therapy for which the new drug is being approved. These SECs must have statutory backing, with the law clearly specifying the qualification criteria and the manner of appointment to the SEC. **Any conflicts of interest with any member of the SEC should be publicly disclosed.** The proceedings of the SEC must be subject to mandatory transparency requirements. Rather than releasing a mere 150-200 words summary of the entire deliberations, we recommend that a verbatim transcript of the entire deliberations be released publicly so that the general public can inform themselves of the deliberations that led to the approval or rejection of a new drug application.

37. After the final recommendations of the SEC has been published, **the regulator must be required by law to invite public comments on the recommendations of the SEC.** The law must specify the time period within which such comments may be submitted, after which the regulator must be required to publish a public response to all substantive objections received from the general public. These proceedings must necessarily be open for the members of the general public.

38. The final decision to approve or reject a new drug application must be vested in the person appointed to head the regulator, based on the recommendations of the SEC, the Drug Assessment Report and the public comments. **Any final decision that deviates from the recommendations of the SEC must be explained in writing by the person heading the regulator.**

39. Once final approval is received for a new drug application, **the law must mandatorily require the pharmaceutical company to submit it labelling, tradename and promotional material for a review process by a specialist committee**. This is important because it is widely known that pharmaceutical companies in India tend to overplay the effectiveness of their drugs during the course of marketing, while underplaying their side-effects. On the issue of tradenames, India has a long history of massive trademark litigation over similar and confusing names used by different pharmaceutical companies for same and different drugs. The Parliamentary Standing Committee, the Supreme Court of India and more recently, the Delhi High Court have repeatedly flagged this issue, pointing out the dangers of confusion caused by similar sounding pharmaceutical names among patients. Globally, the task of approving tradenames of drugs is vested with drug regulators. In India, the recent

discussions in the Delhi High Court have centered around giving this responsibility to the Trade Marks Registry. In our opinion this is bad idea and the new law must specifically vest this function of vetting the name with the drug regulator instead of the drug regulator.[12]

40. For the reasons mentioned above, it is absolutely necessary that the trade-name, labelling and promotional material associated with any new drug be subject to very strict scrutiny by a committee of experts to ensure that the same is in compliance with the scope of the approval by the regulator.

41. **Dealing with the ghost of pre-1988 new drug approvals:** The new law should also deal with the ghost of pre-1988 new drug approvals. The year 1988 is relevant because it was in this year that the Government of India amended the Drugs & Cosmetics Rules, 1945 to finally require all new drugs to be evaluated on the basis of data from clinical trials as a condition for approval. While doing so, the law failed to create a process to vet all pre-1988 approved drugs on the basis of clinical evidence. **It is incumbent on government to rectify this historical mistake and create a process to vet all pre-1988 drugs based on available clinical data, published scientific literature and expert scientific opinion.** It should not be the case that old drugs lacking scientific basis are still being sold in India despite being discontinued in other countries.

42. **Conflict of Interest norms for external experts engaged to advise the regulator on the approval of clinical trials and new drugs:** Given that the regulator is increasingly depending on external experts to participate in key regulatory decisions, it is important for the new law to lay down disclosure norms for such experts in order for the general public to determine whether the experts have a "conflict of interest". In particular **the disclosure norms should require external experts to provide a list of all grants or consultancies that they may have received from the pharmaceutical industry or other related organizations.** Experts should not be allowed to participate in regulatory decisions involving pharmaceutical companies from whom they have received financial support, either in the form of grants or consultancies. Such a prohibition in the law is required to ensure public confidence in the regulatory process and the resulting decisions.

[12] Gireesh Babu, 'Delhi HC issues notice to DCGI on steps taken related to approval of drugs with identical brand names', *PharmaBiz* (April 27, 2022) available at http://www.pharmabiz.com/NewsDetails.aspx?aid=149316&sid=1

E. Reforming the regulatory requirements for approving generic drugs

43. Historically the process for approving generic drugs in India has been unnecessarily convoluted and lacking in any scientific rationale. We say this because generic drugs that get approved within 4 years of the innovator drug being approved by the DCGI were historically subject to different requirements when compared to those generic drugs that are approved after 4 years by state drug controllers. Generic drugs approved by state drug controllers after the initial 4 year period were not required to submit any bioequivalence or stability data until 2017 & 2018 respectively. However, even the mandatory bioequivalence and stability requirements introduced in the last few years have not been clearly articulated. It is important that the new drug regulatory law clarify these issues in abundant detail.

44. **The importance of bioequivalence testing and biowaivers:** The simple aim of bioequivalence testing is to ensure that a generic medicine has the same bioavailability in a patient's bloodstream as the innovator drug which is evaluated through a clinical trial. In essence, bioequivalence testing measures the solubility and permeability of a drug i.e., can the drug permeate through the intestinal membrane to enter the bloodstream and if so, at what rate. Such testing is important because although a generic drug will have the same active ingredient as the innovator drug, its manufacturer may use different excipients, binders etc. which will affect the ability of the drug to dissolve into the bloodstream; this is called bioavailablity. Every drug displays a dose-response, meaning its concentration increases once it is administered and then the body excretes it through normal bodily functions. The highest concentration of the drug in the bloodstream and the total drug available before it is excreted are key measurement criteria to demonstrate equivalence between the innovator formulation and the generic formulation. Once such bioequivalence is established between an innovator and generic drug, the latter can be clinically prescribed as a substitute for the former. This testing to establish bioequivalence is carried on healthy human volunteers rather than patients with the disease as is the case with clinical trials. One of the reasons, that generic drugs are more affordable is because of the fact that bioequivalence studies are simpler and cheaper to conduct than full-fledged clinical trials needed to get regulatory approval for new drugs.[13]

[13] Dinesh Thakur, A petition to reform the legal framework for bioequivalence testing requirements for generic drugs: https://casemindia.org/a-petition-to-reform-the-legal-framework-for-bioequivalence-testing-requirements-for-generic-drugs/

45. When India finally made bioequivalence testing mandatory in 2017, it did so in a convoluted way when it adopted the Biopharmaceutical Classification System (BCS). The BCS divides all drugs into 4 categories depending on the solubility and permeability of the drug in question. As per the amendments to Indian law in 2017, only those drugs falling in 2 of the 4 categories per the BCS classification, having poor solubility characteristics are required to be tested for their bioavailability; except that the law does not clearly lay down parameters for what exactly is high or low solubility. For drugs classified as having high solubility, the law allows for the grant of "biowaivers"; meaning that no bioequivalence data is required for approval. As of today, we have no idea how different state drug controllers are interpreting "high or low" solubility while applying the BCS system to determine which generic drugs that need to be tested for bioequivalence. The law must redress this issue and if it cannot come up with scientifically sensible parameters for solubility and permeability, it should mandate bioequivalence testing for all generic drugs regardless of their solubility or permeability characteristics.

46. **Selecting the "reference product":** A related issue when it comes to testing for bioequivalence is the drug which is to be used as the "reference product" for the purpose of establishing bioequivalence. Usually the "reference product" is the innovator product that has shown to be therapeutically effective clinical trials. As of now, Indian law is completely silent on the process by which state drug controllers are to select "reference products". The new law must tackle this issue and clarify how exactly these products will be determined and create an easy pathway for accessing such "references products".

47. **Drugs prohibited from the biowaiver route:** Last but not the least, when it comes to bioequivalence testing and biowaivers, regulators like the USFDA do not allow for biowaivers for certain kind of medications including drugs demonstrating a Narrow Therapeutic Index (NTI) – these are drugs where even small variations of bioavailability will have significant impact on treatment outcomes. Surprisingly, Indian law does not mention any exceptions to the concept of "biowaivers". This is an issue that must be addressed by the new law on the basis of scientific evidence.

48. **Stability testing requirements:** Similar technical issues exist with regard to the stability testing requirements for generic drugs. The issue of stability testing is critical in guaranteeing that only medicines of standard quality reach patients. This is because most drugs, which are combination of chemical substances (and in the case of biosimilars, proteins and peptides) are inherently unstable over

long durations of time. It takes a feat of chemical engineering to ensure the stability of a drug over a period of several months and in varying conditions over a supply chain that may cross climate zones. If the manufacturing process is anything less than precise, there is a high possibility that the resulting drug will degrade in a manner that affects its therapeutic efficacy. This could have an adverse impact on patients, especially if the drug qualifies as a life-saving drug.[14]

49. The most common environmental factors influencing stability of drugs are temperature, humidity and sunlight. These three factors could severely degrade drugs during their transport and storage. For this reason, almost every country requires all drugs to undergo mandatory stability testing for their entire life-cycle. Such stability testing requires exposing a sample of every batch manufactured to external elements such as heat, humidity and light in special chambers designed for such testing. If the sample fails initial stability testing, it is usually mandated that the batch from where it is drawn to be destroyed in its entirety. Presuming the batch clears its initial stability testing, most countries require the manufacturer to test retained samples from that batch which is shipped to the market at regular intervals until the lifecycle of the drugs expires. If at any stage, the samples so retained fail stability testing, the manufacturer is required to affect a recall across the supply chain. It is possible for a drug to be stable for a few months of its lifecycle and degrade thereafter due to poor manufacturing practices or exposure to high heat and humidity conditions. Since recalls are expensive and deeply damaging to the reputation of pharmaceutical companies, there is a great incentive for these companies to fabricate testing data, especially since most countries require such testing to be done internally with records being maintained for inspections by external regulators. It is no surprise then that multiple Indian companies, starting with Ranbaxy, have been caught fabricating stability data by the USFDA.

50. Despite being aware of the importance of stability testing for a long time now, the Indian government has dragged its feet on making such testing mandatory for all generic drugs. In 2013, both the Drugs Consultative Committee (DCC) and the Drugs Technical Advisory Board (DTAB) did deliberate on the issue before making recommendations to the Government to make stability testing compulsory. In fact, the DCC stated that the lack of a mandatory stability testing requirement was a "serious lacunae" and that "that it is necessary that evidence

[14] Dinesh Thakur, A petition to relook the legal framework governing stability testing of drugs in India: https://casemindia.org/a-petition-to-relook-the-legal-framework-governing-stability-testing-of-drugs-in-india/

and data of the stability of the drug products proposed to be manufactured by the licensee are required to be submitted to the regulatory authorities so as to ensure the stability of the drug formulations licensed in the country by the State Licensing Authorities."

51. Thereafter, one set of amendments to the Drugs & Cosmetics Rules, 1945 was published by the Ministry for comments in 2015. These amendments never became law – for reasons that were never disclosed. In 2018, another, a significantly watered down version was made the law. All generic drugs, even those approved after the first 4 years would be required to submit stability data for approval. But unlike the draft amendments of 2015 which specifically required stability data to be generated as per the requirements of Appendix IX, the version in 2018 did not lay down any specifics on the kind of data that was required to be generated, the sample size for testing and the manner in which the stability of the generic formulation had to be documented. Given that India has 36 different state licensing authorities, it makes no sense to not to specify these requirements in the law. Such ambiguity enables wide interpretations of the law by the state licensing authorities resulting in the prevalence of substandard drug products in our drug supply.

52. In June, 2020 we sent a petition the Ministry of Health flagged this lacuna in Indian law specifically asking for greater clarity on stability testing requirements across the country. Unfortunately, the Ministry did not take any action in this regard. The new law provides an opportunity to rectify this historical mistake by ensuring that all drugs, be it new or generic, are subject to the same stability testing.

53. **Bioequivalence and stability data requirement should apply retrospectively:** To begin with, since there is lack of clarity on whether the bioequivalence and stability data requirements apply retrospectively to generic drugs approved prior to 2017 and 2018; **we believe the new law must specifically require all generic drugs, irrespective of when they received their approval, to mandatorily submit data establishing their bioequivalence and stability**. The new law should mandate a timeline within which all manufacturers of generic drugs submit bioequivalence and stability data to the central regulator. Until such time, **the law must mandate labelling requirements for such drugs to indicate to patients whether a drug has in fact submitted such data on bioequivalence and stability to the regulator**.

F. Making GMP compliance the centerpiece of the new regulatory law

54. For most of Indian history, drug inspectors in India have kept a tab on quality of our drug supply by drawing samples of drugs from the market and testing them in government laboratories. Samples that fail testing have led to the prosecution of manufacturers making drugs that are Not of Standard Quality (NSQ). This is a 19th century model of regulation that focused on products and not processes. The rest of the world has long since transitioned to focusing on compliance with good manufacturing processes (GMP).

55. Around 1988, the Drugs & Cosmetics Rules, 1945 were finally amended to include a rudimentary Good Manufacturing Practices (GMP) Code which was upgraded substantially in 2001. The rules were also amended to make GMP compliance a necessary precondition for the grant of a manufacturing licence. While the terms of granting a manufacturing licence require an annual inspection for GMP compliance by the pharmaceutical company, it is anybody's guest as to whether such inspections are actually being conducted.

56. The proposed Bill does not even mention the phrase GMP. The focus of the drafters has been to continue the old mode of regulation which depends on drawing and testing samples of drugs from the market. In our opinion, this is an erroneous approach to regulation. The process of drawing and testing samples at random from the market is not as thorough or efficient as ensuring GMP compliance at manufacturing facilities.

57. In order to make GMP compliance the centerpiece of drug regulation in India, we believe that it is necessary to shift the legal mandates for GMP compliance from the rules to the parent statute. This should be followed by **creating a legal mandate for publication of all inspection reports related to GMP compliance on a government website for viewing by the general public within a specified timeframe following such inspections**. Such transparency requirements will allow citizens to verify for themselves whether annual inspections are being carried out as required under the law. Further. the inspections reports themselves will be useful for procurement officers in both public and private hospitals in making procurement decisions.

58. A second important step is **to create a presumption in the law that drugs manufactured in violation of the GMP code are "adulterated" and punishable with a jail term**. Indian law already presumes drugs manufactured

in "insanitary conditions" are "adulterated". **By extending this presumption to all drugs manufactured in violation of the GMP code will force all manufacturers to take GMP compliance with the seriousness it deserves.** It is necessary to create legal deterrents that force Indian pharmaceutical companies to take GMP compliance more seriously. Attaching the presumption of "Adulterated" to drugs manufactured in facilities violating the GMP code will help in creating such a legal deterrent. As of today, we are yet to come across a single pharmaceutical company successfully prosecuted in India for failure to comply with the GMP code. This is most likely because violation of the GMP code is not clearly articulated as an offence in Indian law. At most, only manufacturing licences are cancelled for a failure to comply with the GMP code.

59. Last but not the least, if the Ministry continues to let state governments issue manufacturing licences, it may be prudent to ensure that all GMP inspections are carried out by joint teams of central and state drug inspectors. The law was amended in 2018 to allow for joint inspections and the constitutionality of the amendment was upheld by the Madras High Court after it was joint challenged by state drug controllers and the pharmaceutical industry.[15] That amendment however was not clear on whether licences would be renewed in case of a disagreement between the central and state inspection teams. **It is important for the new law to clarify that a manufacturing licence cannot be renewed unless both the central and state teams agreed to renew the same**. All such decisions must be publicly disclosed in a time-bound manner for the benefit of the citizens of the country.

G. Revamping testing strategies, the IPC, testing laboratories and enact a timebound recall law

60. The new Bill continues with the existing requirement under the Drugs & Cosmetics Act, 1940 for drug inspectors to draw samples from the market for testing in government laboratories. Although such as an approach is less efficient and rigorous than ensuring GMP compliance, it does serve as a useful indicator of the drug quality in the market. There are however four challenges in enforcing this model of regulation in India.

61. The *first* challenge is in creating proper sampling guidelines. Currently none of the state drug controllers have a sampling strategy in place to guide drug

[15] All India Drugs Control Officers & Anr. v. The Government of India before the Madras High Court decided on February 28, 2022 available at https://indiankanoon.org/doc/191958036/.

inspectors on the type of drugs they should be drawing from the market for the purpose of testing. This fact coupled with limited budgets ensures that drug inspectors end up purchasing only certain type of drugs from the market. For example, we noticed that antiacids are tested far too frequently in India compared to say oncology drugs or injectables. The law must require sampling to by conducted according to a statistically sound strategy developed in conjunction with experts in statistical sampling.

62. The *second* challenge lies in reforming the functioning of the Indian Pharmacopoeia Commission (IPC). The IPC is responsible for publishing the Indian Pharmacopeia, which contains monographs of various formulations and also selling reference standards to both the industry and the government laboratories that are responsible for testing samples sourced from the market by drug inspectors. While there have not been any detailed studies documenting the shortcomings of the IPC, minutes of the meetings of the Drugs Consultative Committee (DCC) indicate that the IPC is not very efficient in ensuring the timely delivery of reference standards. These delays in suppling reference standards can cause consequential delays in testing by government laboratories. Since samples drawn from the market have to tested before the "Expiry dates" listed on the labels, any delay in procuring reference standards may result in the sample being discarded by government testing laboratories. The new law must endeavour to make the functioning of the IPC more transparent and accountable to stakeholders. One way to achieve this goal is to subject the functioning of the IPC to an annual review by experts from outside the government. An alternative route is for the law to directly revamp the working of the IPC itself by giving it an independent statutory existence under experts rather than the Health Secretary as is the present case. Offering the IPC more administrative flexibility may improve its operational efficiency.

63. The *third* challenge lies in equipping test laboratories with the necessary equipment to conduct all prescribed tests in the pharmacopoeia. It is no secret that in many states, the drug testing laboratories simply do not have the equipment and staff required to conduct timely, efficient and accurate testing. We are aware of state laboratories in poorly governed states that do not even have any working HPLC machines without which it is almost impossible to carry out any tests for the samples sourced by the drug inspectors in that state. Given the importance of these laboratories to the functioning of the regulatory system, the law must consider creating a statutory audit mechanism where the functioning of the labs is audited on an annual basis and the audit reports are made publicly available so as to create some accountability to the citizens of

India. Hopefully such a transparency measure will create pressure on the state governments to ensure that their laboratories are well resourced and functional. A related transparency measure which will go a long way is creating a publicly accessible digital database containing all test reports of all drugs that have failed quality testing. Currently, the https://xlnindia.gov.in/ features testing data predominantly from Gujarat, Maharashtra and Kerala. Creating a single database for the country will go a long way in helping procurement agencies assessing the credibility of drug manufacturers.

64. The *fourth* challenge lies in creating a legal requirement for the government to ensure the recall of the entire batch of drugs once a sample fails testing in government laboratories. This is no easy task. The government has been trying to create such a mandatory recall mechanism since 1976 but has not been able to arrive at a consensus. After a parliamentary committee raised the issue in 2012, the CDSCO did formulate certain recall guidelines but these guidelines lacked the force of law and are hence not binding on any of the authorities. As a result, even after state and central laboratories detect drugs that are not of standard quality, there is no legal mechanism to mandate the withdrawal of the drugs from the market. At most, state drug controllers may write to the manufacturer asking it to withdraw the drug but since state drug controllers cannot operate beyond their state jurisdictional borders, there is no way to verify whether the recall is actually effective. More importantly, there is no procedure to actually follow up and inform patients who may have consumed such not of standard quality drugs. The law must specifically vest this function of overseeing recall of NSQ drugs in the central drug regulator and ensure that the task is performed in a transparent manner.

H. Regulating pharmacies & their supply chains

65. The new Bill is surprisingly silent on the issue of regulating pharmacies and supply chains through which a drug transits from the manufacturer to the patient. Currently some of these issues are dealt with under the Drugs & Cosmetics Rules, 1945; but even these rules are entirely silent on two critical issues. The first is storage rules during the course of transit of medicines to the pharmacy. The second is the precise storage requirements in pharmacies (Currently the law only requires “proper storage requirements for preserving the properties of the drugs”).

66. That the existing framework for transit and storage of medicines is entirely inadequate was acknowledged by the Drugs Consultative Committee (DCC) in its

46th meeting when it setup a sub-committee in December, 2013 to study this issue. At this meeting, the DCC noted "guidelines on Good Distribution Practices for Pharmaceutical products [are] the need of the hour as India is a vast country having major variations in temperature and climate". However, when the sub-committee after studying the situation recommended that the rules be amended to give legal force to a Good Distribution Practice (GDP) code, the DCC refused. The GDP code, which is largely based on a WHO document contained several useful safeguards that would have ensured that drugs did not degrade during transit and storage. As of today, India does not even mandate temperature and humidity sensors in pharmacies. Indian law also does not require pharmacies to mandatorily have power backups, despite some state drug controllers requesting the DCC to consider making this a mandatory requirement given the state of electricity supply in some parts of the country.

67. Separate and apart from the abysmal state of affairs described above, there is also judicial confusion on the issue of whether a licence is even required from the drug controller for the purpose of merely storing drugs. In the two conflicting judgments, *Swantraj* v. *State of Maharashtra*[16] and *Mohd. Shabir* v. *State of Maharashtra*[17] two different benches of the Supreme Court interpreted a comma in Section 18(c) of the Drugs & Cosmetics Act, 1940 in different ways leading to opposing conclusions on the issue of whether a licence is required for storing drugs for merely storage not intended for sale. The new Bill appears to have missed these conflicting judgments since the placement of the comma has not been altered in Section 41(1)(c). Since the drafting committee did not release an accompanying "notes on clauses" or a whitepaper, we do not know whether this was a conscious choice or an oversight.

68. On the issue of e-pharmacies, the new Bill is clear that it intends to licence such pharmacies. While this is a welcome move, the law is entirely silent on three issues pertaining to e-pharmacies. The *first* is the issue of checking potential prescription abuse. Currently the law requires the prescription to be marked by the pharmacist in order to prevent its misuse. One potential solution to this problem is to create legal regime mandating the use of e-prescriptions as in the United States. These e-prescriptions which will be sent directly from the doctor to the pharmacy through a secure digital protocol will ensure greater accuracy in prescriptions, apart from preventing the possibility of patients reusing prescriptions. **The government must seriously consider this route as it also**

[16] *Swantraj vs State of Maharashtra* 1974 SCR (3) 287 (5 February 1974).
[17] 1979 SCR (2) 997

has the benefit of reducing prescription errors. The *second* is the issue of a data protection framework. Online pharmacies will be storing significant amounts of sensitive health data about citizens. Since India does not have a data protection law, it is essential for the Health Ministry to take the lead and **formulate specific data protection rules for online pharmacies.** There is precedent in this regard since Reserve Bank of India has already taken the lead in prescribing specific data protection requirements for some online financial services. The *third* issue is the lack of regulations on storage of drugs during the course of home delivery. Drugs, unlike other products in the e-commerce business can degrade in adverse storage conditions. Hence it is important for the law to lay down specific regulations governing the manner in which drugs will be delivered home to patients from the pharmacy.

I. Revamping regulation of Ayurvedic drugs:

69. Over the last decade, the traditional medicine industry in India has been plagued with scandals ranging from brazenly misleading advertising to adulteration of its products with chemical painkillers and of course, persistent reports of heavy metal contamination. The new bill does little to rectify the situation. We explain three specific issues, which in our opinion, go to the core of the problem.

70. **The farce of standardisation:** In 1940, when the Federal Legislature enacted the Drugs Act, 1940 the definition of "drugs" in that law excluded the "Ayurvedic" and "Unani" drugs. This was a conscious decision because as noted by the Drugs Inquiry Committee in 1931, it was not possible to standardize traditional medicine in the same manner as modern medicine. Since Ayush drugs are prepared from plants and herbs; the "active pharmaceutical ingredient" is usually not known and without this information, these drugs cannot be standardized.

71. Due to these scientific realities, when Ayurveda and Unani drugs were brought into the purview of the Drugs & Cosmetics Act, 1940 (cosmetics were included in 1962) in 1964, these drugs were subject to very light regulation. Basically, the manufacturers had to ensure that Ayurvedic and Unani drugs were as per the formulae laid down in a set of traditional texts recognised by the law, that the same were manufactured in hygienic premises under a qualified person with certified raw materials and the ingredients were displayed on the labelling of the drug. The law neither required data about safety and efficacy or standardization.

It was not even clear as to how government laboratories would ensure that these traditional drugs adhered to the formulae in traditional texts.

72. The draft bill now requires Ayush drugs to meet the "Standards of identity, purity and strength specified in Ayurveda or Siddha, or Sowa-Rigpa or Unani Pharmacopoeia of India". This requirement existed since 1995 in the rules and the drafting committee merely shifted it from the rules to the main statute.

73. In our opinion, this requirement is mostly pointless because most Ayush products in the market are "patent or proprietary" drugs which are anyway not included in the pharmacopoeia. For even the traditional Ayush drugs which find a mention in the Ayurvedic pharmacopoeia, we must point out that this pharmacopoeia is nowhere as scientifically rigorous as the Indian Pharmacopoeia which sets standards for modern medicine. The former does not even prescribe tests for "dissolution", which is the most important test for Ayush drugs being consumed as tablets or capsules. If the government is serious about standardization of Ayush products, it needs to invest in creating scientifically rigorous pharmacopoeias for the systems of medicine covered under Ayush.

74. **The safety and efficacy of "patent & proprietary" Ayush drugs:** A common presumption amongst the general public about Ayush medicine is that most of it as sold in India derives from ancient Indian texts and thousands of years of wisdom. In reality this is not true. In 1982, the law was mysteriously amended to introduce the concept of "patent & proprietary" Ayurvedic and Unani drugs. This amendment allowed the creation of *new* Ayurvedic and Unani drugs using ingredients mentioned in the traditional texts. For all practical purposes, these were new drugs whose safety and efficacy should have been tested just like any other modern medicine – through rigorous randomized double blind clinical trials. But in 1982, India did not legally require even modern drugs to go through such clinical trials. Those requirements were introduced for modern drugs only in 1988 but were never extended to "patent & proprietary" Ayush drugs or to the traditional Ayush drugs. This was a mistake in our opinion because it opened the doors to scandals related to the safety and misleading claims about efficacy of Ayush drugs. In 2010 the government introduced Rule 158B which creates a vague requirement for some kind of testing and there has been significant confusion whether this includes the requirement to conduct "clinical trials".

In 2018, finally the Ministry of Ayush clarified that it was not necessary for the Ayush industry to conduct clinical trials for Ayush medicine.[18]

75. The new Bill creates a new definition for "innovative drug of Ayurveda or Unani" which will have to be tested as per guidelines laid down by a new body called the "Scientific Research Board" (SRB)". This new body is required to be staffed by Ayush "Experts". It is not clear as to why these supposedly "innovative" Ayush drugs cannot be approved by the same body approving modern "new drugs". We ask this specifically because the Ministry of Ayush, which will end up controlling the SRB, will likely pressurize the latter to approve drugs developed by the many research councils under the Ministry of Ayush. The administration of these research councils are the main reason for the existence of the Ministry of Ayush. Given the woeful track record of these research councils, we see this as an inherent conflict of interest. In our opinion, the law must create the same regulatory pathway for all new drugs regardless of whether they are derived from traditional medicine or are completely new. If not, the government will be creating an incentive for some players to game the system by exploiting the gaps between the approval process for modern drugs and that for patent or proprietary Ayush drugs. This does not serve the interests of public health for the citizens of India.

76. **Regulate the advertising of Ayush drugs:** A related issue that became notorious over the last decade in relation to the Ayush industry is that of misleading advertisements. Several new age Ayurvedic drugs were marketed as being capable for treating diabetes and other diseases that were traditionally not treated with Ayush drugs. This despite the drugs not having gone through rigorous randomised double-blinded clinical trials since there was no legal requirement for approving Ayush drugs. The advertisements for some of these new drugs claiming to treat diabetes led to an outrage. While the Drugs & Magic Remedies (Objectionable Advertisements) Act, 1954 already prohibits some advertisements, in 2018 the Ministry of Ayush introduced Rule 170 to regulate advertising by the Ayush industry by creating an approval process for such advertisements. The entire Ayush industry challenged the constitutionality of the rules before the Delhi High Court on a number of grounds including that the government lacked the power to do so through its rule making authority. The new bill presented a great opportunity to partially blunt this constitutional challenge by expressly bestowing upon the government the power to regulate,

[18] Government of India, Ministry of Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homeopathy (AYUSH), *Government Notification* (No K.11020/03/2017-DCC (AYUSH), 4 July 2018)

and even censor, advertisements of Ayush drugs making outlandish claims of treating diseases for which they have no clinical evidence. Strangely, the bill is silent on this important issue. The new Bill must blunt the constitutional challenge by specifically vesting the power to regulate advertisements by the Ayush industry in the government.

77. **Ayush medicines & the heavy metal problem:** Starting 2004, doctors and academics in the West began publishing studies on shocking quantities of heavy metal content in "Made in India" Ayurvedic products that were marketed in the west as "herbal medicinal products".[19] Indian doctors have often published smaller case studies among Indian patients poisoned by Ayurvedic drugs containing heavy metals. After a media outrage, the Ministry of Health issued an order under an obscure provision called Section 33EEB, fixing limits on heavy metals in Ayurvedic products as per an obscure document of the World Health Organisation (WHO).[20] As far as we know there has never been a prosecution for any violation of this order.

    Under existing law, if the order under Section 33EEB fixing heavy metal limits was violated, the law proposed a punishment of 6 months in prison and a fine of Rs. 10,000. The new bill's approach to this issue is surprisingly cavalier. We say this because "heavy metals" are included in the Eight Schedule to the law. This means that as per Section 108(1) of the new law, Ayush products found containing "heavy metals" are punishable with a minor fine of Rs. 50,000 although the safety limits are not mentioned in the law. To reduce punishment for heavy metal poisoning to a mere fine is bizarre given the gravity of the offence. Heavy metal poisoning is a serious health issue and the government should be creating a more effective deterrent under the law in order to eliminate such contamination in Ayurvedic drugs.

78. To briefly conclude, the drafting committee has missed a golden opportunity to push the Ayush industry into the era of modern science.

[19] Robert B Saper and others, 'Heavy Metal Content of Ayurvedic Herbal Medicine Products' (2004) 292 JAMA 2868
[20] [20] Government of India, Ministry of Health & Family Welfare, Department of Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homeopathy (Order F.No.K-11020/5/97-DCC (AYUSH), 14 October 2005).

J. The move to decriminalise certain quality violations under the new bill

79. Two of the most shocking provisions in this new Bill are Section 56(e) and Section 71. Read together, these provisions decriminalise the act of manufacturing 'Not of Standard Quality' drugs provided the drug has been declared NSQ because of a defect listed in the fourth schedule. Section (e) reduces criminal punishment for these defects listed in the Fourth schedule. This however is a smokescreen since Section 71 allows the government to "compound" all the prosecutions under Section 56(e) meaning, that manufacturers of drugs that have one of the defects listed in the Fourth Schedule will not have to face any prison time as long as they pay a monetary fine.

80. In our opinion, this is a hugely problematic approach to the issue of drug regulation. Once the standard setting body, the Indian Pharmacopeia Commission (IPC) sets the standard with regard to quality, we do not think it makes any scientific sense for the government to treat certain quality violations at a lower penalty than others. In our opinion, the 43 exceptions in the Fourth Schedule do not have any scientific or moral justification. For example, one of the exceptions in the Fourth Schedule is if the drug contains at least 70% of the active ingredient mentioned on the labelling. As per the Indian Pharmacopeia, a variation between 90% to 110% for active ingredient is allowed for most drugs. Effectively reducing this requirement to 70% has dangerous consequences for public health. For example, if a strip of 10 antibiotic tablets each has only 70 mg of active ingredient instead of the 100 mg of active ingredient as listed on the label, at the end of a ten-day course of treatment, the patient would have received only 700 mg of the antibiotic instead of the 1000 mg that the doctor prescribed. Not only would the patient not recover completely from the infection, but chances are she is now a carrier of antibiotic resistant bacteria.

81. The treatment outcomes will be several times worse in case the drugs have "narrow therapeutic index" (NTI), where even minor changes in the dosage can lead to significant difference in treatment outcomes. Anyone taking thyroid medication, Levothyroxine can attest to adverse outcomes from small variations in the quantity of active ingredient in their medicine. Likewise, drugs that act on disorders of the brain, like the anti-depressant Budeprion are susceptible to small changes in the amount of drug that is available to treat patients. These are just two cases where the science is indisputable that even a variation of 10% of the labelled dosage adversely affects treatment outcomes.

82. Two other exceptions in the Fourth Schedule are "particulate contamination/foreign matter" and "related substance". In other words, even if a drug is found to be contaminated with foreign matter that can range from glass particles to fungus to bacterial endotoxins, the manufacturer of such drugs will now be subject to a lower punishment; only a monetary fine. Other types of defects included in the Fourth Schedule include the presence of "heavy metals" despite it being well known that heavy metals in drugs can result in poor treatment outcomes, ranging from mild allergies to serious poisoning.

83. We are certain that if this clause is included in a final legislation, it is only a matter of time before the extremely powerful pharmaceutical industry convinces the government to use its power under the proposed Section 58 to expand the range of defects recognised in the Fourth Schedule. We say this based on the history of how statutory committees like the Drugs Consultative Committee (DCC), consisting of state and national drug controllers, have framed prosecution guidelines in the past advising drug inspectors to not prosecute pharmaceutical companies for many manufacturing defects which have now found their way into the Fourth Schedule.

84. **We strongly advise the government to drop the Fourth Schedule, Section 56(e), Section 58 and Section 71 from this Bill**.

Concluding remarks: While we commend the Ministry of Health and Family Welfare to have undertaken this exercise to amend the Drugs and Cosmetics Act 1940, we believe that the draft as published is seriously flawed and does not address the immediate needs of public health of the citizens of India. Nowhere else was this visible than during the last two years of the Covid-19 pandemic where questionable drugs were approved by the national regulator which never found a place in the National Treatment Guidelines for Covid-19. Such actions by the national regulator have essentially served to transfer wealth from poor and unsuspecting citizens of India into the pockets of the powerful pharmaceutical industry. One such example is Fabiflu, which reportedly earned Rs 762 Crores for its manufacturer despite a poorly conducted clinical study. These are just a few glaring examples of the dysfunction within the drug regulatory system which be traced back to the issues we have highlighted in this document.

We sincerely hope that the Ministry rejects the current Bill as it is written and commissions an independent group of experts with knowledge and experience in the area of drug regulation to author a new Bill that is responsive and accountable to public health and the citizens of India.