



Indian Council for Research on International Economic Relations

Policy Brief # 2

# Drug Quality and Safety Issues in India

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## EXECUTIVE SUMMARY

With the exception of pharmaceuticals,<sup>∞</sup> consumers in most cases are able to *ex ante* perceive the quality of goods. At the heart of this statement is the very peculiar nature of pharmaceuticals as credence goods – those whose quality can rarely be ascertained even *ex post* – resulting in inefficient outcomes for public health. Poor quality medicine due to intentional or negligent lapses in manufacturing may lead to grave consequences, including loss of confidence in health systems and consequent economic losses for the industry. The dynamic and complex nature of pharmaceuticals thus warrants quality assurance at all nodes of the pharmaceutical value chain. As such, effective regulation of these processes can largely ensure delivery of safe and high-quality medicines to the masses.

With India being recognized as the pharmacy of the developing world, it is believed that there is need for a strict quality specification and enforcement within the country in the first place. There have been several reports where doubts have been raised regarding quality of medicines available in and from India. The present study attempts to address these issues, firstly, by bringing to fore the differences in the multiple definitions of poor quality medicines and their varied implications. Secondly, the aim is to critically analyze the existing views of diverse stakeholders and look at the best practices followed domestically and internationally, in order to suggest technical and institutional reforms for the Indian regulatory regime and other relevant stakeholders that affect drug quality, directly or indirectly.

This study is based on extensive literature survey and field research conducted in four states (Kerala, Tamil Nadu, Gujarat and Maharashtra) and four countries (USA, UK, China, Indonesia). Restricting ourselves to the realm of quality of drugs manufactured within the country, this study does not broach upon the issues that arise from drug approval processes and clinical trials, nor do we address the concerns of intellectual property rights and pricing issues. Some of these topics will be dealt with in future phases of the Research Program on Drug Regulatory Reforms in India under ICRIER's Health Policy Initiative.

This document summarizes the study's broad policy recommendations along with measures for their operationalization.\* Some of the major policy recommendations include uniformity in the interpretation of legal terminology contained in the relevant act and guidelines, rationalization of work distribution across regulatory personnel, use of technological tools to bridge the gap in the data available to policymakers, and need for driving the industry towards voluntary compliance and self-regulation. Participation of all stakeholders towards making dedicated efforts in these critical reform areas can pave the way for India to become a widely acknowledged source of good quality and efficacious medicines.

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<sup>∞</sup> For the purpose of this study, the terms drug, medicine, pharmaceutical product and pharmaceuticals are used interchangeably to refer to medicinal products intended for prophylactic, diagnostic or therapeutic use.

\* For a detailed analysis of the research findings, please refer to the relevant working paper enclosed herewith and also accessible at <http://icrier.org/publications/working-papers/>.

## CONCERNS ABOUT DRUG QUALITY AND SAFETY IN INDIA

India is home to over 135 FDA-approved pharmaceutical manufacturing units and in 2012, its INR 1.1 trillion – largely generics making – drug industry exported around INR 400 billion worth of drugs across the globe (Unnikrishnan, 2013). Although the industry is growing at double-digit rates, there have been several incidents in the recent years that have created an atmosphere of mistrust among various stakeholders, particularly regarding drug quality.

On several occasions, it has been reported that the prevalence of poor quality drugs in the Indian market is as high as 30 percent while the National Drug Regulator – Central Drugs Standard Control Organization (CDSCO) has argued that such reports are unverified and not backed with sound evidence. It subsequently conducted an independent study in 2009 and reported a prevalence figure of 0.3 percent for the spurious drugs in the domestic market. The Parliamentary Standing Committee on Health and Family Welfare in its 59th Report on the functioning of the CDSCO (henceforth, 59th report) found that the problem is not as simple as it is projected to be, as very often counterfeits are confused with spurious drugs, leading to inaccurate prevalence rates for poor quality drugs. Further, the 59th report notes that the evidence generated from central and state drug testing laboratories shows the prevalence to be around 7-8 percent when sub-standard drugs are taken into account. Above all these skirmishes, there has been a constant overhang of concerns about the drug quality and safety emerging from the largely generic Indian manufacturers. Due to their increasing integration with the global pharmaceutical product value chain, there has been some disquiet about the serious ramifications they might have for healthcare across the globe. Pharmaceutical companies fear damage to their branding from rumors of poor quality, whereas the governments can see such information as undermining confidence in the health system (Cockburn et al., 2005).

Under this ambiguity, it is important to understand the issue of quality of medicines and identify the various technical and institutional mechanisms that play an immensely important role in provision of good quality medicines. The following sections discuss some of the key areas of concern along with actionable policy recommendations in order to secure supply of good quality medicines in India.

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## THEME 1: DEFINING DRUG QUALITY

### Current Scenario

In several countries, the term 'counterfeit drugs' has come to represent poor-quality drugs and is used in common parlance, although there are major differences in definitions or connotations. On account of these differences, there is a great difficulty in exchange of information between countries as well as in estimating the extent of the problem of poor-quality drugs globally. With this view, in 2009, the World Health Organization (WHO) formulated a comprehensive, yet a broad definition of counterfeit medicines, which according to many leads to confusion between legitimate generics and dangerous fakes.

Responding to the above criticism, during the 63rd World Health Assembly, it was proposed that until a consensus is reached on how medical products should be defined, the term 'substandard / spurious / falsely-labeled / falsified / counterfeit medical products' or 'SSFFC' should be used to bring all poor-quality drugs under a single umbrella framework.

### Defining SSFFC in India

There have been several reports of spurious medicines in the Indian market. During the course of our study, it was realized that depending on how poor-quality drugs are defined and interpreted, all such reports (produced worldwide) may or may not be talking about the same class of drugs. It was observed during the interactions with stakeholders that loose interchanging of terms from the SSFFC framework amounted to the aforesaid confusion. To add to the confusion, there are multiple iterations for a single term and in order to understand the issue in the Indian context, it is perhaps wise to codify the Indian laws vis-à-vis terms in the SSFFC framework (see table 1 below).

### Spurious vs. Substandard Drugs in India

Majority of stakeholders interviewed, for want of a more rigorous study on poor quality medicines in India, refrained from putting a number (or percentage) to its prevalence. Also major studies estimating poor quality drugs in India have so far focused on a small number of fast moving brands / generics, while makers of poor quality drugs in order to evade detection might choose to enter the supply chain of slow moving products.

Substandard drugs receive a lot less attention than spurious drugs. According to official data, substandard drugs outnumber spurious drugs amongst poor quality drugs. This viewpoint was also shared by individuals from the regulatory sphere.

## Recommendations

### **A clear description of SSFFC terms should be included in the any ongoing or future study instituted to quantify the extent of poor-quality medicine in India and abroad**

Any study that aims to quantify the extent of poor-quality medicines or spurious drugs in India should clearly contextualize the definition of Spurious Drugs as in the Drugs & Cosmetics Act, 1940, with respect to the SSFFC framework. Terms that constitute the SSFFC framework should be clearly defined both nationally and internationally. The mere inclusion of a section on precise definitions would render such a study a uniform global interpretation and hence lead to better clarity on the nature of poor-quality drugs emanating from India. Such intricacies in definitions and perceptions should be taken into account when a percentage figure is assigned to medicines such as spurious drugs

### **Training directed at a clear understanding of these definitions should be imparted to stakeholders across the country and especially to regulatory officials**

In the absence of uniform interpretation of definitions, stakeholders across the sector seem to infer varying definitions differently, leading to confusions and at times, creating hurdles in the way of genuine products. Therefore trainings directed at clear understanding of these definitions should be imparted to stakeholders across the country and especially to the regulatory officials who have a critical role to play in ensuring that good quality products are available in the market.

### **Any ongoing or future study instituted to quantify the extent of poor-quality medicine in India should focus equally on sampling from both urban and rural settings**

A staggered sampling strategy should be adopted where both fast and slow-moving branded and generic drugs may be included in the sample set from urban and rural settings alike. Besides, generics from small and medium manufacturers should receive as much importance as products from larger manufacturers.



**Table 1: Interpretation of the ‘SSFFC’ framework in India**

Packaging & Labeling <sup>x</sup>	Willful Trademark Infringement	Right Active Pharmaceutical Ingredient (API)	Right Dose of Active Pharmaceutical Ingredient (API)	WHO definition of Counterfeit <sup>∞</sup>	Type of Drug (as defined in India)
Fake	√	√	√	Counterfeit	Counterfeit/Spurious <sup>*</sup>
Fake	√	x	√	Counterfeit	Counterfeit/Spurious <sup>#</sup>
Fake	√	√	x	Counterfeit	Counterfeit/Spurious <sup>#</sup>
Fake	√	x	x	Counterfeit	Counterfeit/Spurious <sup>#</sup>
Fake	x	√	√	Counterfeit	Falsified/Falsely- labeled/ Spurious <sup>~</sup>
Fake	x	x	√	Counterfeit	Falsified/Falsely- labeled/ Spurious <sup>^</sup>
Fake	x	√	x	Counterfeit	Falsified/Falsely- labeled/ Spurious <sup>^</sup>
Fake	x	x	x	Counterfeit	Falsified/Falsely- labeled/ Spurious <sup>^</sup>
Genuine	-	x	√	Counterfeit	Falsified/Spurious <sup>+</sup>
Genuine	-	x	x	Counterfeit	Falsified/Spurious <sup>+</sup>
Genuine	-	√	x	Counterfeit	Substandard/ Spurious <sup>§</sup>

*Legends: <sup>x</sup>A packaging may be called fake if it purports to be the product of a manufacturer of whom it is not truly a product by virtue of either a willful trademark infringement or simply if the label on the product bears the name of an individual or company that is fictitious or does not exist (without any trademark infringements);*

*<sup>∞</sup> See CEBR (2002). Counting counterfeits: defining a method to collect, analyze and compare data on counterfeiting and piracy in the single market”, Final report for the European Commission, Directorate-General Single Market, p. 60*

*<sup>\*</sup>Refers to the definition of spurious drugs under Section 17B (a), (b) & (e) of the DCA only and hence is equivalent to counterfeit.*

*<sup>#</sup>Refers to the definition of spurious drugs under Section 17B (a), (b), (d) & (e) of the DCA only and hence is equivalent to counterfeit.*

*<sup>~</sup>Refers to the definition of spurious drugs under Section 17B (a), (c) & (e) of the DCA only and hence is equivalent to Falsified but are not counterfeit.*

*<sup>^</sup>Refers to the definition of spurious drugs under Section 17B (a), (c), (d) & (e) of the DCA only and hence is equivalent to Falsified but are not counterfeit.*

*<sup>+</sup>Refers to the definition of spurious drugs under Section 17B (d) of the DCA only and hence is equivalent to Falsified but are not counterfeit.*

*<sup>§</sup> Substandard and spurious products may be distinguished by the presence of the word ‘substituted by’ in Form 13 or certificate of test or analysis, i.e. drug test report issued by a ‘Government Analyst’ in a government drug testing laboratory pending investigation by the ‘Drug Inspector’ (application of these criteria was not found to be uniform across the states studied). The ultimate onus of classification of the sample lies on the drug inspector who investigates the matter.*

*Source: Authors’ own compilation from literature and field research.*

## THEME 2: GMP COMPLIANCE

### Current Scenario

#### Absence of clear and uniform interpretation of GMP guidelines

While the rules and guidelines are quite well in place, there exists a non-uniform interpretation of these rules. The Schedule M guidelines have to be read along with the Drugs and Cosmetics Act, 1940, (henceforth, DCA) as well as Drugs and Cosmetic Rules, 1945, and without access to a reference document non-legal experts often find it difficult to interpret the strict legal terminology within these documents. This often results in differences in the expectations of regulatory officials from manufacturers, while the latter seem to be quite unaware of the precise requirements.

#### Quality of API

Since it is not possible to trace the failure of a product to the quality of the API at the end of the process, it is imperative to address the issues at the source itself. As the bulk of our API is imported from China, Taiwan, Korea, among other countries, it becomes important to check the processes put in place to ensure GMP compliance in the manufacture of these raw materials. While some manufacturers conduct GMP audits of their API suppliers before they place their order, this may not be a necessary practice followed across all manufacturers.

#### Contract Manufacturing and loan licensing

In India, at present, manufacturing of drugs is done in three ways—own licence, loan licence and third-party agreements. In case of a loan licence, any company which does not have its own arrangements for manufacturing can use the facilities of another manufacturer. In this scenario, the applicant of a loan licence often provides the necessary raw material to the manufacturer and maintains strict oversight during the entire process. Third-party agreements, on the other hand, just entitle a manufacturer to undertake the manufacturing process on behalf of another entity that would only market the product, with greater autonomy of operation to the former. During our field research, we found an absence of clarity among respondents on the legal liability with regard to quality of products that enter the market through third-party manufacturing. There were mixed opinions about whether the law puts the burden on the firm marketing the product or the one manufacturing it, or if the liability is equally borne by both parties. There is less clarity on this aspect as third-party agreements are not explicitly mentioned in the DCA. An additional issue is the current labelling norms for a product manufactured under a loan licence, which do not require the name of the loan licensee but only the manufacturing licence number to be printed on the product label. In this way, the brand of the product manufactured is allowed to act as a proxy for quality while the consumers are unaware of the true manufacturer of the product.

## Roles and responsibilities of drug inspectors

To ensure the highest standards of quality, it is not only important to have the right set of policy guidelines and processes in place, but also ensuring adherence to these as efficiently as possible. To achieve this goal, the Mashelkar Committee Report (2003) recommended having the ratio of one inspector for every 50 manufacturing facilities and one inspector for every 200 retail facilities.

When we reviewed the situation in the states examined in our study (some of which comprise the best functioning regulatory offices in this sphere), none of them seemed to have met the recommended ratios (See table 2 below).

**Table 2: Inspection Data from State Drug Regulatory Authorities**

State	Total Number of Inspectors (1)	No. of Sr. Drug Inspectors (2)	No. of Drug Manufacturing Facilities to be Inspected~ (3)	No. of Facilities other than Drug Manufacturing Facilities to be inspected* (4)	No. of Licensed Sales Premises (5)	No. of Inspectors Required** (6)
Tamil Nadu	146	14	494	395	43218	234
Gujarat	126	42	2226	994	30887	218
Kerala	47	6	101	286	16598	174
Maharashtra <sup>Ω</sup>	124 (161) <sup>ε</sup>	NA	1523	NA	80417	432

Legends: ~ Only Allopathic Units; \*Does not include retail/wholesale outlets; \*\* Calculated as per Mashelkar Committee Report

<sup>Ω</sup> Figures substantiated from: Kadam et. al. (2013). "Shortage of drug inspectors for inspection of manufacturing and sales units in the state of Maharashtra, India", Draft available at: <http://www.amasa-project.eu/storage/AMASA.London.AbhayKadamIN01.Paper.pdf>

<sup>ε</sup> The figure in the parenthesis shows number of posts sanctioned while the number outside shows the number of posts filled. These figures were obtained from the regulator's office while conducting the field survey

Source: Authors' own compilation from data collected during field research.

Moreover, each drug inspector was burdened with the responsibility of inspecting various kinds of facilities including allopathic drugs, homeopathic drugs, cosmetics, large-volume parenterals and blood banks, and there was no focus on specialists for each of these.

## Penalty and sanctions for non-compliance

Under the current system, the inspectors notify the manufacturers of the lacunae if they fail to meet the requirements under Schedule M through the 'Corrective and Prevention Action' Report (also known as CAPA), after which the latter are supposed to take necessary steps to rectify the major and minor observations mentioned in the report.

In case of failure to correct the processes or repeated instances of non-compliance, the manufacturer's product licence is suspended and in extremely rare circumstances, even cancelled. However, in case a given manufacturer has multiple production lines, then a short-term suspension of a single production licence may not prove to be an effective deterrent.

### **Absence of a national database of manufacturers**

There is no consolidated national list of manufacturers or total number of licences granted, which makes it difficult to devise any concrete national or state policy for regulation of this sector. The absence of a comprehensive state-wise list also stems from incomplete digitization and computerization of the regulatory offices. The private datasets that already exist, do not capture the market in its entirety thus warranting an urgent need for a comprehensive national database.

## **Recommendations**

### **In order to ensure uniform understanding and interpretation by all stakeholders, there is a definite need for a guidance/reference document for schedule M on the lines of those for WHO-GMP guidelines**

This guidance document should be used by regulators, drug inspectors and manufacturers alike. This will ensure that all requirements for ensuring production as per Schedule M are understood and met with uniformity. This document could be prepared by legal professionals in consultation with scientific experts and policymakers, and later disseminated in a series of workshops.

### **Strengthening international monitoring by the Indian government for assessing GMP compliance of supplier nations (for example, API)**

While the complete legal liability of ensuring the API quality rests with the manufacturer of the finished formulation, we suggest that the existing mechanisms for achieving this should be strengthened. A permanent office of the CDSCO in China and other high-volume source countries should be set up for the purposes of drug audit and quality certification. The manufacturer (also the importer of the API) should report any defects in the API to the CDSCO so the latter may investigate this matter further. In case of instances where there are repeat offenders, the CDSCO may come out with an alert list towards warning Indian manufacturers against such suppliers. This initiative can be strengthened through an MOU between India and WHO member countries which, amongst other things, allows easing of the visa process for inspectors and therefore makes it feasible to inspect each other's manufacturing facilities.

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## **Providing clarity with regard to liability for quality in case of contract manufacturing and labelling provisions in case of loan licensing**

It is recommended that an elaborate guidance document for contract manufacturing be prepared on the lines of those drafted by the United States Food and Drug Administration (USFDA) and the International Conference on Harmonization (ICH). As is the case for Schedule M guidelines, such a document would provide uniform guidance to all manufacturers and regulators on the requirements as per the law, and thereby put greater burden on all involved parties to ensure quality. Also, the present labelling requirements need to be revisited, so that the packaging reflects complete information to the consumer with respect to inclusion of name of the loan licensee.

## **Improve existing inspection procedures**

We suggest that the regime of inspections be changed from single-man led jobs to that of team inspections- comprising a mix of senior and junior inspectors. This, apart from having the benefit of providing on-the-job training to the new and lesser experienced inspectors (this model is found to be functioning well in Indonesia), would also improve the efficiency of the inspections conducted. Additionally, it is suggested that that the manufacturers should adopt a quality-by-design approach, while the regulators focus on a risk-based inspection strategy. This implies that each product should be inspected according to its individual risk profile as well as previous inspection history thereby focusing on critical areas.

## **Fostering voluntary compliance: punitive measures and deterrence mechanisms**

It is required that the norms should be made stricter, especially with regard to GMP non-compliance. The submission of response to a CAPA report should be done within a fixed time frame so that the necessary follow-ups can be carried out. In the event of failure to submit the report within the designated time frame, there is a need for strict punitive action such as financial penalty on the defaulter (found to be in use in USA and China) as an alternative to the existing system. Other alternatives to judicial enforcement may be worth considering, such as the EU system of qualified person with the authority to revoke GMP certificates or suspend manufacturing licences by administrative action. In addition, use of 'reputation effects' as a deterrence mechanism can be carried out by regularly updating non-compliance data and making it available in the public domain. This exercise is already being done by the European Medicines Agency (EMA) through the European Union Drug Regulatory Authorities (EUDRA) GMP database.

### **There is a need for a rational distribution of drug inspectors and government analysts**

The drug inspector to inspection sites ratios suggested by the Mashelkar committee may be one way to rationalize the distribution of inspectors, especially if it is implemented in a manner such that there is increased focus on specialists than generalists. We recommend that the state drug regulatory authorities impart more specialised skills to their inspectors and government analysts, either product-based or process-based. This can be achieved by ensuring that each inspector is trained in a niche segment and develops specialty in it through continuous experience. We came to learn that such a practice is being used for government analysts in the state of Gujarat, where each analyst repeatedly carries out tests within a certain class of drugs and thereby achieves proficiency in the process. This has led to reduction in the time taken to carry out these tests as well as in pendency of the number of cases for sample analysis.

### **Consolidation of a national registry of pharmaceutical manufacturers which can be used to assess and revise distribution of human and financial resources across regulators within the country**

The required database can be created using information technology. The precise mechanism for doing so is elaborated in later pages under the section 'Role of Technological Interventions'.

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## THEME 3: DRUG SAMPLING AND TESTING CAPACITIES

### Current Scenario

#### National drug testing capacities

In India, drug testing laboratories comprise eight central government laboratories (six for drugs, one for vaccines and one for r-DNA and diagnostic kits), state laboratories (for most states) and more than 500 private laboratories. However, not all of the six central laboratories are fully equipped and some require upgradation. The present drug testing capacity of the six central laboratories is around 8,000 samples per annum, which is targeted to be increased to 24,000 samples per annum. This too may be insufficient to test all products given that at present the most conservative estimate of total pharmaceutical products in the domestic market stands at a figure of 62,000 products.

The research team visited two state government drug laboratories in order to gauge the capacity that the states' laboratory harbored. In both cases, the equipment was found to be up to date, but there was lack of staff to man the equipment. It was observed that there were posts lying vacant from the pool of total sanctioned posts, while both laboratories reported shortage of hands required to meet the annual targets.

#### Feasibility of routine drug sampling in the post-marketing phase in India

Two completely divergent views emerged from the stakeholder interviews at national and international levels regarding routine drug sampling and testing in the post-marketing phase (not Phase IV). The stakeholders at the international level (in both USA and Europe) doubted the sustainability of routine sampling in the post-marketing phase in terms of the limited budgets of the regulators for undertaking such an exercise and stressed more on quality assurance or a quality-by-design approach.

The above view is in contrast to that taken by stakeholders in India (primarily policymakers), who believed that there is a need to ramp up routine sample collection and medicine testing capacity in order to timely process (test) the samples in the country. Interestingly, the exception to the above viewpoint of the Indian policymakers came through a few retired officials (from the regulatory sphere), who cited the futility of the entire exercise. The most plausible reason cited was that with extended timelines in receiving reports on drug quality, most of the products from that production batch may already be consumed by the virtue of it being present on the sale counters. The extended timelines, in turn exist due to buildup of pendency from unprocessed samples earlier received by the labs.

## Recommendations

**As a short-term measure, National Accreditation Board for Testing and Calibration Laboratories (NABL) accredited private labs should be used to ease the backlog of drug samples in public drug testing laboratories until the in-house testing facilities of central and state drug testing labs are established**

In order to reinforce the drug sample processing capacities, the capabilities available in the private space in NABL accredited drug testing labs should be exploited with adequate checks and balances. The 500-odd labs in the private domain have a subset of NABL accredited labs, which were reported to be at par or even exceed the capacities available in government drug testing labs. Many public drug procurement agencies such as Tamil Nadu Medical Services Corporation (TNMSC) have empanelled such labs for pre-shipment quality check. The capacities of these labs may be used for drug testing with adequate checks and balances.

A double-blinded two-phased drug test may be instituted only in cases where the samples fail the drug testing during the first phase in the NABL lab, which should then be sent to the state drug testing laboratories for the second phase of testing. This measure should only be resorted to until the in-house testing facilities of central and state drug testing labs are established. This measure is recommended to bring down the already existing pendency with the labs and hence improve the timelines for generation of drug test reports.



## THEME 4: DRUG ALERTS AND PRODUCT RECALLS

### Current Scenario

#### Current system of drug alerts

The system of drug alerts typically ensures safety of a product post-marketing phase through identification of poor-quality products. However in practice the system ceases to function very smoothly. Lists of drug alerts are generated both state-wise and independently by the CDSCO, but they are not linked with each other and one has no means of knowing what action is taken after such an alert is posted.

#### Pharmacovigilance in India

At present, the Pharmacovigilance Programme of India (PvPI) has limited outreach among patients as well as health-care professionals, with little or no information provided about the measures taken or recommended after an Adverse Drug Report (ADR) is reported. In addition, this system is not integrated with the drug alerts that are generated through random sampling at both the state and central levels.

#### The system of product recalls in India

There are lists of drug alerts that have been reported by the state and central authorities, however, information about which of these drugs have been recalled is not available in the public domain. This creates lack of clarity as to how the recall process is being carried out. For effective recall, at times the product may have to be recalled from the retail level, which means from thousands of retailers across the country. This poses a problem in cases if a laboratory report identifying a faulty product takes three to four month to process – by then, a large portion of the batch would have already been consumed in the market, especially if they are fast moving products.

### Recommendations

#### Develop an integrated web-based system for drug alerts

A system that integrates the drug alerts generated by the states and the centre, should be developed so to allow effective tracking of poor-quality products. This could be done through creating a common portal where relevant information from each state could be uploaded. Even the actions taken on these alerts such as recall of products could be uploaded on this portal, thereby allowing any individual to track these alerts at one place. Such a system could also be used to send out messages/SMSs in order to notify drug control departments as well as retailers across the country about such products.

### **Strengthening of the pharmacovigilance program and its integration with drug alerts**

While both PvPI and drug alerts may operate independently, their reporting should be done under a common portal. The advantage of doing so also lies in being able to identify the cause of the ADRs—whether due to errors in prescribing/dispensing, clinical properties of the drug or poor-quality of the drug itself. In several other countries like China and the UK, it has been found that pharmacovigilance monitoring operates as an integrated system. In a similar fashion, an integrated network for reporting and collection of data could be developed in India in order to have a well-functioning pharmacovigilance programme.

### **There should be an online monitoring system for product recalls, which requires a manufacturer to provide real-time information about the progress of the recall process**

An online monitoring system for product recalls is necessary not only to ensure that information regarding the recalled products is made available to the public but also to enable the authorities to track the process of recall themselves. Such a system may mandate a manufacturer to provide information about the progress of the recall process from time to time, which will be uploaded on the website. This should function like a courier tracking system only in the reverse direction, wherein it is feasible to see how far the product has been retraced. Finally this information should be disseminated to the public not only through the web but also through other media channels for wider outreach.

The website of the Health Sciences Authority (HSA) of Singapore, is a good example of an online portal for recalled products. The HSA mentions on its website, detailed information regarding the products recalled including its batch number, batch size, expiry date, class and level of recall, reason for recall and manufacturer's name and country.

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## THEME 5: ROLE OF TECHNOLOGICAL INTERVENTIONS

### Current Scenario

#### Track and Trace Technology in India

Track and Trace technologies (referred to hereafter as T&T) are touted to be the game changers in ensuring safe drug distribution chains and instituting quality / expiry recalls. T&T systems allow all interested parties to know where the product is at any time and see a record of where it had been previously. T&T systems rely on serialisation, the assigning of unique identification numbers to products. Products that lack identification numbers, or products with identification numbers that cannot be accounted for throughout the distribution chain, must be treated as falsified and removed from the market, even if they come from licensed manufacturers. The unique identifier may be stored in a barcode, electronic product code, radio frequency chip or it may be a long-digit serial number.

Government of India instituted a task force for studying T&T systems, which submitted its report to the Ministry of Health & Family Welfare, Government of India in March 2012.<sup>1</sup> The task force members looked into hardware and solution providers and suggested that the stakeholders at the lower end of the supply chain could use their existing computers and internet connections to be part of the T&T system. But at the same time they acknowledged that being a system which is not widely used within the pharmaceutical industry, the cost estimated by the stakeholders and solution providers varied greatly. This is in line with the views gathered from the field research. Most stakeholders interviewed were not technically competent to comment on the viability of the system and quoted costs which varied greatly. A much clearer picture emerged only after the research team took demonstrations of this technology at a few manufacturing sites.

#### The roll-out of XLN Software

Another major technological intervention has been the introduction of XLN software (Xtended Licensing, Laboratory & Legal Node). XLN is a software for transparent and speedy disposal of various licensing applications, it also helps reduce the time lag between the collections of samples and declaration of results to dissemination of information among stakeholders. Apart from online processing of manufacturing and sales-premises licences, the software also maintains an online database of batches of spurious and substandard drugs which fail testing at various government approved laboratories. A complete deployment of the tool is aimed at ensuring end-to-end transparency and a

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<sup>1</sup> See *Report of the Task Force on Track and Trace, Ministry of Health and Family Welfare, Government of India, 2012*. Available at: <http://mohfw.nic.in/WriteReadData/1892s/5557266952Report%20of%20Task%20Force%20on%20Drug%20Tracking%20Tracing.pdf>

streamlined drug distribution chain. Even though it was claimed that it had been implemented in ten states and five more states were in the process of implementing the software, it was found that in states other than Gujarat and Maharashtra, XLN was being used only to track licensing of retail pharmacy outlets.

### **Recommendations**

**Rule 96 of the Drugs and Cosmetics Rules, 1945 should be amended for making a provision for bar coding on primary, secondary and tertiary packings of drugs**

**A centrally located T&T solution is highly recommended. In addition to the function of 'Track and Trace', a centrally located database can be used to create the much needed national registry of active pharmaceutical manufacturing firms. Although, sufficient time should be provided for a full blown implementation.**

The system can be implemented in a staggered fashion (by introducing barcodes on secondary packs for the domestic market to begin with) and slowly be retrofitted into every pharmaceutical production line. Hence, sufficient time should be provided to the manufacturers for a primary pack level implementation. Also, this would only be within the reach of manufacturers if the entire life cycle management cost of deploying the T&T system (software development, cloud deployment, database security/management, artwork standardisation, bar code standard selection etc.) is borne by the exchequer.

A centrally located T&T solution may be instituted at the National Informatics Centre, which would roll-out an online portal for every pharmaceutical manufacturer for registration and deployment of software in the firms.

**Use T&T in providing complete information to consumers with respect to the products manufactured via contract manufacturing**

**The T&T system should be integrated with the newly rolled-out Integrated Pharmaceutical Database Management System (IPDMS), also developed by NIC for the National Pharmaceutical Pricing Authority (NPPA) acting as pharmaceutical monitoring and information system**

NIC can periodically forward the data under the integrated database (IPDMS) to CDSCO, which should use this data to formulate a national registry that enumerates all active manufacturing firms in all Indian states along with data on what all pharmaceutical products are being manufactured by these firms including fixed dose combinations. This in itself would serve as a real-time monitoring system for CDSCO and can be used to define the true quantum of duties for the national regulator to institute further reforms. Using such a registry would also make it will also be possible to remove any irrational drugs from the market smoothly.

### **There should be speedy implementation of XLN software across all states**

XLN should be uniformly implemented pan India and the data on spurious and substandard samples should be made public in a precise and cogent fashion. Warnings regarding spurious samples and firms manufacturing substandard products should be issued online, and this should be disseminated using all electronic and print media channels.

## CONCLUDING REMARKS

To secure their health, consumers who have no means for verifying the authenticity or potency of drugs, need to be assured at all times that medicines made available to them are of good quality and safe to use. It thus falls upon other participants at various nodes of the supply chain to provide the much needed assurance. Since provision of good quality medicine is ensured through a participative process, the issues linked with it are intertwined and cannot be dealt with in isolation.

One of the major obstacles that both the industry and regulators face is related to the definition and interpretation of quality standards of the manufacturing process. On the one hand there are differences in quality parameters across countries (although in principle they are broadly aligned with each other), while on the other hand is a concern more immediate within India that emerges from non-uniform interpretation of guidelines within the country. Further, there are complexities arising from the existing federal structure since states have differing regulatory capacities which in turn is the result of insufficiency of trained personnel as well as testing capabilities.

Towards addressing a number of such regulatory bottlenecks, dedicated efforts are required towards harmonizing the interpretation of legal terminology contained in the relevant act and guidelines, rationalizing the work distribution across regulatory personnel, using technological tools to bridge the gap in the data available to policymakers, and driving the industry towards voluntary compliance and self-regulation. While the quality of medicines produced in India currently is under scrutiny, the good news is that the Indian regulator as well as industry are aware of the areas that need to be focused upon. Some recent reform efforts in this direction include the cabinet approval of a proposal to strengthen the drug regulatory system both at the level of the centre and the states.<sup>2</sup> The said proposal, among other things, seeks to upgrade both equipment and manpower in the existing drug testing laboratories as well as set up new laboratories, make provision for a training academy for regulatory and laboratory staff, and foster greater use of information technology enabled services. In addition, a recent report of the task force on enabling private sector to lead the growth of pharmaceutical industry recognizes that there is greater need for creating a conducive policy and operating environment which fosters growth of the industry.<sup>3</sup> Among its several recommendations, the task force highlighted the need to strengthen regulatory support by increasing the available manpower for effective monitoring and control of manufacturing and retail facilities. The present study adds to

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<sup>2</sup> See press release by the Ministry of Health and Family Welfare, Government of India, available at the following link <http://pib.nic.in/newsite/PrintRelease.aspx?relid=124950>. Last accessed September 16th 2015.

<sup>3</sup> *Recommendations of the Task Force on Enabling Private Sector to Lead the Growth of Pharmaceutical Industry*. Government of India, 2015. Retrieved from available at <http://pharmaceuticals.gov.in/taskforce1.pdf>. Last accessed September 16th 2015.

these reform efforts by bringing out the need for not only enhancing the capacity of the regulatory systems but also for improving upon the precise mechanisms for monitoring the sector (such as inspections, testing, etc.) with the aim of making them more effective. By channeling resources in these areas and actively engaging various stakeholders, India can become a widely acknowledged source of good quality and efficacious medicines. be banked upon to deliver safe and efficacious medicines for all.

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## SNAPSHOT OF POLICY RECOMMENDATIONS

Problem	Recommendations	Intended Impact
Conflating definitions	<p>Inclusion and description of SSFFC definition in each study that attempts to quantify the problem.</p> <p>Training regulators towards uniform interpretation of definitions.</p>	<p>More clarity on the nature of poor quality drugs emanating from India.</p> <p>Homogenous interpretation of what constitutes poor quality drug.</p>
Absence of clear and uniform interpretation of Schedule M guidelines	Creating a reference document of Schedule M guidelines for manufacturers and regulators alike.	More uniform interpretation of guidelines leading to ease of compliance.
Poor quality API	Setting up of CDSCO office in source countries so as to coordinate between exporters and importers.	Address quality of API at source rather than at the end of process.
Legal liability for quality in case of contract manufacturing and loan licensing	Separate guidance document for rules with regard to contract manufacturing.	Greater burden on all involved parties to ensure quality.
Absence of strong mechanisms for voluntary compliance	<p>Revision of punishment from suspension of single production licence to financial penalty.</p> <p>Update non-compliance data and make it available in the public domain.</p>	<p>Stronger and more credible threat towards ensuring compliance.</p> <p>Reputation effects will trigger deterrence towards non-compliance behavior.</p>
Single man led inspections of facilities	Team led inspections with mix of experienced and new inspectors. Also focus on creating teams of specialists.	Provides on the job training to new inspectors and reduces time taken, thereby improving efficiency.

Problem	Recommendations	Intended Impact
Absence of a national database of manufacturers and licences granted	A national database compiled from all states onto a common portal using IT.	Can be used to assess and revise distribution of human and financial resources. Also improves transparency and ensures that only authentic products move in the supply chain.
Low capacity of testing laboratories	As a short term measure, rope in private NABL accredited labs in two phased testing until the government labs are able to upgrade in-house capacity.	Reduced pendency of samples and improved timelines for generation of drug test reports.
Segregated list of drug alerts	All state and central drug alerts (along with action taken) should be brought together on a common portal.	Ease of tracking substandard products.

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