A Safe Medicines Chest for the World

Preventing substandard products from tainting India's pharmaceuticals

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Executive summary

Shocking headlines about substandard and counterfeit medicines are frequently featured in the Indian media. Some recent examples from 2009 are as follows (and a far larger list is presented in Appendix 1):

- "Fake drug racket busted", Times of India, 23rd December 2009
- "Fake medicine sale rampant, cops helpless", Indian Express, 1st December 2009
- "Six commonly used drugs found substandard", Pharmabiz.com, 18th August 2009
- "Fake cancer drugs make it to your homes", The Times of India, 24th March 2009

In 2010 a huge fake drugs racket was exposed in Chennai. At the time of going to print, over 30 suspects had been arrested in relation to the scam, which involved putting fake labels on expired products. Over half the pharmacists we interviewed in this study (prior to the Chennai case hitting the news) said that the most popular method of counterfeiting was to re-label expired drugs with a new expiry date.

But anecdotes merely give a loose impression, and so this paper presents analysis of data based on surveys of Indian pharmacies and drug traders in Delhi and Chennai.

The paper refers to both "substandard" and "counterfeit" medicines – with a full explanation of our definitions explained in Appendix 2.

Substandard drugs supplied by pharmacies

Bate et al. (2009) surveyed a small random sample of pharmacies in Delhi and Chennai.

- 12 per cent from Delhi pharmacies were substandard.
- 5 per cent from Chennai pharmacies were substandard. [1]

While the majority of drugs were high quality, it is very worrying that 80 per cent of the sampled Delhi pharmacies were providing *some* substandard products. In Chennai the situation was much better, but there remained a 38 per cent chance that the pharmacist [in Chennai] would be issuing *some* substandard medicines.

In Delhi, nearly all the drugs with zero active ingredients (probably counterfeits) came from the worst seven pharmacies. Our findings suggest that a significant minority of pharmacies are knowingly selling high levels of substandard and counterfeit drugs.

Substandard drugs supplied by drug traders

The researchers then set out to compare the findings obtained from pharmacies with a study of the same five drug types procured from four Delhi drug traders.

- 7 per cent of tested samples from traders were substandard.

While lower than the results from pharmacies, this is still a significant number and suggests that the problem affects the whole supply chain in India.

The failure rates observed at individual traders varied hugely, from 1 per cent to 18 per cent (see Figure 3). The trader with the 18 per cent failure rate was clearly selling a mixture of legitimate and counterfeit goods.

Of all the samples from traders, 3.6 per cent had zero

active ingredient (most likely counterfeit medicines) – all of which were from the two worst traders. Some drugs contained chalk or talcum powder, plus a pain reliever to trick and defraud patients.

Substandard and counterfeit Indian drugs abroad

Accurately estimating the proportion of exported Indian drugs that are substandard is fraught with difficulty: exported drugs typically enter a complex global supply chain, and there is no simple market from which to buy drugs exclusively for export. As independent non-government non-industry researchers, it was impossible to obtain a decent sample for such a survey. We therefore observed evidence from elsewhere.

Bate et al. (2008) found that 35 per cent of antimalarial drugs sold in shops and pharmacies in six major African cities failed basic quality control tests. 31 per cent of the samples purportedly of Indian origin were found to be substandard.[2] However, as some were counterfeit medicines, we cannot be sure that they were all certainly from India. A counterfeiter can fake a "Made in India" label, just as they can lie about any other aspect of packaging.

In 2008, about half of all medical products detained at EU borders arrived from India – most of them for trademark infringement.[3]

Some seizures in the EU became notorious in late 2008 and 2009, following cases of pharmaceuticals from India being detained, apparently on suspicion of patent-infringement (even though the drugs were not patented in either the source or destination country). The governments of India and Brazil are now challenging the European seizures at the World Trade Organization (WTO).

Had customs officials in the EU limited themselves to instances of trademark infringement (which, in any case, made up the majority of seizures[4]), their actions would have been beyond reasonable criticism. Trademark infringement is a form of counterfeiting, and authorities are correct to clamp down on it.

Elsewhere in the world, the Nigerian government has banned imports from certain Indian pharmaceutical firms,[5] and set up an office for their regulator in India.[6] And in November 2009 the Sri Lankan government banned imports from four Indian companies following the discovery of dangerously substandard products, including vials containing broken glass or plastic.[7] A month later Kenji Toda, chairman of the Japan Pharmaceutical Manufacturers Association, stated that the bad reputation of the quality of medicines and concerns about counterfeits are a barrier to the growth of Indian-produced pharmaceuticals in Japan.

Quality concerns seem the only stumbling block to an otherwise thriving industry.

Causes of substandard and counterfeit drugs

Weak legal systems

The growth of the Indian economy has been mitigated by the emergence of counterfeiting. The Confederation of Indian Industry (CII) singled out pharmaceuticals as one of two worst instances in this area.[8]

The CII are correct to highlight these two weaknesses that allow counterfeits to thrive:

- Lack of enforcement of existing laws.
- Weakness of civil law and the rule of law.

The enforcement of existing laws relies on a quick and fair court system – for both civil and criminal cases. As the old saying goes, justice delayed is justice denied. Yet the Indian legal system is famously sclerotic. In May 2010 the Indian pharmaceutical website Pharmabiz.com reported that a Delhi court had convicted a man for manufacturing counterfeit cosmetics. According to the report: "The case was filed in 1987."[9]

Reliable trademark protection in the courts does not favour Western corporations above Indian industry. On the contrary, Indian brands need to be able to protect themselves from counterfeiters. Figure 5 shows two versions of a well known Indian brand generic medicine, Ciprotab. The medicines in one of the packages passed all quality tests, while those in the other failed them all. The latter is a counterfeit.

Corruption

While studying the quality of drugs procured from Delhi and Chennai pharmacists, qualitative interviews were used to investigate how substandard medicines were arriving at pharmacy counters.

- 73 per cent (19 of 26) acknowledged that not only was there a serious problem with substandard drugs but that some of their fellow pharmacists were complicit in their sale.
- 19 per cent of pharmacists (5 of 26) claimed that their competitors bought from merchants selling sub-potent or otherwise suspect medicines.
- 92 per cent (24 of 26) claimed that at one time or another they had been approached by a trader offering sub-potent drugs at cheaper prices.

The situation is not necessarily improved by adding layers of state regulation. Indeed, in some cases it may simply result in additional bribery and corruption:

- 73 per cent (19 of 26) expressed concern about the government's attempts to regulate drug quality.
- Over half expressed concern that inspectors would demand bribes.
- Almost one in four (6 of 26) claimed that bribes had been demanded in the past.

Local investigator Suresh Sati explains that while counterfeit medicines often arrive through complicit pharmacists and corrupt officials, they also enter the supply and distribution chains through corrupt deals between hospitals' buyers and wholesalers and manufacturers.

In December 2008, a "thriving racket" supplying substandard drugs into government hospitals of Orissa was exposed. A report said: "In most cases, spurious drugs circulation is carried out with the knowledge and connivance of officials of the drug controller, [in] Orissa, and local drug inspectors who are on the payroll of unscrupulous dealers."[10]

Political obfuscation

In November 2009 an article in the newspaper Mint appeared under the headline "Supply of fake drugs grossly overstated."[11] It was based on a governmental claim that only 10 of 24,000 (or 0.04 per cent) sampled medicines were found to be 'spurious' – a quite incredible figure. These headline statistics were leaked to an Indian pharmaceutical industry website, while the study itself is yet to be published at the time of this paper going to print. The underlying methodology and holistic data are unavailable, casting doubt over how robust and impartial the survey really is.

The methodology behind an earlier governmental report (Mashelkar, 2003) is also questionable. Consider these striking regional differences: in Haryana state, substandard drugs account for an astounding 40.4 per cent of those sampled, compared with 5.3 per cent in neighbouring Delhi, 2.1 per cent in Tripura, and zero per cent in Arunachal Pradesh, Daman and Due, and Goa. Given the likely significant leakage across state borders, such differences call into question the methodology by which they were obtained – and also whether each location followed the same methodology in practice.

Furthermore, the study relied on unverified data reported by state authorities and on data frequently drawn from samples of small size. Some states reported no data at all.

It is vital that the Indian government makes available its data on levels of counterfeit and substandard medicines across the nation, and the full research methods of the survey – especially when it releases headline findings to media outlets. Headlines that misleadingly dismiss the problem risk encouraging people to buy drugs from sources which supply substandard and counterfeit medicines – hence fuelling such trade.

Conclusion and recommendations

Many high quality drugs are manufactured in India, and the sub-continent has become the largest generics manufacturing location in the world. But it also has a significant problem with counterfeit and substandard drugs.

The enforcement of private rights (notably trademarks) must be given more support, both domestically and in international fora such as at WHO and with respect to the EU.

Further, the Government of India should not sponsor and promote reports which contain much misleading information concerning drug quality in India. Worse, some state governments have been very lenient towards local counterfeiters. In some instances officials have been directly bribed, and nearly all courts throughout the country have considerable backlogs of cases – allowing traders of potentially lethal products left free to ply an odious trade.

Our surveys show that a small but significant proportion of drugs purchased at retailers and traders in Delhi and retailers in Chennai fail at least one quality test. A significant minority of actors (manufacturers, wholesalers, pharmacies) are intentionally supplying counterfeit and substandard medicines in order to line their own pockets.

Fortunately private companies are finding innovative ways of preserving the identity of their products from counterfeiters, through serialisation systems (utilising new technologies) and more secure supply chains.

But such measures can only go so far. These companies, and patients, need the protection of the law, operated under efficient, independent and fair courts – both civil and criminal. Their prosperity and health relies on it.

A Safe Medicines Chest for the World

Introduction

Clinically faulty medicines (substandards) and products that breach trademark or labelling laws and defraud patients (counterfeits) are a serious problem in India. Anecdotal reports suggest that the manufacture and distribution of such products is widespread throughout the country. In 2009 alone, seizures of counterfeit medicines were reported in Bangalore, Mumbai, Delhi, Jaipur and a range of other areas (see Figure 1). In Appendix 1 we list 28 stories from 2009, an average of more than two a month, that exposed counterfeit drugs in India – and these are only from the English-language media. Meanwhile, shortly before this paper went to press in May 2010, a huge swindle was uncovered in Chennai, involving the re-sale of expired medicines.[12] The implications for patient safety are ominous.

> *"India's domestic pharmaceutical market will grow to $20 billion by 2015. Yet this growth surely depends on a strong reputation for high quality products."*

But anecdotes merely give a loose impression. In order to provide a clearer picture of the scale of the problem, and as importantly to provide insight as to where and how the problem occurs, this paper presents analysis of data based on surveys of Indian pharmacies in Delhi and Chennai and wholesale traders in Delhi.

These data enable us to provide a limited evaluation of the levels of substandard medicines (some of which are counterfeits) in two Indian cities. The data also allow us to give some preliminary answers to important questions, including: (1) In which parts of the supply chain are problems occurring; (2) To what extent are the problems a result of negligence (for example, the result of poor manufacture or improper storage) and to what extent are they the result of deliberate foul play, such as counterfeiting?

The paper also considers cases of counterfeit and substandard drugs exported from India (and drugs mislabelled as having been manufactured in India). As the Indian pharmaceutical sector has grown into a global industry, the international reputation of India as a source of such medicines has become increasingly important. McKinsey estimates that India's domestic pharmaceutical market will grow to $20 billion by 2015.[13] Yet this growth surely depends, at least in part, on a strong reputation for high quality products.

We then consider the origins and implications of the political furores that recently erupted over two seemingly arcane issues: the World Health Organisation definition of a 'counterfeit drug' and the seizure and temporary withholding by European customs officials of drugs exported from India.

Finally, the paper explores the factors driving the spread of substandard and counterfeit medicines, and concludes with policy recommendations that would, we argue, considerably reduce the problem of such medicines – benefiting patients in India and around the world, as well as the manufacturers and distributors of good quality medicines.

Methodology & definitions

Samples gathered in our surveys were tested for three qualities:

1. Whether amounts of the active ingredient were approximately consistent (within 10–20 per cent confidence) with the dose and formulation stated on the packaging.

Figure 1 **A small selection of Indian media headlines from 2009**

Note: For a fuller list of examples see Appendix 1.

2. A basic measure of whether the product was capable of being taken up by the human body in sufficient amounts to be effective (product disintegration within 30 minutes in warm water). More substantive dissolution testing was not undertaken. Furthermore, neither impurity assessments nor product contamination assessments were undertaken.
3. More sophisticated analysis was done on a subset of samples using a handheld raman spectrometer.

The full methodology is outlined in Appendix 3. The techniques chosen are those which can be deployed in the field and hence do not give a precise assessment of quality but rather a reasonable approximation. In this sense the first two tests are more forgiving than a laboratory assessment. For example, samples in a laboratory assessment would be considered to fail if the active ingredient was outside of the range of 95–105 per cent of the stated amount. Because of the less precise nature of the tests employed here, only products with less than 80 per cent of the stated dose were said to fail. A drug was considered 'substandard' if it failed either the ingredient assay or basic disintegration.

A handheld raman spectrometer was used to assess authentication of products and where possible assessing underlying ingredients, if different than stated on the packaging. This technology can be as precise in identification of products as lab techniques.

As we explain in Appendix 2, our categorisation of "counterfeit" and "substandard" drugs does not precisely match the World Health Organization (WHO) definitions of those terms. The WHO definitions involve questions of deliberate intent and regulatory authorisation, which can be extremely complex and expensive to prove. They also complicate the central issue – the standard of drugs on sale to the Indian public. We do, however, refer to the WHO definitions when they are relevant.

Where there is reasonable evidence of a deliberately counterfeited drug (for example, where it contains none of the stated active ingredients, or where the trademark is clearly faked) then we point this out as supporting evidence. The level of evidence required to prove a case of counterfeiting in a court of law is higher than the standard that most "reasonable" people concerned about public wellbeing would use, and we therefore take the approach that emphasises concerns about health.

Evidence of substandard Indian medicines

Substandard drugs supplied by pharmacies

Bate et al. (2009) surveyed a random sample of pharmacies in Delhi and Chennai. The study, published in the online peer-reviewed journal PLoS One, found that 12 per cent of five classes of medicines sampled from 26 Delhi pharmacies were substandard.[14] Meanwhile in Chennai, approximately five per cent of the same five medicines were found to be substandard.

> *"12 per cent of medicines from Delhi pharmacies were substandard."*

More detailed analysis of the figures reveals the following risks of purchasing drugs in pharmacies:

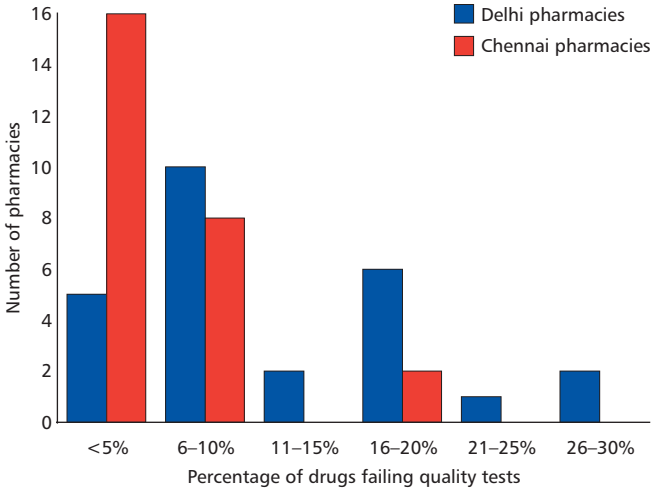
In Chennai, the situation was positive, with well over half the pharmacies selling only high quality medicines (62 per cent, 16 out of 26). However, this still left a 38 per cent chance that the pharmacist would be issuing *some* substandard medicines. In Delhi, there was an 80 per cent chance (21 / 26) that the pharmacy would be selling some substandard medicines as well as high quality medicines. For this majority, the proportion of the drugs they sold that were substandard ranged between 6 per cent and 30 per cent. Focusing on the more worrying end of this group, there was a 27 per cent chance (7 / 26) that the pharmacy would be selling medicines of which a fifth or more (20 per cent to 30 per cent) were substandard. Furthermore, these same pharmacies also supplied 10 of the 11 samples with no active ingredients at all (which suggests they were counterfeits, 'deliberately and fraudulently mislabeled').

These results were discussed with local counterfeit drug inspectors who agreed that some pharmacists are purchasing large amounts of substandard drugs, some of which are counterfeits. (See the section entitled "Corruption" for evidence of pharmacists being complicit in the sale of counterfeit and substandard medicines.)

In other words, a small but significant minority of pharmacies are (perhaps knowingly) selling high levels of substandard and counterfeit drugs. Furthermore, a slight majority are currently unable to guarantee entirely safe supplies of high quality medicines. Both situations harm the reputation of Indian pharmaceuticals, Indian pharmacists and endanger the lives of vulnerable patients.

Moreover, it is possible that the situation is worse in poorer, rural parts of India (average per capita income in Delhi and Chennai is considerably more than the Indian average and an order of magnitude higher than in poorer rural areas), where drugs are often purchased from informal street vendors. A security specialist and counterfeit drug investigator, Suresh Sati, has stated that most buyers of substandard medicines from traders come from rural areas, where they are likely selling them to rural pharmacies. Levels of substandard medicines, he feels, are far higher in areas where people are less literate, less educated, and where government inspectors very rarely visit.

Figure 2 **Percentage of tested samples failing quality tests by number of pharmacies sampled in Delhi and Chennai**



Note: All pharmacies with fewer than 5 per cent failures actually had zero failures.

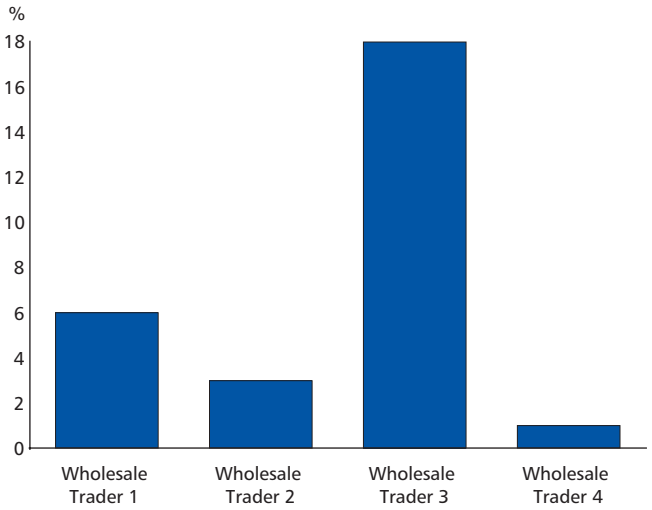
It should be noted that the sample sizes are small and could over or understate the problem. But it is interesting that over 90 per cent of drugs found to be substandard in this study failed quality tests 1 *and* quality tests 2 – they exhibited low levels of active ingredient *and* a failure to dissolve properly. This likely reflects counterfeit products with large amounts of substances designed to look good in pills, but which will not dissolve properly, meaning that any active ingredient in these pills is unlikely to be available to the patient. Furthermore, all samples tested after the initial study was published, with Raman spectrometry, indicated very little if any active ingredient present. Most samples did contain active ingredients, but they were not as stated, often containing aspirin or acetaminophen.

See Appendix 3 for the complete methodology and further detailed findings.

Substandard drugs supplied by traders

It is possible that fake drugs mainly enter the supply chain when criminal suppliers deal directly with retailers, such as pharmacies. If this were the case then one would expect only a small problem with small-scale wholesale traders, and specifically those which

Figure 3 **Percentage of tested samples failing TLC or disintegration, as supplied by four traders in Delhi**



distribute drugs openly to pharmacists and rural traders. We therefore set out to compare the findings obtained from pharmacies with a study of the same five drug types procured from Delhi-based traders.

Overall, 7 per cent of tested samples from traders were substandard.

The rate is lower than that discovered from pharmacies, but since all traders assessed had at least some drug failures, these results suggest that the problem of substandard drugs sold on the domestic market affects the entire supply chain, from manufacturer to pharmacist.

The failure rates observed at individual traders varied from 1 per cent to 18 per cent (see Figure 3). In the case of the trader with a 1 per cent failure rate, only one drug type (erythromycin) failed one or more tests, and this failure was almost certainly a result of product degradation due to a broken blister pack – in other words it was a storage and transportation problem, not a manufacturing one. And if we had acted like any sensible pharmacist would have done and discarded this obviously degraded product there would have been no failures from this trader. By contrast, the trader with the 18 per cent failure rate was clearly selling a mixture of legitimate and counterfeit goods. Indeed, this backs up anecdotal evidence provided by drug investigators, who sometimes masquerade as covert buyers to trap counterfeiters. They say that some traders actually provide two price lists for trusted buyers, higher prices for legitimate products and lower prices for products without genuine provenance.

The trader findings broadly mirror those obtained from pharmacists. In each case, some actors are providing high quality medicines, while others are providing a mix of good and substandard products. This suggests that the presence of substandard drugs is not accidental, nor is it merely a problem of inadequate storage; some suppliers are knowingly selling counterfeit and substandard drugs.

Sampling of traders from one wholesale location, as done in this study, might well bias the results. This is a point that we could not establish to any degree of certainty, but should be born in mind in the discussion.

Of all the samples, 3.6 per cent had zero active ingredient; of these, the majority (12 of 14) were from the worst performing trader; the other two were from the next worst performer. In other words, most of the presumably counterfeit drugs came primarily from one trader.

"… the presence of bad drugs is not accidental; some suppliers are knowingly selling fake drugs."

It is interesting that the spectral profile of the drugs was similar to the failures found in the pharmacies – containing a pain reliever and either chalk or talcum powder and not the correct active ingredient.

We spoke to investigators about who would normally buy from the traders we had sampled from and the consensus was buyers would be split between rural traders and a few local pharmacies. So although it is quite possible that these results are representative of the situation across India, they may not even reflect the situation across all of Delhi. Sample sizes and limited locations can only give a snapshot of the potential problem. However, the results are consistent with the notion that some of the problem of substandard drugs is probably due to poor storage and poor quality but otherwise legitimate manufacturing (and possibly resold expired drugs), but much of the problem is due to deliberate, illegal activity. This finding is reinforced by

the numerous cases of deliberate counterfeiting exposed by the media and listed in Appendix 1.

See Appendix 3 for the complete methodology and further detailed findings.

Substandard and counterfeit Indian drugs abroad

Substandard Indian drugs sold overseas harm the lives of patients and the reputation of the Indian industry. Given the need and demand for low-cost generic pharmaceuticals throughout the world, and especially in low- and middle-income countries, it is crucial that levels of inferior products are significantly reduced.

Accurately estimating the proportion of exported Indian drugs that are substandard is fraught with difficulty. Exported drugs typically enter a complex global supply chain, with any single batch ending up in numerous different countries. From a practical standpoint, there is no market from which to buy drugs exclusively for export. Ignoring illegal activity, legitimate deals are done between companies or major wholesalers in India and overseas buyers, including wholesalers, pharmacy chains, donor agencies, procurement agencies and government entities. Unless one goes through the major and expensive effort of setting oneself up as an importer of drugs from a foreign land, and doing deals with various Indian exporters, it is therefore not possible to obtain a decent sample, for independent non-government non-industry researchers.

"In 2008, about half of all medical products detained at EU borders arrived from India – most of them for trademark infringement."

Given our resource constraints, we decided instead to utilise data from (not necessarily representative) samples of many drugs collected in major cities in Africa. Bate et al. (2008) found that 35 per cent of antimalarial drugs sold in shops and pharmacies in six major African cities failed basic quality control tests. 31 per cent of the samples purportedly of Indian origin were found to be substandard.[15] However, the study did not attempt to prove that all these samples were definitely from India. The case in 2009 of counterfeit medicines from China being labeled "Made in India" quickly became infamous among a wave of outrage. Yet it is obvious that counterfeited medicines often include false information regarding their origin – and if some of the apparently "Indian" samples were counterfeits (rather than other forms of substandards) it is feasible they could have been produced elsewhere.

Nevertheless, the industry's reputation is damaged by the amount of Indian counterfeit drugs found by foreign customs authorities. The European Commission's latest report on intellectual property right (IPR) infringement at EU borders claims that IPR-infringing medicinal products primarily come from India.[16]

In 2008, about half of all medical products detained at EU borders arrived from India – most of them for trademark infringement.[17] Seizures in the EU became notorious in late 2008 and 2009, following cases of pharmaceuticals from India being detained, apparently on suspicion of patent-infringement (even though the drugs were not patented in either the source or destination country). The problem arose because customs officials sought to clamp down on the importation of IPR infringing goods into Europe and included goods being trans-shipped. Had the customs officials limited themselves to instances of trademark infringement (which, in any case, made up the majority of seizures[18]), their actions would have been beyond reasonable criticism (according to the EU, seizures during the "Medi-fake" operation included the interception of 600,000 counterfeit antimalaria pills. Given the high level of counterfeit and substandard antimalaria treatments in Africa, the health benefits of such seizures must be recognised.)[19] Unfortunately, by also targeting goods that infringed patents held in the EU, they made themselves the enemy of the exporters, the importers and a range of activist groups who have for years claimed that patents restrict access to medicines. DG Shah, the head of the Indian Pharmaceutical Alliance (IPA), explained that he was not aware of a single European importer or Indian exporter who had been prosecuted for trading in these allegedly counterfeit medicines – the implication being that the whole point of stopping their generic drugs was to prevent competition, rather than to save lives. He quipped, in the EU's eyes "if it's a generic it's counterfeit, it makes it

Figure 4 **The methods of storage (top) and production (cement mixer, bottom) discovered during a raid on a counterfeit drugs manufacturer in Haryana State, India, 2008**

simple doesn't it?"[20] We sought a response on this matter from the European Commission through e-mails and phone calls, but were not provided with an answer before going to print in May 2010.

A counterfeit drug is one that is "deliberately and fraudulently mislabeled", according to the World Health Organization. Faking a trademark clearly counts as an act of mislabeling; it is an attempt to deceive purchasers regarding the source of the product. While it is theoretically possible to provide high quality, genuine medicines within counterfeit packaging, there is little motivation to do so. Indeed, since the central purpose of selling counterfeit pharmaceuticals is to make money through deception, and since it is generally more profitable not to manufacture pharmaceuticals to high standards, the probability that counterfeit pharmaceuticals will also be substandard is extraordinarily high.

The apparently large volumes of counterfeit drugs originating in India and finding their way to other parts of the world should be of huge concern to the Indian pharmaceutical sector. The Nigerian government, facing one of the highest levels of counterfeit drugs in the world, has banned imports from certain Indian pharmaceutical firms,[21] and even set up an office for their regulator, NAFDAC, in India.[22] And in November 2009 the Sri Lankan government banned imports from four Indian companies following the discovery of dangerously substandard products, including vials containing broken glass or plastic.[23]

A month later, in December 2009, Kenji Toda, chairman of the Japan Pharmaceutical Manufacturers Association, speaking at a conference in Chennai, stated that the bad reputation of the quality of medicines and concerns about counterfeits are a barrier to the growth of Indian-produced pharmaceuticals in Japan. Otherwise, he said, India is an extremely attractive region for investment due to cost-savings, the clinical research environment and large number of English-speaking professionals.[24] Again, quality concerns seem the only stumbling block to an otherwise thriving industry.

> *"The Nigerian government, facing one of the highest levels of counterfeit drugs in the world, has banned imports from certain Indian pharmaceutical firms, and even set up an office for their regulator, NAFDAC, in India."*

Causes of substandard and counterfeit drugs

Weak legal systems

The remarkable growth of the Indian economy has been accompanied by the birth of the Indian power brand, states a 2008 report by the Confederation of Indian Industry (CII). However, it noted that this success story is mitigated by the growth of "grey-market" goods, and counterfeits which taint the reputation of Indian brands and threaten patient safety. It singled out pharmaceuticals as one of two worst hit areas.[25]

The CII are also correct to highlight two weaknesses that allow counterfeits to thrive: lack of enforcement of existing laws and the inadequacy of the legal system and the rule of law. In both cases, the ineffectiveness of the courts stifles actions against counterfeiters and peddlers of substandard drugs.

The CII report states: "A number of recent anti-counterfeiting conferences in India have focused on the need to usher in greater enforcement of existing laws…" Tackling the lack of enforcement is not simply a matter of increasing regulatory and police resources (indeed, the cases of corruption among officials, outlined in the next chapter, suggest that adding extra layers to regulatory bodies can sometimes be damaging). Rather, the enforcement of existing laws relies on a quick and fair court system – for both civil and criminal cases. As the old saying goes, justice delayed is justice denied. And the Indian legal system is famously sclerotic, as the 2003 Mashelkar Report noted: "most of the prosecution cases pertaining to offences related to spurious drugs remain undecided for years. There is no greater deterrent than a 'severe', 'sure' and 'swift' punishment. This problem needs to be solved squarely by making a separate provision for speedy trials of such offences."[26] In May 2010 the Indian pharmaceutical website Pharmabiz.com reported that a Delhi court had convicted a man for manufacturing counterfeit cosmetics. According to the report: "The case was filed in 1987."[27]

The situation, certainly in civil courts, has improved little in the past seven years. The CII notes that laws to protect trademarks do exist, yet the ability to enforce them is lacking. Its report states: "there remains a general view that prosecuting such civil offences is a lengthy and cumbersome process, often resulting in less than desirable outcomes."[28] Indeed, it is also widely observed that investigations which lead to failed prosecutions further undermines the reputation of the entire pharmaceutical business.

"Most of the prosecution cases pertaining to offences related to spurious drugs remain undecided for years."

Criminal law is no better. The CII report continues: "counterfeiting rarely produces dire consequences in terms of incarceration or redress, and…perpetrators are often back in society only to become re-engaged in their practices. As a result, some brand owners have become resigned to a mindset that IP theft is simply one of the components of the Indian business environment that must be tolerated."[29]

Beyond the implications for patients, this last point is extremely worrying for those seeking to attract investments to India's emerging brands, especially in the realm of pharmaceuticals. The reputation of Indian generic medicines producers is threatened by counterfeit versions, within India or in foreign markets.

Figure 5 shows two versions of a well known Indian brand generic medicine, Ciprotab. The medicines in one of the packages passed all quality tests, while those in the other failed them all. Ciprotab is marketed by Fidson, a Nigerian company working with the producer, the Indian company VS International. Fidson's product is a generic version of ciprofloxacin, a powerful antibacterial drug.

According to Vidhyut Shah, the Managing Director of VS International of Mumbai, "Ciprotab is one of our leading brands and also the No. 1 brand of ciprofloxacin in Nigeria. We are aware that the product is being faked and consequently we have incorporated a number of anti-counterfeit measures to protect the integrity of the product and to ensure that only the original product reaches the consumer." [30]

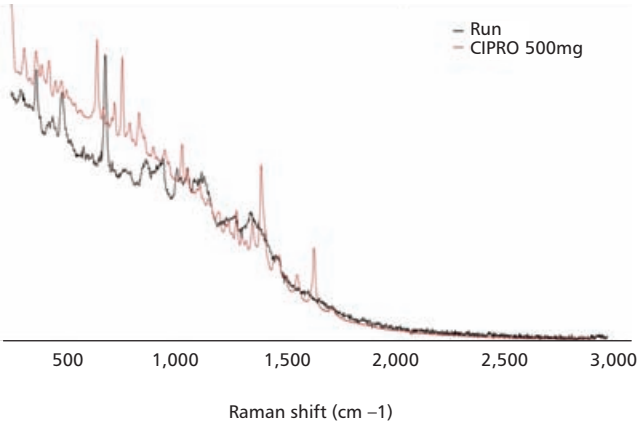
When brands like Ciprotab are faked the reputation of the company and of Indian generics as a whole may become compromised. The trademark could be faked by counterfeiters within India, or from elsewhere. In either case it is important that VS International and other companies producing brand pharmaceuticals be able to protect their brands and take action against those who infringe them – at the very least within India.

Dabur India, one of the country's leading consumer goods companies, is another example of a successful Indian enterprise under attack from counterfeiters. The firm has to work with India's authorities to defend its brand from vast amounts of counterfeiting. Their director of corporate affairs, P. D. Narang explained recently: "Through the initiatives of Dabur India, raids have been conducted at various locations and goods worth over 15

Figure 5 **Ciprofloxacin samples**

Tablets sampled from the packaging on the left failed quality tests, while tablets from the packaging on the right passed all three tests. The package on the left is a counterfeit of the genuine Indian generic. It has the batch number VM610. According to Dr Deshpande of VS International. "We have not produced Batch No. VM610 in 2008. Batch VM610 was manufactured by us in the year 2006 and exported to Nigeria in the same year"33. In other words the counterfeiters have taken a real batch number and pretended their product was that batch but produced and hence expired two years later than the real product. Photograph by Jennifer Moretta

Figure 6



The spectra in red is genuine Ciprotab/ciprofloxacin (on the right in Figure 5), the black is the fake Ciprotab – which is primarily made from talcum powder – as one can see the spectra do not match. These spectra were made with the Truscan raman spectrometer discussed elsewhere in this paper.

million rupees (around $325,000) have been seized so far through the raids." He believes that Indian industry loses $6.4 billion per annum due to counterfeiting.[31]

In January 2010 an article in the newspaper Business Standard explained the devastating effect of counterfeiting and piracy on Indian industry:

"According to the estimate by the industry, the music industry alone suffers a loss of Rs 600 crore [approximately $130m] every year owing to large scale piracy which is about 40 per cent now. Movie industry faces a loss of Rs 2,000 crore [approximately $425 m] every year. A FICCI study conducted last year found that 37 per cent of the automobile parts available in the market today were counterfeits."

The article notes the more tangible, damaging effect of medicines counterfeiting:

> *"The piracy is more visible in case of counterfeit drugs which flood the market under the same name and brand as the original ones thus leaving the buyers clueless about their authenticity. The industry estimates that 20 per cent of the drugs available in the market today are spurious."*[32]

Counterfeiting has the capacity to damage the reputation of Indian pharmaceuticals in general. In Nigeria, a large quantity of counterfeit drugs were discovered with the labels stating "Made in India", but investigations revealed that they were in fact produced in China. If a producer is able to fake a trademark, they can also fake anything else on the packaging, including the expiry date, source of the product, ingredients and so on. The fake drugs that claim to be "Made in the USA", discovered in our sampling, provide further evidence of this.

> *"… some brand owners have become resigned to a mindset that IP theft is simply one of the components of the Indian business environment that must be tolerated."*

Admittedly it is not the fault of the Indian system or US system if counterfeit versions of Indian or American medicines are produced in other countries. However, it is noteworthy that the problems experienced by countries such as Nigeria in the fight against counterfeit and substandard medicines are often the same as those in India. In a speech written for a conference in Ghana in November 2009, the head of NAFDAC Dr Paul Orhii stated:

> *"In Nigeria the litigation process is very, very sluggish. Some cases last for more than 10 years in one court … and get so protracted that the judges die in the process, and the cases are started over."*

Dr Orhii makes an important point – if companies cannot efficiently defend their trademarks in courts, and patients are not able to obtain redress from the culprits

who damage their health with fake products, there is little to deter criminals from producing counterfeits, or negligent companies from producing substandard products.

A stifled legal system is worsened by another problem too often ignored in debates on counterfeit and substandard medicines, yet recognised by Dr Paul Orhii who stressed in his speech: "corruption and conflict of interests." These are explored in the next sections.

Corruption

While studying the quality of drugs procured from Delhi and Chennai pharmacists, qualitative interviews were used to investigate how substandard medicines were arriving at pharmacy counters.

Although owners and managers were initially wary of speaking with researchers,[34] when assured that their responses would remain anonymous, 73 per cent (19 of 26) of pharmacists acknowledged that not only was there a serious problem with substandard drugs but that some of their fellow pharmacists were complicit in their sale. Some pharmacists knowingly bought substandard drugs in order to enrich themselves, they said.

Over half the interviewed pharmacists and assistants (15 of 26) said the most popular method of counterfeiting was to re-label expired drugs with a new expiry date. Twenty-seven per cent (7 of 26) said some companies readily supplied new labels. Even without these labels, altering a drug's expiry date is a simple process: according to Harinder Sikka, a director at the Indian pharmaceutical company Piramal Group, "All one needs is a nail polish remover."[35]

Nineteen per cent of pharmacists (5 of 26) claimed that their competitors bought from merchants selling sub-potent or otherwise suspect medicines. Nearly all pharmacists (92 per cent) claimed that at one time or another they had been approached by a trader offering sub-potent drugs at cheaper prices. No pharmacist said they could guarantee that all the drugs they sell are always of good quality.

"… a strong majority acknowledged that that some of their fellow pharmacists were complicit in the sale of fakes."

The situation is not necessarily improved by adding layers of state regulation. Indeed, in some cases it may simply result in additional bribery and corruption. A strong majority of pharmacists (19 of 26) expressed at least some level of concern about the government's attempts to regulate drug quality. Over half expressed concern that inspectors would demand bribes, while almost one in four (6 of 26) claimed that bribes had been demanded in the past.

Moreover, the problem is by no means limited to the pharmacy-level of the supply chain. Local investigator Suresh Sati explains that while counterfeit medicines often arrive through complicit pharmacists and corrupt officials, they also enter the supply and distribution chains through corrupt deals between hospitals' buyers and wholesalers and manufacturers.

In December 2008, a "thriving racket" supplying substandard drugs into government hospitals of Orissa was exposed. In this instance health department officials were said to be in league with the manufacturers of counterfeit medicines, with state drug inspectors also party to the scam. A report into the case said: "In most cases, spurious drugs circulation is carried out with the knowledge and connivance of officials of the drug controller, [in] Orissa, and local drug inspectors who are on the payroll of unscrupulous dealers."[36]

Around the same time a medical officer, Ranjit Das, exposed the supply of counterfeit drugs to Danapur Railway Hospital. His suspicions had been aroused after patients failed to respond to drugs, such as antidepressants and painkillers, supplied by three firms in particular. The drugs were tested in laboratories in Kolkata and Delhi and confirmed to be seriously substandard.[37]

Notorious counterfeiters of Haryana state have been filmed by the BBC, for the TV program Bad Medicine, discussing how to adulterate medicines to fool basic quality tests (and how to bribe ministers). In 2008, a research colleague approached another noted counterfeiter in Haryana posing as a buyer for a southern African pharmacy chain. He was offered rifampicin, a critical tuberculosis drug – at 15 per cent strength. Fifteen per cent is

"enough to pass colour dye tests and is much cheaper than 100 per cent," the counterfeiter told him.

Perhaps the worst case of which we are aware occurred at the Osmania General Hospital in Hyderabad, where patients were given substandard anaesthetics. One patient who was supposed to be under anaesthetic for two hours woke up after 30 minutes. In the end the hospital's doctors had to give three times the normal dose to ensure patients stayed unconscious throughout their procedures. This outrageous practice happened because the authorities did not prosecute the company that was supplying the substandard drugs, even though the complaint has continued for over a year.

Meanwhile, private investigators say that, in spite of authorities seemingly attempting to improve their performance against counterfeiting, the problems persist, and bringing culprits to justice remains a struggle.

This is by no means a uniquely Indian problem, but part of a pattern that can be observed in many parts of the world – especially where government control is strong but the rule of law is weak.

In 2009 a couple of high-profile cases demonstrated the often-strong link between government corruption and the supply of counterfeit medicines. In Russia, a company named Bryntsalov A was found to have manufactured over 50 brands of counterfeit medicine. Two leading figures in the company are siblings Vladimir Bryntsalov and Tatyana Bryntsalova, the former being an ex-candidate for President of Russia, and both therefore said to have extremely strong political links. In spite of being caught and convicted, the so-called punishments they received were merely token fines of no more than $1,500 each – raising strong questions over the independence of the judicial process.[38]

Meanwhile, in Argentina it emerged that a counterfeit medicines and money laundering ring was linked to key supporters of the president. Police subsequently arrested the heads of a trade union and pharmaceutical company and, crucially, senior officials in the local ministry of health. [39]

Figure 7

Top, reels of labels for counterfeit medicines, discovered during a raid in Ghaziabad, Uttar Pradesh State, India, 2009. Bottom, the labels once attached to counterfeit bottles of Benadryl, a cough medicine. The dangers of counterfeit cough medicine are shown in the numerous deaths of victims, many of whom are children, who have died due to products containing diethylene glycol, commonly known as anti-freeze, instead of glycerine, a sweet tasting syrup.[44]

Corruption in China reached the very top of the State Food and Drug Administration (SFDA), judging from the prosecution and subsequent execution of former head Zheng Xiaoyu for accepting bribes. Indeed, reports of corruption typically follow occurrences of counterfeit and substandard medicines.[40] There are allegations in Sri Lanka that the aforementioned cases of substandard medicines were procured by state departments.[41] In Uganda, members of parliament have accused National Drug Authority officials of "conniving with unscrupulous companies … to import the drugs which they said are a threat to the health of the people in the country" according to a report.[42] In Bolivia a massive street market in which counterfeit

> *"Over half [pharmacists] expressed concern that inspectors would demand bribes, while almost one in four claimed that bribes had been demanded in the past."*

drugs are sold alongside counterfeit DVDs operates freely because officials are "too corrupt" to take action. One peddler of counterfeits said he would "just pay off all the right people" if any measures were taken to thwart his business.[43]

While these may be extreme examples, from countries with high levels of corruption, they stress the need for strong, independent courts so that private actions can be taken and thereby deter counterfeiting and negligent manufacturing.

Political obfuscation

The debate on counterfeit and substandard drugs is often punctuated by claims that 'spurious' medicines make up less than one per cent of the Indian market. And in November 2009 an article in the newspaper Mint appeared under the headline "Supply of fake drugs grossly overstated."[45]

The basis of these claims are figures published by Indian authorities that show significantly lower, even negligible levels of what they call 'spurious' medicines.

In 2003, the Mashelkar Report (produced by the Ministry of Health and Family Welfare)[46] announced that eight consecutive years of data showed levels of 'spurious' drugs ranging between just 0.24 per cent and 0.47 per cent of the market. By comparison, the high levels of *substandard* drugs discovered and reported by Mashelkar (8.19 to 10.64 per cent) raise serious issues that are often hidden because of the headline-grabbing, low levels of 'spurious' drugs. See Appendix 2 for an explanation of how the Mashelkar report defines 'spurious'.

Meanwhile, even Mashelkar's figures for substandard drugs seem highly questionable. Consider these striking regional differences: in Haryana state, substandard drugs account for an astounding 40.4 per cent of those sampled, compared with 5.3 per cent in neighbouring Delhi, 2.1 per cent in Tripura, and zero per cent in Arunachal Pradesh, Daman and Due, and Goa. Given the likely significant leakage across state borders, such differences call into question the methodology by which they were obtained – and also whether each location followed the same methodology in practice.

Officials from the Government of India caution that these numbers may not be representative because they rely on unverified data reported by state authorities and are frequently drawn from samples of small size. Some states reported no data at all (eight of the 30 states assessed by India's Ministry of Health and Family Welfare reported no quality testing).[47] States that lack adequate testing facilities or fail to assess quality for financial or political reasons are precisely those most likely to harbour producers of low-quality products.

There are also concerns about the methods of data collection, and collusion between different groups. Vijay Karan, the former head of the Delhi Police Department, and an expert panel advisor to the Mashelkar Committee, claims that government interfered with the sampling methodology by telling at least some of the pharmacies in advance that they would be surveyed.[48]

Several investigators with whom the authors spoke were even more concerned about figures that first appeared on an Indian website in late August 2009, regarding new government data on levels of 'spurious' medicines.[49] The statistics claim that only 10 of 24,000 (or 0.04 per cent) sampled medicines were found to be 'spurious' – a quite incredible figure. These headline statistics were originally leaked to an Indian pharmaceutical industry website, while the study itself is yet to be published at the time of this paper going to print – although it continues to influence media headlines, such as the one in Mint in November 2009 referred to above. The underlying methodology and holistic data are unavailable, casting doubt over how robust and impartial the survey really is.

Other surveys and reports (including our own, outlined above) consistently show serious problems with substandard drugs in India. In 2002, a year prior to the publication of the Mashelkar Report, the World Health Organization (WHO) reported that Indian pharmaceutical manufacturers themselves estimated 20 per cent of drugs in major Indian-city markets were substandard or illegal.[50] More recent media reports, as outlined in Appendix 1, continue to tell a similar story.

If levels of substandard and counterfeit drugs are as low as the government claims, it is unclear why it keeps proposing new initiatives and clampdowns. The

Mashelkar Report itself recommended harsh fines, life imprisonment and even the death penalty as punishments for offenders. More recently, plans have emerged to allow drug inspectors to arrest pharmacists,[51] and a range of punitive measures announced. In August 2009, health minister Ghulam Nabi Azad said: "short of capital punishment, everything will be done to stamp out the circulation of spurious drugs."[52] The government has signalled its intention to regulate exported drugs, with validation checks and obligatory exporting licences.[53] A 2009 report from Delhi cited a health official as saying that "Ghaziabad and Faridabad are some of the areas where spurious and adulterated drugs are manufactured and circulated in large quantities" and that "harsh measures" such as more frequent raids were required to deal with the situation.[54] The Federal Government in Delhi has even introduced a "whistleblower policy", to reward people who report on cases of counterfeit drugs[55] (although a recent report indicates this policy is not working[56]). Combined, these do not seem to be normal levels of response to an allegedly negligible problem.

It is vital that the Delhi government makes available its data on levels of counterfeit and substandard medicines in India, and the full research methods of the survey – especially when it releases headline findings to media outlets. Headlines that misleadingly dismiss the problem risk encouraging people to buy drugs from sources which supply substandard and counterfeit medicines – hence fuelling such trade.

Furthermore, blocks on international cooperation against counterfeit medicines must be stopped. The International Medical Products Anti-Counterfeiting Taskforce (IMPACT) constantly has its progress at the World Health Organization thwarted. The taskforce was born from a WHO conference in Rome and mainly consists of drug regulatory authorities; and while research-based pharmaceutical companies are consulted, so are generics-producing pharmaceutical companies. Although IMPACT was probably unwise in not allowing the Indian Pharmaceutical Alliance (IPA), the body most closely associated with Indian generic producers, to become an NGO member of its effort. Although there were legitimate membership rule-based reasons for denying IPA a greater role, the result is probably the main reason why IMPACT is distrusted and attacked in India with conspiracy theories that claim it is being used to stifle the global trade in generics.

While it is possible that some western interests may use almost any argument and any fora to oppose Indian generic exports (e.g. patent-based drug seizures), attacks on the WHO in India appear misguided and ultimately counterproductive, given WHO's historic support for access to essential medicines. In December 2008, IMPACT amended its definition of 'counterfeit drugs' to make absolutely clear that generic drugs are not confused with counterfeits. The definition states: "disputes concerning patents must not be confused with counterfeiting." The European Generic-medicines Association (EGA) welcomed this augmentation, explaining that it "puts an end to any confusion with alleged patent infringement products which have nothing to do with counterfeiting."[57]

Nonetheless, the resolution to endorse IMPACT was still blocked the following month, and failed to make progress in 2009's World Health Assembly – on both occasions amid protests against IMPACT from the Indian government. Currently, some Indian pharmaceutical groups object to any use of the term 'counterfeit' at the WHO, even when it categorically does not include issues of potential patent-infringement.[58]

The conspiracy theories, worryingly, often stem from Indian government officials. In an article in India's Economic Times entitled "India to thwart attempt by MNCs [multi national companies] to get generics tagged spurious by WHO", an unnamed government official is quoted as saying:

> *"Not only are they [Western corporations] trying to influence African countries against buying generics produced by India by feeding them false information, they are also trying to influence international law making."*

The same article also quotes a (this time named) government official, D.K. Mittal, as saying: "We are all together in our mission to protect our generic industry…"[59]

Following an incident of dangerously substandard Indian medical products being supplied to Sri Lanka, the

reaction of the Indian government was to leap to the defence of the potentially culpable companies. It quickly called on the Sri Lankan government to drop the import bans imposed on the companies suspected of supplying substandard products.[60]

The role of Indian authorities should not be to protect domestic industries in this way, nor lobby on their behalf. All Governments promote their own industries, but promoting dangerous producers is unacceptable. There is a legitimate role to be played in international politics, warning against poorly-worded legislation that could confuse counterfeit drugs with high quality generic drugs. Authorities should encourage all measures which protect patients from counterfeit and substandard drugs, while ensuring that patent protection is dealt with as a separate issue and that generic drugs are not penalised. The aim should be to ensure high standards of pharmaceuticals throughout the world – not for western and Indian interests to use any potential conflict as an excuse for geo-political games.

Conclusion and recommendations

Many high quality drugs are manufactured in India, and the sub-continent has become the largest generics manufacturing location in the world. But it also has a significant problem with counterfeit and substandard drugs. Its Government has brought in new policies, including new legislation, to combat counterfeiters. But it also appears to be negligent in its inadequate enforcement of private rights (notably trademarks), less so domestically but more so in international fora, such as at WHO and with respect to the EU. The Government of India also sponsors reports which contain much misleading information concerning drug quality in India. Worse, some state governments have been very lenient towards local counterfeiters, in some instances officials have been directly bribed, and nearly all courts throughout the country have got such a backlog of cases of all types, that pharmaceutical actions can sit dormant for years, with traders of potentially lethal products left free to ply an odious trade.

We have shown, on the basis of a small set of independent surveys, that a small but significant proportion of drugs purchased at retailers and traders in Delhi and retailers in Chennai fail at least one quality test. The problem appears to be more serious in Delhi (averaging around 10 per cent in our survey) and also appears to be more serious at some pharmacies and some traders than in others. We conclude that the problem is largely due to a minority of actors (manufacturers, wholesale traders, pharmacies) who are intentionally supplying counterfeit and substandard medicines in order to reap the higher profit margins available from such transactions. In addition to posing a grave threat to the health of patients, the presence of such fakes undermines confidence in the medical system as a whole (and discourages patients from using allopathic medicines), and creates concerns outside India – potentially threatening the lucrative legitimate businesses producing good quality medicines.

Private enforcement of rights does occur but could be improved. As we have shown, many suppliers of counterfeit and substandard medicines are operating openly – complex police manoeuvres are not always required to catch the culprits, and therefore a problem seems to be with completing successfully legal action against them. This applies to both criminal and civil actions. Strong and independent courts must be available: for individuals to obtain redress, when harmed by substandard products; for victims to take action against counterfeiters guilty of misrepresentation; and for private companies to take action against counterfeiters who copy their trademarks.

Fortunately private companies are finding innovative ways of preserving the identity of their products from counterfeiters. F Hoffmann La-Roche Ltd announced in November 2008 that they were rolling out a serialisation system covering all their products in India.[61] Serialisation involves packages, or even individual pills, being given unique numbers which are stored in a central database. When a patient obtains the package, or a pharmacist administers a medicine, they can check the number against the database. This informs them whether or not the product is genuine and within its expiry date. The system signals an alarm when duplicate numbers are reported.

Some companies have developed serialisation systems based on SMS technology. A patient, upon buying

medicine, can find a unique number behind a scratch panel – they then send the number via a mobile phone to the central database, which tells them whether or not the drug is counterfeit. Developers of this system have signalled their intent to bring it to India this year.[62]

But India is not just expected to become a target for technologies developed elsewhere. New identity-preserving technologies are emerging from within India itself. A Pune-based company, for example, launched barcode systems involving nanotechnology and fingerprinting. Other Indian technologies, such as those which guard against tampered packages, have been discussed on the well-known Indian blog Spicy IP.[63] On the blog, Prashant Reddy commented:

> *"the government machinery is simply too incompetent to rein in such a serious threat to public health. It was therefore up to the market forces to innovate on effective anti-counterfeiting strategies in a bid to save the consumer from fake drugs…"*[64]

Spicy IP have stated that there are 27 anti-counterfeiting technologies on the Indian 'Bigpatents' database.

These technologies offer great hope to patients, and also show the drive from within India for new innovations and high quality products. As another counter to the threat of counterfeit medicines, organised pharmacy chains (such as Apollo Pharmacy and Fortis Health World) have centralised procurement directly from authorised distributors. "We deal with large established distributors representing big companies only, physically check every strip and bar code on them so that no unwanted supplies can trickle in," says Ashish Pandit formerly chief executive of Fortis HealthWorld (later known as Religare Wellness).[65]

These two companies are part of a large and growing trend of retail pharmacies which are undertaking vertical integration, from manufacture to distribution, retail and even medical practitioner. Fortis is allied with the drug manufacturing giant, Ranbaxy, and Apollo has developed from the Apollo Hospital Group. Other big players include Subhiksha and Zydus Cadilla and, interestingly, Reliance Health Venture, a sideways move for Anil Ambani , using his retail expertise to develop a complete chain, including the acquisition of a generic drug producer.

The new style pharmacy and healthcare stores, projected to increase by thousands of outlets over the coming years, also offer non-medicinal products that are in high-demand.[66] And many premises offer clinical services such as diagnostics, counselling and home visits.

Taken together, these commercial innovations could go a long way towards solving many of India's fake drug problems. Notably, our survey procured drugs from three of these pharmacies – all of which passed the quality testing.

Such innovative companies, and producers of high quality medicines, are examples of the organisations which drive India's economy forwards, and enhance the global reputation of Indian industry. They deserve to be able to protect their trademarks; and they deserve protection from the minority of miscreants who exploit not only their good reputations, but also the vulnerability of some of the world's poorest patients.

Ultimately, technology can only provide part of the solution; political will to enforce federal law, as well as the enforcement of private rights are urgently required to limit lethal drugs on the market.

Appendix 1 – A selection of reports of counterfeit and substandard medicines in India from 2009

28th December 2009
"FDA conducts raids to check fake drugs"
The Times of India
The town of Muzaffarnagar is identified as the "hub of substandard and fake drugs" in Uttar Pradesh. Large volumes of substandard and counterfeit medicines have been seized by authorities throughout Uttar Pradesh.
http://timesofindia.indiatimes.com/city/lucknow/FDA-conducts-raids-to-check-fake-drugs/articleshow/5385971.cms

23rd December 2009–31st December 2009
"Fake drug racket busted" (23rd December 2009)
"Drug racket: Raids at 30 more places" (25th December 2009)
"Drug racket made holograms to get rewards" (27th December 2009)
"Drug kingpin swindles Rs 36 lakh from pharma cos" (31st December 2009)
The Times of India
A series of large raids in Jaipur, Ragasthan, discover production of counterfeit drugs and a racket involving the production and dumping of counterfeits prior to informing the authorities or large drug manufacturers and fraudulently claiming rewards.
http://timesofindia.indiatimes.com/city/jaipur/Fake-drug-racket-busted/articleshow/5367574.cms
http://timesofindia.indiatimes.com/city/jaipur/Drug-racket-Raids-at-30-more-places/articleshow/5376526.cms
http://timesofindia.indiatimes.com/city/jaipur/Drug-racket-made-holograms-to-get-rewards/articleshow/5385702.cms
http://timesofindia.indiatimes.com/city/jaipur/Drug-kingpin-swindles-Rs-36-lakh-from-pharma-cos/articleshow/5397335.cms

23rd December 2009
"Drug manufacturer, retailer fined Rs 10,000 each"
Tribune News Service
Court imposes fines on a Haryana manufacturer and a Haryana retailer for supplying substandard drugs into the Indian market.
http://www.tribuneindia.com/2009/20091224/haryana.htm#12

1st December 2009
"Fake medicine sale rampant, cops helpless"
Indian Express
Counterfeit drugs are "sold rampantly in the state [of Gujarat]". A police inspector says "Fake medicines sell more than the original ones."
http://www.indianexpress.com/news/fake-medicine-sale-rampant-cops-helpless/548280/

14th November 2009
"Cops identify fake drugs 'kingpin'"
Times of India
Chandigarh police target Delhi-based man named as "Sandeep", under allegations of supplying counterfeits to the Kumar Brothers chemists.
http://timesofindia.indiatimes.com/city/chandigarh/Cops-identify-fake-drugs-kingpin/articleshow/5228983.cms

13th November 2009
"Cops smell fake drug racket"
Times of India
Chandigarh, India: Kumar Brothers chemist is suspected of supplying counterfeit equipment, including counterfeits of Johnson and Johnson Ltd.
http://timesofindia.indiatimes.com/city/chandigarh/Cops-smell-fake-drug-racket/articleshow/5224552.cms

20th October 2009
"Natco Pharma faces criminal action"

Economic Times
Regulator looks to initiate criminal proceedings against pharma company for supplying substandard drugs (a generic version of a patented breast cancer treatment).
http://economictimes.indiatimes.com/news/news-by-industry/healthcare/biotech/pharmaceuticals/Natco-Pharma-faces-criminal-action/articleshow/5137815.cms

30th September 2009
"Counterfeit drugs are killing bottle manufacturers"
DNA India
Trade in counterfeit Indian drugs is harming Indian packaging industry according to Arun Kumar, spokesman of the All India Glass Manufacturers' Federation. He says "The reuse is happening only at the facilities of the spurious drug manufacturers … The empty glass bottles are picked up either by kabadis or rag pickers. These are then washed in unhygienic conditions. Unscrupulous businessmen use empty glass bottles of reputed brands to sell their inferior products."
http://www.dnaindia.com/money/report_counterfeit-drugs-are-killing-bottle-manufacturers_1293881

25th September 2009
"Bad medicine"
Bangalore Mirror, India
In Bangalore, the "State Drugs Controller B R Jaga Shetty said, 49 drugs were found to be substandard out of the 900 samples tested. When the stocks of these 49 drugs were seized, they had already been sold in the market."
http://bangaloremirror.com/index.aspx?page=article&sectid=10&contentid=20090925200909250124224539 00f93bd&sectxslt=

29th August 2009
Karnataka drugs control dept seizes stocks of 5 substandard drugs from retail chemists
Pharmabiz.com
"Karnataka drugs control department has seized stocks of 5 different drugs in surprise inspections at the premises of pharmacists and the tests have proved that these products are not of standard quality."
http://www.pharmabiz.com/article/detnews.asp?articleid=51422&sectionid

24th August 2009
"Ignoring bills aids fake drugs biz"
The Times of India
State Drug Control Organisation (DCO) seized fake drugs in Jaipur.
http://timesofindia.indiatimes.com/articleshow/4926002.cms

21st August 2009
"Unregistered drugs being smuggled from India and China"
The News International [Pakistan. Story involves counterfeit drugs from India]
"…most common unregistered drugs found on sale in almost all markets of the country are being smuggled from India and China. Market sources informed 'The News' that a number of smuggled drugs of Indian origin are being brought into the country illegally through KSA and UAE … fake, counterfeit drugs – copies of many imported drugs – are being prepared in Pakistan while some importers are getting the copies from India and China on order."
http://www.thenews.com.pk/daily_detail.asp?id=194125

18th August 2009
"Six commonly used drugs found substandard"
Pharmabiz.com, India
Drug authorities found commonly used drugs to be substandard in Kerala, Karnataka, Tamil Nadu.
http://www.pharmabiz.com/article/detnews.asp?articleid=51230&sectionid=

12th August 2009
H1N1? Just fake it
Times of India
Article evaluates concerns over counterfeit swine flu drugs. "Periodic surveys have discovered that in some urban and semi-urban areas in the country, more than 30 per cent of the drugs randomly subjected to analysis were found to be spurious."
http://timesofindia.indiatimes.com/articleshow/4882012.cms

3rd August 2009
"Warning against substandard drug"
The Hindu, India
Bangalore: Chemists, wholesalers, and medical staff

warned not sell or use drug after it's found to be substandard.
http://www.hindu.com/2009/08/03/stories/2009080359400400.htm

18th June 2009
"Jailed for manufacturing substandard drug"
The Hindu, India
Magistrate in Hyderabad convicts person for manufacture and distribution of substandard drug. Sentence is one year in prison and a fine.
http://www.thehindu.com/2009/06/18/stories/2009061859240300.htm

10th June 2009
"Kerala DCA seized counterfeit of AstraZeneca's antibiotic from private hospital"
Pharmabiz.com
Counterfeit version of AstraZeneca drug found in private Indian hospital in Kerala.
http://www.pharmabiz.com/article/detnews.asp?articleid=50130&sectionid=

27th May 2009
"Spurious medicine racket busted"
The Times of India
Counterfeit drugs factory raided by the special operations group (SOG) of Ghaziabad police.
http://timesofindia.indiatimes.com/Delhi/Spurious-medicine-racket-busted/articleshow/4581364.cms

16th May 2009
"Counterfeit drugs"
Hueiyen News Service, India
Drugs deemed 'not of standard quality' by the government of Maharashtra are allegedly being sold in Manipur
http://www.e-pao.net/GP.asp?src=Snipp8..170509.may09

5th May 2009
"Two illegal drug trader caught"
Hueiyen News Service, India
Manipur Chemists' and Druggists' Association (MCDA) expose two alleged pushers of substandard medicines.
http://www.e-pao.net/GP.asp?src=29..060509.may09

29th March 2009
"Monitoring misuse of the WHO name and emblem in medicine promotion in India" *Indian Journal of Medical Ethics*
A report finds that "the name or emblem of WHO has been used extensively for unethical promotion of drugs … in India."
http://www.ijme.in/171ar10

24th March 2009
"Fake cancer drugs make it to your homes"
The Times of India
Bangalore: "The state health department has unearthed an anti-cancer drug racket where crucial medicines for treatment of the disease were not only illegally manufactured, but re-bottled and sold after expiry dates … Initial investigation has proved that these drugs have hit the market and consumed by patients."
http://timesofindia.indiatimes.com/Cities/Fake-cancer-drugs-make-it-to-your-homes/articleshow/4302988.cms

18th February 2009
"Over 120 kgs (265 lbs) of Fake Viagra Bound for America and Europe Seized"
UK Medix News [not an Indian media source, yet story concerns India]
In Haryana police make "one of the largest seizures" of counterfeit Viagra in a supposedly closed manufacturing plant.
http://www.ukmedix.com/viagra/over_120kgs_of_fake_viagra_seized4453.cfm

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The Times of India
FDA found that pharmaceutical firms sold substandard drugs in Maharashtra. http://timesofindia.indiatimes.com/Mumbai/FDA_review_reveals_sale_of_inferior_drugs/articleshow/4039057.cms

Appendix 2 – Defining Terms

The data shown in Appendix 3 and Appendix 4 were accrued through in-the-field surveys – selecting drugs from Indian pharmacists and wholesale traders and testing them for quality. This reveals the extent to which poor quality drugs exist in those markets; drugs that are of such poor quality as to be ineffective, or even directly harmful. This evidence is extremely helpful, yet the central finding – whether or not a drug is of an acceptably high pharmaceutical standard – does not fall neatly into the World Health Organization definitions of either 'counterfeit' or 'substandard'.

The WHO defines counterfeit medicines as follows:

> *"counterfeit medicine is one which is deliberately and fraudulently mislabeled with respect to identity and/or source. Counterfeiting can apply to both branded and generic products and counterfeit products may include products with the correct ingredients or with the wrong ingredients, without active ingredients, with insufficient active ingredients or with fake packaging."*[67]

The key point with this definition is that a product is only counterfeit if it has been *deliberately and fraudulently* mislabeled. On an aggregate level, in order to ascertain what proportion of drugs are counterfeit, it would therefore be necessary to investigate the history of every medicine in the sample, tracing each back to its source and discovering (if possible) whether there was deliberate intent behind its deception.

Such investigation is theoretically possible by deploying forensic evidence. To do this, however, can be extremely expensive and time-consuming, especially where samples are large. It is therefore not possible for our surveys to declare with confidence what percentage of the samples are definitely 'counterfeit' according to the WHO definition.

It is also worth bearing in mind that such a definition could include high quality medicines with deceptive packaging – although it is unlikely that anyone would bother to create counterfeit packaging, and then use it to sell high quality medicine.

The WHO defines substandard medicines as follows:

> *"Substandard medicines (also called out of specification (OOS) products) are genuine medicines produced by manufacturers authorized by the NMRA [National Medicines Regulatory Authority] which do not meet quality specifications set for them by national standards.*

Normally, each medicine that a manufacturer produces has to comply with quality standards and specifications. These are reviewed and assessed by the national medicines regulatory authority before the product is authorized for marketing."[68]

Determining the proportion of our sampled medicines that are defined as substandard by the WHO would be easier than calculating the level of 'counterfeit' medicines. However, even this would involve confirming the source company of each sample, ensuring that it is definitely not a counterfeit version, and checking that the company is authorised by the regulator. Further, there can be complications in determining which NMRA is considered responsible for the quality of drugs when they are traded between countries (often via other countries), and different NMRAs may have different standards, and varying decisions regarding which drugs are authorised and which are not.

For example, in November 2009 the Sri Lankan government banned imports from four Indian companies following the discovery of dangerously substandard products (as outlined on page X). If products made by these companies were subsequently

discovered in the Sri Lankan market would they automatically be excluded from being defined as 'substandard' (irrespective of their quality) because the manufacturer was not authorised? And if the contents were below acceptable standards, would the package be defined as 'counterfeit', while an equally substandard product from an authorised company would be defined as 'substandard'?

The term 'spurious' is often used in Indian debates, including in the Mashelkar Report in 2003. The report notes that the Drugs and Cosmetics Act by the Amendment Act of 1982. Section 17-B defines that a drug shall be deemed to be spurious:-

a. if it is manufactured under a name which belongs to another drug; or

b. if it is an imitation of, or is a substitute for, another drug or resembles another drug in a manner likely to deceive, or bears upon it or upon its label or container the name of another drug, unless it is plainly and conspicuously marked so as to reveal its true character and its lack of identity with such other drug; or

c. if the label or container bears the name of an individual or company purporting to be the manufacture of the drug, which individual or company is fictitious or does not exist; or

d. if it has been substituted wholly or in part by another drug or substance; or

e. if it purports to be the product of a manufacturer of whom it is not truly a product.

Interestingly, given the political pressure in India referred to on page X, the definition alludes mainly to intellectual property, and specifically trademarks – deeming a drug to be spurious if its packaging contains the name of another producer, for example. In point d. the definition also refers to the deliberate production of a substandard product.

However, both this definition, and the WHO definition of 'counterfeit', leave a considerable grey area. For example, if a manufacturer knowingly operates a shoddy facility, at high risk of producing substandard drugs, are they culpable of *deliberately* producing substandards?

Even in specific cases, proving deliberate deception can lead to a legal minefield.

Overcoming such complications, this paper argues that all drugs failing basic quality tests pose a serious health hazard to the public. We refer to all drugs of unacceptable quality as 'substandard'. See the methodology on page X for details on how our tests determine whether a drug is satisfactory or substandard.

Where there are clues as to whether a product is a deliberate counterfeit, rather than a poorly produced (or maintained) attempt at a genuine drug, we elucidate on this evidence. For example, we assume that a product has been deliberately counterfeited when it contains no active ingredients whatsoever (although many deliberate counterfeits also contain *some* active ingredient). Equally, we do not evaluate the trademark status of every sample, yet reveal cases in which a trademark has clearly been faked, as this provides useful supporting evidence. In this sense, products breaching trademark and labelling laws are 'counterfeit', as explained in the opening line of this paper. A drug produced from incorrect ingredients, deliberately made to deceive patients, is clearly a 'counterfeit' irrespective of trademark issues. Yet such a drug would typically come in packaging which misleadingly declared it to be the real thing, and would therefore still fall under our definition of 'counterfeit'. The authors accept that it is possible for such a drug to be sold 'loose', as part of a deceptive sale, and that this would still be a counterfeit. While there is a public health case to be made for defining deliberately faked drugs as 'counterfeits' above and beyond trademark issues, our research (as explained above) cannot comprehensively evaluate the likelihood of deliberate intent behind every sample.

The paper also argues that its proposed solutions would combat the unnecessary scourge of all substandard and counterfeit medicines, however they're defined, and increase the standard of medicines across the board.

Appendix 3 – Methodology and Summarised Findings

Survey of medicines obtained from pharmacies in Delhi and Chennai

In June 2008 and March 2009, samples of drugs were procured from store-front pharmacies in Delhi and Chennai respectively.

Five classes of drugs were obtained, with the number of samples tested in brackets:

- Ciprofloxacin (103)
- Chloroquine (119)
- Erythromycin (117)
- Isoniazid (84)
- Rifampicin (118)

All are included in the World Health Organization's Model List of Essential Medicines.[69] The level of substandard drugs found among the different classes was relatively consistent, yet the drug Isoniazid had slightly higher levels of substandard samples than the others, at 12 per cent. If the rates of substandard anti-TB drugs (Isoniazid 12 per cent and Rifampicin 9 per cent) assessed in this study were reflected across India , then at any time around 200,000 tuberculosis (TB) sufferers could be taking substandard medicines.[70] This is not to mention the many patients outside India consuming substandard Indian anti-TB drugs. With TB resistance becoming rampant in India and elsewhere, the portent of the situation is worryingly clear. In September 2009, Dr James Sitienei of the Kenyan health ministry blamed substandard drugs for the emergence of multi-drug-resistant tuberculosis (MDR-TB) and the problems with tackling the disease in Kenya.[71]

In total 541 samples were tested (281 from Delhi and 260 from Chennai) with only the better-performing sample in the duplicate pair being considered – a generous assumption which could understate the levels of substandard drugs.

The survey's findings were originally published in the peer-review academic journal PLoS One in June 2009.[72]

Overall of the drugs obtained 12 per cent from Delhi pharmacists were substandard, and 5 per cent of those obtained from Chennai pharmacists were substandard.

Of the 52 pharmacists surveyed (in both cities), 21 provided drugs only of high quality.

However, 18 pharmacies provided a small proportion of substandard drugs (6 – 10 per cent). More seriously, in 13 pharmacies over 10 per cent of medicines purchased were substandard, whilst in seven of these 13 pharmacies one in five (or more) drugs purchased were substandard (see Figure X, page X).

91 per cent of the substandard drugs failed *both* kinds of standard testing: thin-layer chromatography tests (which measure the levels of active ingredients) and disintegration tests (which measure if the drug successfully disperses the ingredients at 37°C in less than 30 minutes). To fail the thin-layer chromatography test, the drug must have had less than the required amount of active ingredient, which equates given confidence in the technology to about 80 per cent of the stated active ingredient. These findings demonstrate the degree to which the failed drugs were significantly substandard, and thus the high danger posed to patients. If the drug does not dissolve in reasonable time in body temperature water there is likelihood that even if it has the right ingredients in it, it will not dissolve appropriately when ingested, which would indicate

lower bioavailability of the product, and hence clinical failure of the drug.

The studies in Delhi and Chennai did not forensically test which medicines were likely to be counterfeits, and which simply substandard medicines – yet almost 3.9 per cent of drugs purchased in Delhi (11 from 281) had zero active ingredients, indicating that these were likely to be counterfeit medicines – these results were confirmed by assessment with the Truscan raman spectrometer which showed the products did not have the correct, if any, active ingredient. Around half of these appear to involve blatant trademark-infringement, faking the brands of two large, global pharmaceutical producers – one American company, and one Indian company. The fact that these were available from regular, respectable-looking store-front pharmacies is a cause for real concern.

Almost all (97 per cent) of the drugs sampled were labelled as being made in India, with the rest labelled as drugs from the USA. Four "Made in USA" drugs failed quality testing, and all had zero active ingredients – suggesting they are counterfeits. The packaging information, therefore, is also likely to be deliberately misleading.

N.B. Full product authentication using the Truscan raman spectrometer requires background samples of known good substances in order to create a method against which a sample can be tested. For example, to be sure a counterfeit and substandard product exists of Brand X, one would need quality assured pills of Brand X from the manufacturer, or randomly bought Brand X pills assessed in detail for quality – this would entail full compendial assessment, perhaps using High Performance Liquid Chromatography. If the manufacturer of Brand X did not send samples or if no access to a laboratory to undertake compendial assessments is possible, then full product authentication could not be undertaken. For the vast majority of samples collected we had neither known good samples from the manufacturer or proven samples from compendial studies. Attempts to gather samples from manufacturers met with mixed responses so a complete library was not possible.

However the spectrometer still provides useful information. Each sample spectra can be compared with known spectra of each drug class. For while we may not have the brand in question, and its unique formulation and hence unique spectra, we knew that the spectra of any drug claiming to contain ciprofloxacin should contain certain spectral peaks. If they are absent we know the active ingredient is absent. This meant for example in the case of Ciprotab that we could see that the fake version had no ciprofloxacin in it.

Using the spectrometer in this way we can confirm drug quality failures. But the real advantage of the spectrometer, its speed and ease of use is unfortunately lost since detailed analysis of every spectra has to be undertaken by a spectroscopist (our thanks to spectroscopist Robert Brush of Thermo Fisher Scientific for help with analysis of various spectra in this study).

If companies would supply good quality samples, then an independent assessment of drug quality, of thousands of samples, could be undertaken quickly. We hope that perhaps the Indian pharmaceutical companies were to sponsor such an assessment.

Survey of medicines obtained from wholesale traders in Delhi

In April and May 2009, Indian nationals from Delhi posed as drug buyers, purchasing large quantities of drugs from four wholesale traders in one wholesale market of Delhi. The drugs purchased were the same classes as those examined for the survey of pharmacists. The same methodology was used as outlined in the section above.

A total of 1,563 treatment packs were purchased from the wholesale traders. The numbers of drugs purchased are broken down as follows:

- Ciprofloxacin (302 treatment packs)
- Chloroquine (208)
- Erythromycin (325)
- Isoniazid (315)
- Rifampicin (313)

Bulk amounts of the drugs were purchased by Delhi

residents to simulate normal transactions between local drug-buyers, and traders.

The drugs were procured from the four wholesale traders in the following quantities:

- Wholesale trader 1: 407 treatment packs
- Wholesale trader 2: 401
- Wholesale trader 3: 374
- Wholesale trader 4: 381

Of these treatment packs, researchers selected an approximate 25 per cent representative sample of the different brands of each drug type from each trader, resulting in a sample of 390, which were then tested.

Drugs procured directly from wholesale traders, which supply some local pharmacies in the Delhi area, as well as rural drug traders, had a worryingly high failure rate (7 per cent), but which was noticeably lower than the failure rate of the drugs procured from Delhi-area pharmacies (12 per cent). The distributions of brands purchased for specific drugs in the two studies were similar but not identical.

It is notable that even for this relatively small sampling, for every drug class assessed, the failure rate is higher for pharmacists than wholesale traders. This would be consistent with some product degradation due to inappropriate transportation and storage from wholesalers to pharmacists and within pharmacies. Furthermore, there may be further opportunity for substandard product infiltration into the distribution chain between wholesalers and pharmacists. Also, poorly manufactured drugs which pass tests at production are more likely to degrade faster, which could contribute to slightly worse results at the pharmacy level.

As with the survey of drugs from pharmacies, significant levels of substandard drugs were found in all five drug classes procured from wholesale traders, with levels of active ingredient ranging from around 6 per cent to 11 per cent. For wholesale traders, failure rates ranged from 6 per cent for chloroquine to 11 per cent for isoniazid; for pharmacies, failure rates ranged from 9 per cent for chloroquine to 17 per cent for isoniazid. At pharmacies, isoniazid had the highest failure rate (17 per cent, 8/48), followed by erythromycin (13 per cent, 8/61), rifampicin (12 per cent, 8/66), ciprofloxacin (10 per cent, 5/50), and chloroquine (9 per cent, 5/56). At wholesale traders, isoniazid had the highest failure rate (11 per cent, 9/79), followed by rifampicin (10 per cent, 8/78), erythromycin 7 per cent (6/81), ciprofloxacin (7 per cent, 5/75), and chloroquine (6 per cent, 5/77). No specific drug type had zero failures and no specific drug type had all, or nearly all, failures. This suggests that the problem of counterfeiting is not limited to only a few types of pharmaceuticals.

A subset of the above drugs was tested with a Raman spectrometer. Not all drugs could be tested since it requires an assured quality product as reference for each brand, as discussed above. The spectrometry analysis will continue over time, as more quality assured samples are gathered. But what can be concluded from the limited analysis undertaken so far is that where products are in testable form, the spectrometer confirms all the failures found with analysis undertaken by the Minilab (TLC and disintegration) as described above. It also finds a slightly elevated failure rate than with Minilab tests, but the sample size is as yet too small to draw more concrete conclusions.

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18. The report (Ibid.) is slightly unclear on the proportion of seized medicines that were stopped specifically on suspicion of trademark infringement. According to a graph on page 25 of the report, it seems that over 65% of medicines detained at EU borders were infringing trademarks. Other figures mentioned on the proportion of trademark infringements range from 54.92 per cent to 93 per cent, but both of these may refer to all products, not just medical products. We sought clarification on this matter from the European Commission, but were not provided with an answer before going to print in May 2010.

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According to a 2009 World Health Organization report (''Global tuberculosis control: a short update to the 2009 report'', Table 1, page 5, http://www.who.int/tb/publications/global_report/2009/update/tbu_9.pdf [accessed 17/05/10]) the latest estimated prevalence rate of TB in India is 2,186,402, while DOTS coverage is 100 per cent. If at least 9 per cent of the market is fake, then at least 9 per cent of this number are exposed to substandard drugs – giving the figure of 196,776 affected patients.

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