COUNTERFEIT AND SPURIOUS DRUGS: BIG CHALLENGES TO THE
HEALTH CARE SYSTEM WORLDWIDE

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ABSTRACT

Counterfeit drugs are one of the key challenges facing pharmaceutical supply chains and the safety of patients. Counterfeit drug is a pharmaceutical product which is produced and sold with the intent to deceptively represent its origin, authenticity or effectiveness. It may contain inappropriate quantities of active ingredients, may be improperly processed within the body or may contain ingredients that are not on the label, and is often sold with inaccurate, incorrect, or fake packaging and labeling. Spurious drugs are a great threat to patient’s life, the genuine pharmaceutical manufacturer and the image of the country as a whole. According to WHO, 25% of medicines consumed in poor countries could be counterfeit or below standard. An estimate suggests that these drugs are a $200 billion industry worldwide. India could be an easy target for counterfeits, as the manufacturing costs is 40% cheaper here as compared to other countries. India is fast becoming capital of counterfeit drugs, accounting for one third of the counterfeit drugs produced worldwide. It is estimated that 40 per cent of the pharma market in our country, i.e. Rs 8000 crore is under the grip of spurious and black marketed drugs. Not only is the people’s health at stake but also there is a serious loss to the exchequer of both central and state governments as they are deprived of huge amounts on account of sales tax and excise duty. Proper drug quality monitoring, enforcement of laws and legislation, an effective and efficient regulatory environment, and awareness and vigilance on part of all stakeholders can help tackle this problem. The uses of holograms, 2D bar codes, Quick Response (QR) codes, tracers, traggants and inks, plastic tags, radio frequency identification, mass encryption technology are some other techniques to limit the counterfeiting of drugs.

Keywords: spurious, counterfeit, substandard drug, 2D bar codes, QR codes, Holograms, Radio Frequency Identification (RFI).

INTRODUCTION

The Indian pharma industry has become third biggest in the world by volume and is poised to touch $20 billion mark by 2015, up from $12 billion. The domestic industry players have a major role in ensuring safety and quality and providing drugs at affordable prices. The Indian pharmaceutical companies have an extensive presence in many parts of the world, and our pharmaceutical products are known to be of good quality, safety and efficacy. Indian generic drugs have helped in bringing down the cost of treatment of various diseases worldwide, which includes HIV/AIDS.
Drugs administered to patients prove their relative safety, efficacy and improved quality before they are introduced into the markets but medicines are increasingly becoming the victim of counterfeits in recent time. Between January 1999 and October 2000 alone, 46 confidential reports relating to such drugs were received by WHO from 20 countries. The consumption of paracetamol cough syrup prepared with diethylene glycol (a toxic chemical used in antifreeze) led to 89 deaths in Haiti in 1995 and 30 infant deaths in India in 1998. A study conducted in WHO's South-East Asia Region in 2001 revealed that 38% of 104 antimalarial drugs on sale in pharmacies did not contain any active ingredients. Counterfeit drugs are those drugs which are sold under a product name without authorization and which are sold with the intention of misleading the customer into believing that the drug is original. Counterfeiting is one of the major problems facing healthcare systems across the world. It is more prevalent in developing countries where there is limited control over the flow of drugs through the supply chain. Low-Quality Medicines poses hazards at all levels of the population and the impact of this menace can range from one section of population or escalate to full blown volcano eruption. Counterfeiters find weak links in the supply chain to introduce fake drugs and so counterfeiting market thrives in developed countries where the movement of goods in the supply chain is not strictly regulated. In the developing countries of Africa, Asia and Latin America, counterfeit drugs constitute considerable portion of the total pharmaceutical market. Counterfeiting of drugs is an economic and social menace and over the years this has grown into a well - organised criminal activity in the country. Only a sustained and concerted action backed jointly by the government, drug industry and consumer action groups can tackle it. Along with this, innovations in packaging technology have come to play a stellar role in helping the consumers identify the authentic products and to ward off counterfeiters. Poverty, high cost of medicines, lack of an official supply chain, legislative lacunae, easy accessibility to computerized printing technology, ineffective law enforcement machinery, and light penalties provide the counterfeiters with an enormous economic incentive without much risk. The consequences of the use of such medicines may vary from therapeutic failure to the occurrence of serious adverse events and even death.
SPURIOUS AND COUNTERFEIT DRUGS³

In accordance with Black’s law dictionary, the term “counterfeit drug” may be used to describe a drug made by someone other than the genuine manufacturer, by copying or imitating an original product without authority or right, with a view to deceive or defraud, and then marketing the copied or forged drug as the original. In reality, however, counterfeit drug is defined differently in different countries.

In India, The Drug and Cosmetic Act 1940 and Rules 1945, a central piece of legislation regulating the manufacture, sale, and quality of drugs and formulations, provides a definition of “spurious drugs” under section 17-B.⁴

1. If it is manufactured under a name which belongs to another drug; or
2. If it is 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
3. If the label or container bears the name of an individual or company purporting to be manufacturer of the drug, which individual or company is fictitious or does not exist; or
4. It has been substituted wholly or in part by another drug or substance; or
5. If it purports to be the product of manufacturer of whom it is not truly a product.

According to WHO definition, 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.”⁵-⁷ In other cases, drugs which have been rejected by regulators or manufacturers may be sold in markets and should be considered counterfeits.⁶

The same holds true for drugs which have expired and have been relabeled with a fake later expiry date. Indian drugs laws, however, do not define or make note of the term “counterfeit drugs” throughout the statute, although there is an immediate need to incorporate this term under its purview. Bearing in mind the fact that India has emerged as a bulk manufacturer and exporter of drugs and pharmaceuticals, the quality of drugs manufactured in India and its regulatory mechanisms are of paramount importance, not
only for India but also for the whole world. In developing countries, drugs used to treat life threatening conditions such as malaria, tuberculosis, HIV/AIDS, etc, are generally counterfeited. In developed countries, counterfeiters generally target newer and costly drugs like hormones, steroids, psychiatric medicines, anticancer drugs, etc.\(^5\),\(^7\)

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.

Spurious and counterfeit drugs are not synonymous with each other and a clear line of demarcation needs to be drawn between the two (table 1).

**TABLE 1: DISTINCTION BETWEEN SPURIOUS AND COUNTERFEIT DRUGS**

<table>
<thead>
<tr>
<th>Spurious drugs</th>
<th>Counterfeit drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. The drug product/formulation is without any active ingredient/salt</td>
<td>1. The drug product/formulation contains labeled drug</td>
</tr>
<tr>
<td>2. Sample will fail when tested in the laboratory</td>
<td>2. Sample may pass when tested in the laboratory</td>
</tr>
<tr>
<td>3. It may or may not resemble in packing, design, look, etc with popular original brand</td>
<td>3. It will resemble in packing, design, look with popular brand. The batch number, manufacturing date, expiry date, labels on the product may be from the original pack. Even the physician/pharmacist may not be able to detect it</td>
</tr>
<tr>
<td>4. Injurious to health; may cause problems even death of the patient</td>
<td>4. May not be injurious to health</td>
</tr>
<tr>
<td>5. Normally the medicines are sold without bill</td>
<td>5. Medicines may be sold on valid invoices by licensed chemists</td>
</tr>
<tr>
<td>6. There is criminal intent behind producing and supplying these drugs</td>
<td>6. Criminal intent may or may not be there</td>
</tr>
</tbody>
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**MAGNITUDE OF THE PROBLEM**

The problem of spurious and counterfeit drugs has been escalating the world over in spite of tough provisions provided in drug laws in most countries to counter this problem. Between 1984 and 1999, there were 771 reports of counterfeit drugs with 78% of these coming from developing countries. From January 1999 to October 2000, 46 reports of
counterfeit drugs were received from 8 countries; 60% from developing countries and 40% from developed nations 9.

The International Federation of Pharmaceutical Manufacturers Associations (IFPMA) has estimated that 7% of all drugs sold around the world are counterfeits 10.

In India, the death penalty has been discussed as a penal action in case of conviction in a spurious drug case. 11 Fake drugs are estimated to represent 13–30% of the pharmaceutical market in India. 12–14

A survey suggested that in India’s major cities one in every five medicines sold was fake. 15

According to another report released by the European Commission, 75% of global cases of counterfeit medicines originated from India. 16

India is also the major exporter of counterfeit drugs to the least developed countries such as Nigeria, including anti-HIV drugs. 17

The human right to a standard of living adequate for health and well-being is an important right that is recognised in the International Bill of Human Rights. 18

Although the Indian Constitution does not explicitly mention health or health care as a fundamental right, the legal right to health is based on right to life and liberty (article 21 in part III of the Constitution of India). This right to health has to include the right to access quality medicines to be of any value; thus, the state is duty bound to provide quality medicines to its people.

Types of Counterfeit Drugs and their consequences

Illegal drugs are often produced and sold with the intent to deceptively represent their origin, authenticity or effectiveness. The nature of these fraudulent drugs ranges from those containing no active ingredient (eg. when a bag of powdered lactose claimed to be cocaine), with insufficient active ingredient or with some diluents (e.g., Baking soda or lactose) or sometimes with a wrong active ingredient (e.g., when methamphetamine is sold as cocaine) or with a fake packaging 19-20. The various types of counterfeit drugs are:

1. Counterfeit drugs containing same dose of the active ingredient,
2. Mislabeled medications,
3. Counterfeit drugs containing an incorrect dose of the active ingredient,
4. Counterfeit drugs which do not contain the active ingredient,
5. Counterfeit drugs which have the active ingredient

Counterfeit drugs containing some dose of the Active Ingredient: They are close replicas of the genuine drug with the same dose of the active ingredient. They constitute only 5% of the fraudulent medicines. Even though they contain the same active ingredient as the originals they are of poor quality as it is not manufactured according to the rules of good manufacturing practice approved worldwide. The dissolution profile of the drug may vary, so the amount of drug available for absorption by the body may vary and finally the efficiency of the drug is less. The inactive ingredients in this type of drugs are not documented and they can be detected only by laboratory analysis. Sometimes these inactive ingredients can cause health risks.

Mislabeled medications: Mislabeled medicines are those which are sold in the package of another brand medicine. The label of counterfeit medicine also contains batch number, manufacturing number and other details which are fraudulent. Counterfeitors put labels of firms which may not even exist on the packaging of their drug products, so as to bypass the penal action by administrative and law enforcement agencies.

For example in 2006 the US government issued a public warning against buying brand name medicines off the internet. This was after the case of prescription weight loss medication Xenical (orlistat). The packaging appeared authentic but the batch number; (a genuine one) did not matched with the expiry date for the batch by the manufacturer. Another ploy is to use the name of one drug in a class to label another drug in the same class which is cheaper—for example, ciprofloxacin tablets are labelled as levofloxacin tablets. There may be cases where the manufacturer does not have any intention of undue monetary benefits, yet the product can be of substandard/spurious/adulterated quality. Sometimes inadvertent error in the manufacturing process leads to genesis of substandard/spurious quality products. This computer technology has made the task of copying the labels/ cartons of reputed pharmaceutical companies so effortless and accurate that it is difficult to differentiate between the original and the fake.

Counterfeit drugs containing an incorrect dose of the active ingredient: This can lead to much health related problems. In case of antibiotics low dose therapy may not kill the bacteria but may lead to the emergence of resistant strains.

Counterfeit drugs which do not contain the active ingredient:
1. Counterfeit drugs containing a potentially harmful substance: Contamination of, or substitution in, medicines of diethylene glycol has occurred in many countries including Argentina, Bangladesh and Nigeria, resulting in the loss of over 500 lives.\(^{23}\)

2. Counterfeit drugs containing an unlisted active ingredient: This type of counterfeiting is commonly found in recreational drugs which may contain some herbal ingredients. Even though they are natural they may exhibit some pharmacological actions in the body. So it should be taken into consideration and use of such type of drugs should be discussed with the health care provider.

3. Counterfeit drugs containing an inert material: Manipulations in the active raw materials during the manufacture of drug products may lead to the genesis of a spurious drug product. Substitution of API (active pharmaceutical ingredient) with inert material (for example, making a tablet of alprazolam with simple sugar instead of the legitimate raw material); the purchase of raw material of short expiry or unknown expiry or unlabelled raw material or purchase from an unauthorized / doubtful source so as to reduce the manufacturing cost.

4. Counterfeit drugs having Substitution of the API with a cheaper API: Substitution of the API with a cheaper API which has a very similar therapeutic action (for example, cefotaxime with ampicillin; analgin with paracetamol) may all lead to the generation of spurious / counterfeit drug products.

Counterfeit drugs which have the active ingredient:

1. Counterfeit drugs having Raw material with inactive ingredients / excipients: If the swallowed tablet passes through the patient and out with the stool, without disintegrating in the stomach, it is useless to the patient even if it contains the required quantity of therapeutically active ingredient. The solvent (excipient) added to dissolve the drug powder paracetamol may prove fatal if it is not pure. Herein lies the importance of these hidden materials, which do not contribute to the therapeutic efficacy, but may result in a heavy cost if their quality is not ensured or is compromised by the manufacturer. Such materials are known as excipients, fillers, and vehicles.
2. Counterfeit drugs having Non-uniform mixing of the active ingredient with the excipients: Because of faulty mixing procedure This problem is usually seen in cases where the quantity of active ingredient is very small compared with the total bulk in the mixer (for example, bethamethasone / dexamethasone).

3. Counterfeit drugs prepared by using poor quality solvents/vehicle—for example, purified water, glycerine, propylene glycol, etc—in the formulation may lead to a spurious/adulterated/sub-standard product. Poor microbiological quality of water in the manufacture of large volume parenterals can be fatal when given intravenously.

4. Counterfeit drugs prepared by using Use of inadequate/incompatible preservative or vehicle: Use of inadequate/incompatible preservative or vehicle, either by oversight or deliberately or as part of cost reduction exercise, may lead to a substandard drug product.

5. Counterfeit drugs having poor Storage Condition: Most of the drugs require particular storage conditions; if they are not stored in these mandatory storage conditions, they tend to lose their potency. Drugs such as ampicillin, gentamycin, oxytocin, insulin, vitamins, etc, require storage at controlled temperatures and specified humidity throughout their process of manufacture and afterwards. Usually no strict compliances are made to their storage conditions by the manufacturers/traders in developing countries, affecting the quality of the product to the detriment of the end users—the patients.

6. Counterfeit drugs having poor attention at the manufacturing stage: Stability problem which causes formulation may be unstable at the manufacturing stage. Formulations containing vitamins, antibiotics, etc—where due care towards inherent stability of the API is not given before the start of process, leading to an unstable final product. Even the improper / faulty storage of such sensitive drugs in the retail / wholesale chemist shop may alter their quality to the risk of the patient.
CONSEQUENCES OF THE USE OF SPURIOUS AND COUNTERFEIT DRUGS

The consequences of the use of counterfeit and spurious medicines may vary from therapeutic failure to occurrence of serious adverse events and even deaths. In the case of anti-infectives, development of drug resistance is the major threat.

For diseases that are treated with combination therapy—for example, falciparum malaria, tuberculosis, and HIV—poor quality drugs risk the spread of resistance.\(^{24}\)

Contamination of, or substitution in, medicines of diethylene glycol has occurred in many countries including Argentina, Bangladesh and Nigeria, resulting in the loss of over 500 lives.\(^ {25}\)

The consumption of paracetamol cough syrup prepared with diethylene glycol (a toxic chemical used in antifreeze) led to 89 deaths in Haiti in 1995 and 30 infant deaths in India in 1998.\(^ {26}\)

More than 10 patients lost their lives after receiving doses of impure glycerine at JJ Hospital Bombay in 1986.\(^ {27,28}\)

In 2000 in Cambodia counterfeit malaria tablets caused death of 30 people.\(^ {29}\)

Over hundred children died in Nigeria in 1993 due to the harmful substance in the counterfeit cough syrup. Similar cases were reported in China and India in 1990-2007 and in Panama due to ethylene glycol in cough syrup instead of glycerol. In 2002 more than 190,000 deaths occurred due to polyethylene glycol contamination in paracetamol syrup.\(^ {30}\)

Factors Encouraging counterfeiting of Drugs\(^ {31}\)

A variety of factors account for why medicines are attractive for counterfeiting. Medicines are high value items in relation to their bulk and the demand for medicines is infinite. Furthermore, for the counterfeiter, ingredient costs can be very low if cheap substitutes are used or if these are omitted altogether, as is often the case. Producing counterfeit drugs may not require building huge infrastructure or facilities. They can be produced in small cottage industries or in backyards or under the shade of a tree. There are also no overhead costs due to quality assurance or meeting Good Manufacturing Practices (GMP) standards, since such standards are never implemented and gross margins are therefore very high.

A counterfeit drug has a better capacity to deceive, particularly if it is copied to make it look like the original product and if it comes from a supposedly legitimate source so that
purchasers are unlikely to be suspicious. Moreover, the process by which patients get their drugs is different from that for other consumer goods: doctors or health workers prescribe them. Even when patients choose their own drugs they may lack the specialized knowledge to detect whether the product they are buying is of good quality let alone be able to detect whether the product is counterfeit. Other factors that encourage counterfeiting of medicines are discussed below.

Lack of political will and commitment

Drugs are unlike other consumer goods in that they are crucial to meeting the important objective of improving public health and so they should not be treated in the same way as other commodities. Their development, manufacture, import, subsequent handling within the distribution chain and use require specialized knowledge and skills. Consequently, they should conform to prescribed standards and their quality should be rigorously controlled. However, this would require strong government will and commitment to establish and operate strong national drug regulatory authority.

Lack of appropriate drug legislation

Legislation and regulations form the basis for drug regulation. Where legislation and regulations do not exist for proper control of medicines, the otherwise criminal activity of counterfeiting of medicines is not treated as a crime. The absence of deterrent legislation encourages counterfeiters since there is no fear of being apprehended and prosecuted. Inadequate resources for drug regulation activities and absence of training of national drug regulatory authorities' personnel may also manifest itself as inefficiency and incompetence of national drug regulatory authorities.

Absence of or weak drug regulation

Drugs need to be safe, effective and of good quality in order to produce the desired effect. Ensuring these properties requires the creation of competent national drug regulatory authority with the necessary human and other resources to control the manufacture, importation, distribution and sale of medicines. At present, out of the 191 WHO member states about 20% are known to have well developed drug regulation. Of the remaining member states, about 50% implement drug regulation at varying levels of development and operational capacity. The remaining 30% either have no drug regulation in place or
very limited capacity that hardly functions. Inadequate, ineffective or weak drug regulatory control could promote unregulated importation, manufacture and distribution of drugs, leading to the proliferation of counterfeit drugs in the national market.

The problems in the regulatory system in the country are primarily due to:

- inadequate or weak drug control infrastructure at the State and Central level;
- inadequate testing facilities;
- shortage of drug inspectors;
- non-uniformity of enforcement;
- lack of specially trained cadres for specific regulatory areas;
- non-existence of data bank; and
- non-availability of accurate information.

Absence of adequately staffed or technically equipped to monitor

Majority of the States are not either adequately staffed or technically equipped to monitor the quality of drugs manufactured and sold in their State. There is a strong need to strengthen the organizations with competent and trained manpower and with adequate budgets. This will enable them to detect, investigate and take quick action in spurious/counterfeit drug cases.

Weak enforcement and penal sanctions

Enacting deterrent anticounterfeiting legislation alone will not solve the problem. It needs to be enforced. Where existing laws are not enforced crime is perpetuated as criminals are not afraid of being arrested and prosecuted. Lenient punishments for offences tend to encourage criminal activities such as medicines' counterfeiting, particularly when the penalties for counterfeiting non-medicinal products are more severe. Moreover, disregarding trademark rights may encourage large scale counterfeiting of drugs.

Corruption and conflict of interest

The efficiency of personnel is adversely affected by corruption and conflict of interest resulting in laws not being enforced and criminals not being arrested, prosecuted and convicted for their crimes. Governments need to develop strategies to reduce corruption. One approach could be to empower public interest and consumer groups to participate in drug regulation and to make regulatory authorities accountable and their decisions transparent.
Demand exceeding supply
When demand for medicines exceeds supply, criminally minded people tend to profit by manufacturing and distributing counterfeit medicines as substitute for genuine medicines.

High prices of medicines
When prices of medicines are high and price differentials between identical products exist there is greater incentive to supply cheap counterfeit medicines.

Inefficient cooperation between stakeholders
Intersectoral cooperation between regulatory authorities, police, and customs services and the judiciary is essential for effective control of the national drug market and enforcement of drug legislation. When such cooperation is ineffective, counterfeiters can escape detection, arrest, and penal sanctions. Equally, the cooperation of the pharmaceutical industry, wholesalers, and retailers to report to the national drug regulatory authority cases of counterfeit drugs is necessary in combating counterfeit drugs.

Lack of regulation by exporting countries and within free trade zones
Pharmaceuticals made for export are not regulated by many exporting countries to the same standard as those produced for domestic use. In addition, pharmaceuticals are sometimes exported through free trade zones where drug control is lax and where repackaging and re-labeling take place. This kind of trade arrangement can provide better opportunities for counterfeiters to introduce illicit material into the distribution chain even when the system is highly regulated.

Trade through several intermediaries
Trade in pharmaceuticals rarely takes place between the manufacturing country and the importing country. Currently, it takes place through one or more intermediate countries or trading houses. Activities in trading houses may sometimes involve repackaging and re-labeling which may be carried out without any controls under conditions that do not comply with good manufacturing practices’ requirements.

HAZARDS AND IMPACT OF THIS MENACE
Low-Quality Medicines poses hazards at all levels of the population and the impact of this menace can range from one section of population or escalate to full blown volcano eruption. Some of the sectors are highlighted as follows:
Impact on public health

In most cases, counterfeit drugs are not equivalent in safety, efficacy and quality to their genuine counterparts. Even if they are of the correct quality or contain the correct amount of active substance, their production and distribution are not within the control of the drug regulatory authority of the country concerned. This means that any associated defects and adverse reactions will not be easily recognized or monitored and, if needed, an effective product recall would not be possible.

So far counterfeit drugs that have been discovered have rarely been efficacious. In many cases they have been found to be without active ingredients, or with wrong ingredients or with incorrect quantities of active ingredients. The use of such drugs can prolong treatment periods as patients may not respond as quickly as they should and exacerbate conditions being treated. Treatment with ineffective counterfeit drugs such as antibiotics can lead to the emergence of resistant organisms and may have deleterious effect on wide section of the population. In extreme cases, counterfeit drugs may even cause death. As a consequence of such damaging effects, counterfeit drugs may erode public confidence in health care systems, health care professionals, the suppliers and sellers of genuine drugs, the pharmaceutical industry and national Drug Regulatory Authorities (DRAs). Incorrect labeling as to the source can also be detrimental to the reputation and financial standing of the original and/or current manufacturer whose name has been fraudulently used.

There is no simple solution or remedy that can be applied to eliminate counterfeit medicines nor can the problem be solved by an individual company or government. The problem has reached global dimension and needs global approach.

Effect on Patient: The very fact that patient looks up to us as life savers, in their hour of need we turn out to be prescribers of low quality drugs even though the diagnosis is genuine. It will not be surprising that patients lose their confidence in the health care system, where the final toll will be the financial burden of both the patient and the government. Low quality of anti-microbials is a major global public health concern. These medicines are contributing to the development of resistance strains of microorganisms.

www.pharmasm.com
Effect on Industry: There is huge financial loss for the companies producing the genuine product. The reputation of the original product is damaged and the pharmaceutical companies which invest huge resources in developing innovative products suffer financially. The loss here is immense; this lead to loss of reputation, loss of genuine of the brand, the company earns the mistrust of Authorities, Health Practitioners and Consumers.

Effect on Government: The respective authority must pay the price of loss of reputation both national and international, mistrust of importers with heavy loss of revenue. New law enforcement and analytical methods further lead to more expenditure. Therapeutic failure or adverse events result in loss of confidence in the health system and the systems of drug control and enforcement. The state also loses revenue from the taxes and duties that would be payable on the legitimate product. Developing countries with lax regulatory environments for drugs are also disadvantaged in their ability to attract direct foreign investment.

Effect on Ethics: Issues on ethics takes the highest level because it points out corruption of the highest order. Country’s drug and pharma industry needs to set up wing to assist the agencies in ensuring quality drugs as Government alone cannot identify unscrupulous producers. It is the responsibility of every healthcare provider to ensure that the quality and safety of medicines are not compromised. There are instances of spurious drugs, which are harmful to health, being produced. This is a crime and an unethical practice.

**STEPS TO COMBAT COUNTERFEIT MEDICINES**

Government tightens rules to curb spurious drugs production: To minimize the manufacture of substandard drugs in the country and making the regulatory control more effective, the 12th Five Year Plan contains substantial provision for further strengthening the drug regulatory system both at central and state level.

Role of International Regulatory Authorities

a) The officers needed to be specially trained for the purpose.

b) To detect and eliminate the manufacturing and training of counterfeit medicines.

c) Increase awareness of importance of quality, safety and effective use of medicines.

d) Should promote policy for the easy availability of good quality medicines with a special focus on drugs used in life threatening conditions like HIV, TB and Malaria.
e) A database of all known sources of counterfeit drugs, whether substantiated or not, needs to be developed by the key players. This database would become a reference for all countries, whether they are importing from or exporting drugs to a country specified as a source of counterfeit drugs.

f) The pharmaceutical companies need to open the lines of communication with their sources of information to keep track of underground counterfeiting operation and should divulge all information to agencies Interpol or to the National police force of any country in which companies suspect counterfeit version of their products are being sold.

**Role of National Governments**

a) Awareness campaign to the people regarding these risks through the media.

b) Drug legislations to inhibit provision, manufacture, import and sale of counterfeit medicines should be strict & vigilant.

c) Surveys to control and check the menace of counterfeit medicines in each and every corner of the country.

d) Products which are provided through established and licensed supply channel (from manufacturer to wholesaler to pharmacy to patient) should be ensured of proper safety throughout the channelling system.

**Role of State Government**

a. The drug control organizations in States should be adequately strengthened. Additional manpower, infrastructure, technical capabilities and financial resources should be made available to the organization. They should have continuous vigilance facilities and strategies to implement an effective system to monitor and control the manufacture and distribution of spurious drugs.

b. States should set up Intelligence cum legal cells under the supervision of trained senior officer. State Governments should put in place efficient mechanism for timely police help to these officers.

c. States should establish a proper surveillance system for keeping a watch over suspected individuals. Watchers should be employed to purchase samples from suspected persons without disclosing their identity. Secret funds should be made available for intelligence activities.
d. States, which have a large number of drug distribution outlets, should set-up a well-equipped testing laboratory to enable them to test all categories of drugs in shortest possible time. All States should plan to take more samples to check the quality of drugs manufactured and sold in the market.

e. States should set up an efficient communication network system between the Center and other States in order to facilitate exchange of information and rapid investigation in cases involving inter-state movement.

f. States should also monitor the source of purchase and quality of drugs stocked by dispensing registered medical practitioners through their drugs inspectors.

Role of the Drug testing Laboratories

a) Drugs and Cosmetics Rules should be amended to include GLP norms as statutory requirement for approved testing labs and also the in house testing labs of manufacturers.

b) Accreditation with NABL should be made mandatory for all testing laboratories including the Government laboratories.

c) The Central Government should initiate a programme to have coded samples of the same product tested at different central and state labs from time to time and have the results assessed by experts for their proficiency testing.

d) The state testing labs should be frequently audited by a team of experts to ensure their proper functioning.

e) A separate Division needs to be established under CDA to oversee the overall working of drug testing laboratories in the country.

Role of Drugs Regulatory Authority

a) Registration of new drugs in India needs to be strengthened to ensure safety, efficacy and quality before they are made available to the consumers.

b) Drug Inspectors should be given the right to enter manufacturing or packaging premises, collect samples for test, and not allow sale of drugs until they check the result of the tests.

c) Setting up of special courts to deal with summary trials would help control the entry of spurious and substandard drugs in the supply chain.

Role of Pharmacist:
a) Should be trained to be aware to purchase products only from reputable companies after good quality analyses.

b) Report to the state regulatory authority if suspected counterfeit medicines have been offered or supplied

c) The pharmacist should co-operate in investigation to detect the counterfeit suppliers.

Whistle Blower Policy:

a) Govt. of India, Ministry of Health & family Welfare has announced the Whistle Blower Policy to reward informer of manufacturers /distributors of spurious drugs.

b) Identity of the informer will be kept secret.

c) Details of the reward Scheme has been put on the official site of CDSCO. The zonal/sub zonal officer under control of DCG(I) in all over the country will act as a nodal officer for receiving the information & for operation of the scheme till the unearthing of the racket of spurious / counterfeit drugs.

Reward for Information of Fake or Spurious Drug

According to Drug Controller General of India (DCGI), a vigilance cell is being set up in every state to monitor fake or spurious drugs. The ministry had earlier received tip-offs from states like Himachal Pradesh, Haryana and Rajasthan in the northern region and one from a southern state, but none produced concrete results. The policy stipulates that the reward of a maximum of 20% of the total cost of consignments seized would be paid to the informer, which will not in any way exceed Rs 25 lakh in each case. In respect to an officer in the government or the Central Drugs Standard Control Organization (CDSCO), the reward would not exceed Rs 5 lakh for one case and a maximum of Rs 30 lakh in h/his entire service. The reward would be given only when there would be confirmation of the seizure of spurious drugs, cosmetics and medical devices by the designated officers of CDSCO.

The policy said that once the fake drugs are seized, the government would engage senior advocates who have sufficient experience of cases relating to drugs to help punish the guilty. To ensure speedy trials, these cases will be filed before the designated/special courts set up for the purpose of drug-related issues, as per provisions of the Drugs and Cosmetics Act. The health ministry estimates that 5% of drugs in India are counterfeit, while 0.3% are spurious.
Role of the Pharmaceutical industry
a) Use their well-developed marketing network to identify distribution channel and persons involved in spurious drug trade.
b) Assist to identify spurious/counterfeit drugs by cooperating with the regulatory and/or police authorities.
c) Prepare a checklist for the guidance of manufacturers, wholesalers and retail sellers to identify and distinguish between the spurious and genuine products.
d) Establish a close interaction with regulatory authorities and extend full cooperation to eliminate the menace of spurious drugs.
e) Ensure proper storage of products during transit as well as at places of distribution.

Role of the Pharma Trade Association
a) Play a proactive and visible role to contain the menace of spurious/counterfeit drugs
b) Develop its mechanism in identifying the persons directly or indirectly involved in abetting the distribution of spurious, counterfeit or questionable quality drugs
c) Prepare a checklist for the guidance of members and widely publicize it for information of all members
d) Sub Rule 3 of Rule 65 (4) of Drugs & Cosmetics Rules requires that the supply by retail of any drug shall be made against a cash/credit memo. This condition of license should be strictly adhered to by all retail licensees.
e) Every chemist/pharmacist to act as a watchdog to prevent entry of any spurious/doubtful quality drugs or those purchased from unauthorized sources or without proper bills in the supply chain.

Recommended Action by the Consumer and other Professional Associations
a) There is an urgent need for an awareness campaign to educate the consumers and the medical and paramedical professionals.
b) The Consumers and health professional/associates should play an active and visible role to create awareness about the hazards of spurious drugs.
c) They should undertake campaigns at the national level to educate the public on the ways and means of detecting spurious drugs and the advantages of purchasing from licensed sources with valid cash memos.
The penalty for sale and manufacture of spurious drug
a) The penalty for sale and manufacture of spurious drug that causes grievous hurt or death should be enhanced from life imprisonment to death. Even the penalty for manufacture and sale of spurious drugs that do not cause grievous hurt or death should also be made more severe.
b) The offences related to spurious drugs should be made cognisable and non-bailable. The bail, if considered by the court should be granted only after a period of three months.
c) The penalty for not disclosing the source of purchase of drugs by a dealer should be made stringent.
d) A provision should be included in the Drugs and Cosmetics Act to enable the Central and State Governments to designate special courts for speedy trial of spurious drugs cases.
e) Under Drugs and Cosmetics Act, besides the Drug Inspectors, Police should also be authorized to file prosecution for offences related to spurious drugs.

The gist of the recommendations to tackle the spurious drugs problem is as follows:
- Creation of effective interaction between the stakeholders i.e. industry and regulators, industry and consumers, trade and regulators and medical professional and regulators.
- Creation of intelligence cum legal cells in State and Central offices.
- Discouragement of proliferation of drug distribution outlets.
- Making changes in law to provide enhanced penalties, making the offences cognisable and non-bailable in the light of similar provisions in Narcotic Drugs and Psychotropic Substances Act.
- Designation of special courts to try the cases of spurious drugs.
- Preparation of dossiers of suspected dealers and manufactures.
- Provision of secret funds and incentives to informers.
- Creating effective networking system between States
- Checking on drug supplies to practitioners who buy and supply drugs to their patients.
- Creation by the industry of its counterfeit drug strategies, better surveillance and efficient complaint handling system.
- Creation of better surveillance system by the Trade Association on defaulting members and to take strict action against them.
• Creation of better awareness amongst consumers.

The Quality Control of Drugs that imported into the Country

The Quality Control of Drugs that imported into the Country has been kept under strict vigil. The quality of the drugs imported into the country is regulated under the provisions of the Drugs and Cosmetics Act, 1940 and Rules made there under, through a system of registration, import license and checking of the consignments at the time of their import at the designated ports. Drugs found spurious and sub-standard are not permitted to be released for import by the customs authorities. The cases of import of spurious drugs in 2009-10 were investigated by the Central Bureau of Investigation (CBI) and prosecutions launched on the basis of evidences available as per the provisions of law.

The imported cases of spurious and sub-standard drugs on the notice of the government during the last three years and the current year have decreased considerably. The health ministry data has revealed that during 2009-10, the spurious drugs reported were seven in number. At the same time, the sub-standard drugs were 35, which continued to be the same in 2010-11. Again in 2011-12, 34 drugs were found to be sub-standard. During 2013, there were 18 cases of such drugs reported as sub-standard. Between 2010 to early 2013, there was not a single case of spurious drugs that was reported in the country.

Working Group on SSFFC

The first meeting of the Member State Mechanism (MSM) on Sub-standard/Spurious/Falsely-labeled/Falsified/Counterfeit (SSFFC) medical products met from November 19-21, 2012 in Buenos Aires. The meeting decided to establish an open-ended working group to identify the actions, activities and behaviors that result in SSFFC medical products.

In order to actively participate in the working group, the Ministry of Health and Family Welfare set up a cell comprising three experts in the Indian Pharmacopoeia Commission on January 15, 2013 to address the issues pertaining to strengthening international cooperation for harmonization of practices on SSFFC.

Drug Alert system for Consumer

In order to regulate the import, manufacture, distribution and sale of drugs, medical devices and cosmetics in India, it has been decided that the CDSCO is required to be informed about the quality defect in the medicinal products which require recall or
restriction on supply. Where a product is considered to be a risk to public health, the marketing authorisation holder will withdraw the affected product from use and the CDSCO as well as concerned state drug regulatory authority are required to be informed about such products so that suitable drug alert is issued for the information of the public. This is the first concerted attempt to develop a pan-India drug alert system for consumers, which some states like Gujarat have already started. The Gujarat drug controller regularly sends out SMS alerts on substandard drugs.

CDSCO’s drug testing laboratories have also been instructed to send regular updates to the headquarters on drugs that fail the test. With the emphasis in the 12th five year plan on a gradual shift from voluntary disclosure for pharma companies to mandatory disclosure, this is one of the first steps in that direction.

The heft of CDSCO is such that even in the absence of laid down punitive provisions, a pharma firm that is found to have concealed information about substandard products may find the going tough in getting future clearances.

The Drug Controller General of India (DCGI) has made it mandatory for all pharma companies and laboratories to report cases of substandard drugs. All details of such substandard/spurious/adulterated/ misbranded drugs will be uploaded on the website of the Central Drugs and Standards Control Organisation (CDSCO) every month.

Vision of CDSCO

A vision paper prepared by the CDSCO, quantifying how much funds are needed under the 12th Five Year Plan (2012-17), According to health minister India would require Rs 3,256 crore to strengthen its drug regulatory system. This includes cost of upgrading state laboratories, improving manpower by 2,500, creation of additional labs, mobile drug testing labs and the CDSCO’s pharmaco-vigilance programme. CDSCO estimates that in the next five years, drug exports may rise from Rs 42,000 crore to Rs 2 lakh crore.

Guidelines for Action to be taken on Sub-standard Drugs

Sub-standard drugs have been categorized into Category A and Category B defects. Category A defects are those, which are considered to be serious in nature and affect the quality of a drug (examples, active ingredient content below 70%; tablets failing in disintegration/dissolution tests and in content uniformity; liquid preparations showing
presence of foreign matter or fungus and parenteral preparations failing in sterility or pyrogen test etc.).

Category B defects are minor in nature (examples, broken or chipped tablets or presence of spots or discoloration; cracking of emulsion or liquid preparations showing sedimentation or change of colour and parenterals showing isolated cases of particulate matter or fungus growth etc.).

The suggested action for category A defects is immediate recall of batch and stop further sale by the manufacturer. The regulatory authority is required to investigate the matter immediately and take appropriate action according to the results of the investigation.

No uniform system is followed. The cases are referred to the concerned state drug controller but the response is usually delayed and complete details of every individual case is i.e. GMP status of concerned manufacturers, recall of products etc. is usually not available. In most cases, the test reports are received after six months or even a year and by that time the product is invariably consumed. Also, due to multi-layered distribution system, involving number of stockists, wholesalers, sub-wholesalers etc., the follow up on recall is difficult.

A view has been expressed that it is likely that many sub-standard reports may in fact be a result of:

i. Improper methods of analysis;
ii. Use of improper chemicals/reagents;
iii. Incorrect interpretation of prescribed standards; and

iv. Improper storage conditions after a drug leaves the manufacturing premises.

Recommendation

a) The Drugs Consultative Committee (DCC) should deliberate on the issue of action to be taken on substandard drugs and review the existing guidelines. It should analyse the nature of substandard reports and status of concerned manufacturing units as well as the system of distribution; and

b) The existing classification by DCC of defects found in substandard drugs into category A and category B and the action to be taken on each category of defects needs to be reviewed and updated.
Technological Ideas to Curb Counterfeiting: Technologies are increasingly employed to protect and authenticate products. The various technologies available today vary considerably in the degree of sophistication and in the principles on which the protection against counterfeiting is based. The various technologies are as follows:

Holograms: Several Indian pharmaceutical companies have implemented changes in their packaging formats as a way of reducing the impact of counterfeit activity. Holograms are now widely available in a variety of formats such as:

(i) Holographic shrink sleeves to protect branded bottled products against counterfeiting and refilling,
(ii) Blister packaging aluminum foil,
(iii) Pharmaceutical PVC, where the hologram is applied as a thin stripe to PVC sheets used to make blister packs,
(iv) holographic induction cap seals,
(v) polyester-based tamper evident labels used to seal packages and
(vi) holographic hot stamping foil where the hologram is fused to the host surface by heat and pressure.

Advantages

(i) They are difficult to counterfeit & are recognizable to the consumer,
(ii) They can feature covert tools such as nanoimagery, micro-imagery, digital watermarks and hidden images,
(iii) They are relatively cheap & allow the tracing/tracking of products through the distribution chain.

Disadvantage

(i) They are generally costly (10–25 paisa) and this can add significantly to the MRP of low-end medicines.
(ii) The holograms themselves can also be eventually duplicated by counterfeiters.
(iii) Finally, passive technologies such as holograms do not provide the brand owner with an implementable protocol for supply chain management, track-and-trace ability (e-pedigree), or with the intelligence that is required in the event that counterfeiting occurs. Hence, an expertly produced counterfeit medicine with a hologram cannot be distinguished from the genuine product, nor can the brand owner trace the origin of the fake products.
Tracers, taggants and inks: Additions of chemical and biological tracers to the packaging and/or product have been relatively commonplace as an anticounterfeiting measure. According to Prebble \(^{42}\), “verification ranges from simple to complex, with certain paper systems authenticated using specially developed color change pens.” With respect to inks, many types are available and these include UV fluorescent, phosphorescent, thermochromic and those at specific light frequencies. These are typically applied on product labels and packaging. When exposed to either heat or light they change color, and when exposed again the color reverts to the original. Inks have also been developed that are invisible to the human eye but which can be read by barcode scanners. These have been used in the fragrance and pharmaceutical industries to authenticate products. Security taggants are four major types \(^{43}\): Spectroscopic, Biological, Chemical and Physical taggants.

Use of Plastic Tags: A microscopic tag is a virtually indestructible, microscopically small plastic particle of random irregular shape, constructed from up to ten different colored layers. The sequence of colors denotes the unique code (ranges up to 4.5 billion). The tags can be applied to both product and packaging in a number of ways, including incorporation in clear varnish.

Radio- Frequency Identification: The technology is based on an electronic chip that emits radio frequency waves encoding a specific ID or code. This information is then captured by a specialized chip reader as the products proceed through the supply chain.

Advantage
(i) No line of sight is required. The chip can be embedded in cartons or pallets in a hidden manner that resists tampering.

Disadvantage
(i) This technology is costly (5 to 15 rupees) readability, and lack of item-level protection. Although this is a manageable cost if the chips are only applied to product batches (e.g., cartons or pallets), the price becomes simply unacceptable at the item level.
(ii) The readability problem has a technical origin and constrains the use of this technology due to high error rates (>2.5%).
The final impediment to use of RFID is that it is not yet possible to implement it at the item level, for two reasons. The first is the cost and another one is that the consumer does not carry RFID readers, which are electronic devices that decode the radio signal. As such, RFID simply cannot be implemented at the item level and thereby fails to include the consumer in the authentication process. Pfizer is the first pharmaceutical company to put in place a comprehensive program of this type focused on EPC authentication as a means of deterring counterfeiting.

Mass Encryption Technology: In this technology, every product is given a unique digital identity that is generated by a computer based encryption engine. The same software is able to decrypt the digital code. The encrypted code itself is usually a 16-digit alphanumeric code that can be displayed in:

A linear format—

![Linear Format](image1)

Scripted format-- HJ 21WF OH U20KB8N 7

2-D Data Matrix barcode—

![2-D Barcode](image2)

2-D barcodes, which are now becoming the industry standard, are printed on packaging during manufacture and therefore provide each medicine with the identity before it enters the supply chain. In addition to the encryption and decryption of the codes, the software that supports this technology allows brand owners to fully manage their supply chain, i.e., track-and-trace. Pharmaceutical companies are empowered to track their shipments from the factory through all intermediate nodes right down to the retail level, in much the same way that courier companies track their shipments as they wind through the shipping chain. By this technology pharmaceutical companies are better able to manage any recalls, should they be necessary.
A major advantage that mass encryption enjoys over all other currently available technologies is that it empowers the consumer to authenticate a drug. Given that the codes can be printed on blister packs and vials in script form, the consumer can simply verify the authenticity of the drug by entering the code into an internet site or via SMS.

**AUTHENTICATION PROCESS BY CONSUMER INVOLVING EITHER SMS OR INTERNET** Counterfeit drugs will either contain no code or have an invalid code, which will not pass the authentication process. It is simply impossible for a counterfeiter to make up arbitrary codes because the combinatorial possibilities are astronomically large for a 16-digit alphanumeric format. The Drug Consultative Committee (DCC) in its last meeting in February 2011 has approved the proposal that for every strip of medicine available in India ought to have a 2D bar code a unique randomly generated numeric code (UID). A phone number will be mentioned above the bar code, where the consumer can SMS the UID. A message will tell the consumer whether the drug is original or not. Once approved, India will join Italy, Malaysia and the European Union to make 2D bar code and UID mandatory in an effort to curb spurious and counterfeit drugs.

**Quick Response Codes:** Quick response (QR) codes are also being tested. These printed squares are an advanced version of the 2D barcodes. Anyone with a camera-enabled phone and web access can scan the code and be taken instantly to the pharma company website to authenticate the drug.

**Unique Identification Mobile Verification:** A pharmaceutical company, PharmaSecure, has come up with a technology called UIMV - unique identification mobile verification. It is a unique code for each product which can be verified by sending texts to the number given. Manufacturers print these codes on packaging, and monitoring begins the minute the product leaves the factory. This way consignment is protected while in transit until they reach their destination.
E-Pedigree: An epedigree (sometimes referred to as e-pedigree or electronic pedigree) is simply an electronic document which satisfies a pedigree requirement. The primary purpose of an epedigree is to protect consumers from contaminated medicine or counterfeit drugs. According to the U.S. Food and Drug Administration (FDA) "A drug pedigree is a statement of origin that identifies each prior sale, purchase, or trade of a drug, including the date of those transactions and the names and addresses of all parties to them."

CONCLUSIONS

Sub-standard / Spurious / falsely-labelled / falsified / counterfeit (SSFFC) medicines are found everywhere in the world. They range from random mixtures of harmful toxic substances to inactive, ineffective preparations. Some contain a declared, active ingredient and look so similar to the genuine product that they deceive health professionals as well as patients. But in every case, the source of a SSFFC medicine is unknown and its content unreliable. SSFFC medicines are always illegal. They can result in treatment failure or even death. Eliminating them is a considerable public health challenge.

Worldwide health care system is in a big challenge due to the Counterfeit and spurious drugs. It poses a public health risk because their content can be dangerous or they can lack active ingredients. Their use can result in treatment failure and contribute to increased resistance or even death. Poverty, lack or weak of drug regulation and legislation, and light penalties makes this a flourishing business in the developing countries. To achieve the goal of health for all, the menace of counterfeit drugs needs to be controlled. A strong political will, an efficient regulatory environment, and enforcement of rules, strict laws, national / international awareness, technological update and financial rewards are keys in combating this phenomenon. In a rapidly globalising world, international cooperation is necessary in order to counter this menace effectively. The counterfeit drug industry and regulatory and enforcement conditions in India should be of concern to the world at large, as reports show India to be a major producer of counterfeit drugs in the world. It should also be of concern to the Indian pharmaceutical industry and government as it can be injurious to their reputation, and adversely affect India’s rapidly growing pharmaceutical exports. Continuous surveillance by the
government with active co-operation from each one of us will promote quality medication use and thereby ensuring that patients lives are safeguarded and that they get maximum benefit from the medications. Country’s drug and pharma industry needs to set up wing to assist the agencies in ensuring quality drugs as Government alone cannot identify unscrupulous producers. It is the responsibility of every healthcare provider to ensure that the quality and safety of medicines are not compromised. There are instances of spurious drugs, which are harmful to health, being produced. This is a crime and an unethical practice.

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REFERENCES

1. The speech of President Pratibha Patil, inauguration, 71st World Congress of Pharmacy and Pharmaceutical Sciences, 4th September, Hyderabad.


33a. www.cdsco.nic.in
33b. The report of Drug Controller General of India (DCGI), The Economics Time, Kounteya Sinha, Sep 9, 2012,
34b. The report of Drug Controller General of India (DCGI), The Economics Time, Kounteya Sinha, Sep 9, 2012,
38. The report of Drug Controller General of India (DCGI), The Indian Express, 19.03.13
41. Ron Weinstein RFID: A Technical Overview and Its Application to the Enterprise
42. R. Jotcham, Understanding and Evaluating Security Technologies for
   Pharmaceuticals, in Combating Pharmaceutical Fraud and Counterfeiting, SMI
   2003.
44. "FDA 2006 Compliance Policy Guide for the Prescription Drug Marketing Act"
45. WHO, May 2012
46. The speech of President Pratibha Patil, inauguration, 71st World Congress of
   Pharmacy and Pharmaceutical Sciences, 4th September, Hyderabad.