INTERNATIONAL JOURNAL OF ADVANCE RESEARCH, IDEAS AND INNOVATIONS IN TECHNOLOGY

ISSN: 2454-132X
Impact factor: 4.295
(Volume3, Issue3)
Available online at www.ijariit.com

Current Trends in Regulatory Authority Actions against Misbranded and Adulterated Drugs

Doni Prakash Kumar
Pharmaceutics & Drug Regulatory Affairs
dprakashkumard@gmail.com

Umasankar .K
Pharmaceutics
umasankar73@gmail.com

Alagusundaram .M
Pharmaceutics
alagusundaram77@gmail.com

Jayachandra Reddy .P
Krishna Teja Pharmacy College,
Chadalawada Nagar, Tirupathi-517506, Andhra Pradesh
krishnateja.b.pharmacy@gmail.com

Abstract: Globally every country is the victim of misbranded or adulterated drugs, which result in life threatening issues, financial loss of consumer and manufacturer and loss in trust on health system. For minimizing adulterated and misbranding drugs or not of standard quality drugs, there is urgent requirement of more stringent regulation and legal action against the problem. The adulteration and substitution of crude drug is a burning problem. substitution is helpful in places where unavailability of particular crude drug and or unwanted adverse effects of desired crude drug are there and have a choice of other drug with similar pharmacological effect and less unwanted after effects. But in most cases, it is unacceptable because the conversion of authentic drug into substandard drug may cause variety of adverse effects from mild and moderate to severe life threatening reactions. So, understanding of all the ways of adulteration and substitution is necessary to rectify this illegal act and maximizing consumers' safety. However, India has taken some preventive steps in the country to fight against the poor quality of regulatory organization drugs for protecting and promoting the public health.

Key words: Adulteration, Misbranding drugs, Crude drug.

INTRODUCTION

The adulteration more precisely defined as crude drug appears, at first sight, to be genuine as its morphological similarity and sometimes chemically indistinguishable. It is the deliberate or accidental substitution of a crude drug partially or completely with other substances which are either free or inferior in therapeutic or chemical properties. Substitution of the herbs is the need of the hour when required medicinal plants becoming red listed. An essential criterion for substitution is the pharmacological activity rather than morphology or constituents. Substitution of herbs achieved many goals though basic was to provide the similar therapeutic effect as that of the original drug. It provided a greater scope for the physician to utilize herbs that are easily available, cost-effective and most appropriate for the clinical condition. The adverse reaction of the drug in which required drug have unwanted adverse.**[1]**

The unwanted aspect of substitution lies under substandard conditions. Which sometimes become life threatening. Adulteration caused a variety of adverse effects from mild (allergic reactions, fatigue, gastrointestinal upset, mood disturbances or muscle weakness, nausea, pain, and respiratory complaints) to moderate (confusion, convulsions, dermatitis, lethargy or seizures, leucopenia, sensory disturbances, vomiting) to severe (carcinomas, cerebral oedema, coma, intracerebral haemorrhage, poisoning, metabolic acidosis, multi-organ failure, nephrotoxicity, prenatal stroke, renal or liver failure or death) life threatening effects.**[2]**

HISTORY

In the early 21st century, cases of dangerous adulteration occurred in the People's Republic of China. In some African countries, it is not uncommon for thieves to break electric transformers to steal transformer oil, which is then sold to the operators of roadside food stalls to be used for deep. When used for frying, it is reported that transformer oil lasts much longer than regular cooking. The downside of this misuse of the transformer oil is the threat to the health of the consumers, due to the presence of PCBs.**[3]** Adulterant use was first investigated in 1820 by the German chemist Federick Accum, who identified many toxic metal colourings in food and drink. His work antagonized food suppliers, and he was ultimately discredited by a scandal over his alleged mutilation of books of the Royal Institution Library. The physician Arthur Hill Hassall conducted extensive studies in the early

1850s, which were published in The Lancet and led to the 1860 Food Adulteration Act and other legislation.**[4]** At the turn of the 20th century, industrialization in the United States led to a rise in adulteration which inspired some protest. Accounts of adulteration led the New York Evening Post to parody: Mary had a little lamb and when she saw it sicken, She shipped it off to Packing town, And now it's labeled chicken.**[5]**

DISCUSSION

Adulteration

Adulteration is the practice of substituting original crude drug partially or wholly with other similar-looking substances, but the later is either free from or inferior in chemical or therapeutic properties. Adulteration involves different conditions such as deterioration, admixture, sophistication, substitution, inferiority, and spoilage.

Deterioration is the impairment in the quality of a drug.
The admixture is the addition of one article to another due to ignorance or carelessness, or by accident.
Sophistication is the intentional or deliberate type of adulteration.
Substitution is the different substance is added in place of the original drug.
Inferiority refers to any sub-standard drug.
Spoilage: deterioration due to the attack of microorganisms.

Types of Adulterants

Generally, the drugs are adulterated by substitution with sub-standard commercial varieties, inferior drugs, or artificially manufactured commodities.

The following types of adulteration are common

1. **Substitution with Sub-Standard Commercial Varieties**
   The adulterants here may resemble the original crude drug in morphological, chemical, or therapeutic characters, but are sub-standard in nature and hence are cheaper in cost. This is a rather most common practice of adulteration e.g. Strychnous nux-blanda or S.potatorum in place of S.nux-vomica, Capsicum annuum in place of C.minimum, Indian senna is substituted with Arabian senna or dog senna, medicinal ginger is substituted with inferior varieties of African, Japanese, or Cochin ginger.
2. **Substitution with Superficially Similar Inferior Drugs**
   These inferior drugs used may or may not be having any chemical or therapeutic value as that of the original drug. Due to their morphological resemblance to the authentic drug, they are marketed as adulterants. Belladonna leaves are substituted with Ailanthus leaves, Saffron is admixed with dried flowers of carthamus tinctorious, and bees wax is substituted with Japan wax.
3. **Substitution with Artificially Manufactured Substances**
   It has been also observed that substances artificially prepared to resemble the original drug are used as substitutes. This practice is followed for much costlier drugs. Compressed Chicory in place of coffee, yellow coloured paraffin wax for bees wax properly cut and shaved basswood for nutmeg.
4. **Substitution With Exhausted Drug**
   The same drug is admixed but is devoid of any medicinally active constituents as they are already extracted out. This practice is more common in the case of volatile oil containing drugs like fennel, clove, coriander, caraway etc. Sometimes natural characters of exhausted drugs like colour, and taste are manipulated by adding other additives and then it is substituted, e.g. exhausted gentian made bitter with aloes, artificial colouring of exhausted saffron, etc.
5. Besides these common practices, sometimes other methods are also employed like the use of synthetic chemicals to enhance the natural character as in the case of addition of benzyl benzoate to balsam of peru, citral to citrus oils like oil of lemon and orange oil, etc.
6. **Presence of vegetative matter from the same plant**
   Sometimes, the other miniature plants growing along with medicinal plants are admixed with the authentic drug, due to their resembling colour, odour, and in some cases constituents. The lower plants like moss, liverworts, and epiphytes growing on bark portion are mixed with cascara or cinchona, the stem portions are mixed along with leaf drugs like stramonium, lobelia, and senna.
7. **Harmful Adulterants**
   Sometimes the waste from the market is collected and admixed with the authentic drug. This is particularly noticed for liquids or unorganized drugs. The examples like pieces of amber coloured glass in colophony, limestones in asafoetida, lead shot in opium, white oil in coconut oil, cocoa butter mixed with stearin or paraffin. The addition of rodent fecal matter to cardamom seed is a very harmful adulteration.
8. **Adulteration of Powders**
   Besides the entire drug, the powdered forms are frequently found to be adulterated. Examples: dextrin in ipecacuanha, powered liquorice or gentian admixed with powdered olive stones, exhausted ginger powder in powdered colocynth or ginger, red sanders wood in capsicum, etc.**[6]**

Criteria for desirable substitution

The drug should exhibit similar chemical constituents and therapeutic effects.

A. Substitution with totally different drug

- Clerodendron indicum and Solanum xanthocarpam (Yellow-berried Nightshade) have shown antihistaminic activity and employed in diseases related to respiratory system.

- The chemical constituents of Tribulus territories (Chota Gokhru) Family: Zygophyllaceae and Pedalium murex (Large Caltrops / Bara Gokhru) Family: Pedaliaceae are different. Tribulus terrestrial contains chlorogenin, diosgenin, rutin, rhamnose, and alkaloids. Whereas, Pedalium murex possesses ursolic acid, vanillin, flavonoids, and alkaloids. But both species are proved as a nephroprotective, diuretic and hepatoprotective effect.

B. Substitution of species belonging to the same family

The chemical constituents of Datura metal (black datura) and Datura stramonium (thorn apple) Family: Solanaceae are alkaloids as scopolamine, atropine, and hyoscyamin. These alkaloids are proved as bronchodilator and inhibitor of mucus membrane secretions in the respiratory tract. So, both species are beneficial in the disease of the respiratory tract.

C. Substitution of different parts of plant

The roots of Sida cordifolia considered as an official drug. The root contains sitoindoside and acyl steryl glycoside. The whole plant contains alkaloids, hydrocarbons, fatty acids, and ephedrine. Various plants extracts exhibit antibacterial, antioxidant, hypoglycemic, hepatoprotective and cardiotonic activities. Roots and aerial parts both are equally effective in above-mentioned conditions. **[7]**

Reasons of adulteration

A. Confusion in Vernacular names

Same vernacular name of different species and different vernacular names of same species creates confusion and invites adulteration. In Ayurveda, Parpatta refers to Fumaria parviflora. In Siddha, Parpadagam‟ refers to Mollugo pentaphylla. Owing to the similarity in the names in traditional systems of medicine, these two herbs are often interchanged or adulterated or substituted.

B. Lack of knowledge about authentic source

Nagakesar is one of the important drugs in Ayurveda. The authentic source is Mesua ferrea. However, market samples are adulterated with flowers of Chlorophyll uminophyllum because suppliers are unaware of it. Authentic flowers can be easily identified by the presence of two-celled ovary whereas in the case of spurious flowers they are single celled.

C. Similarity in morphology

Mucuna prurient adulterated with other similar Papilionaceae seeds having similarity in morphology. Mucuna utilise (sold as white variety) and Mucuna deeringiana (sold as bigger variety) are popular adulterants. Apart from this Mucuna Cochin chinensis, Canavalia virosa and Canavalia ensiformis are also sold in Indian markets. Authentic seeds are up to 1 cm in length with shining mosaic pattern of black and brown color on their surface. Mucuna deeringiana and Mucuna utilise are bigger (1.5-2 cm) in size. While Mucuna deeringiana is dull black and Mucuna utilise is white or buff colored.

D. Lack of authentic plant:

Hypericum perforatum is cultivated and sold in European markets. In India, availability of this species is very limited. However, the abundant Indo-Nepal species Hypericum patulum, sold in the name of Hypericum perforatum. The market sample is a whole plant with flowers and it is easy to identify them taxonomically. Anatomically, transverse section of Hypericum perforatum stem has compressed thin phloem, hollow pith, and absence of calcium oxalate crystals. Whereas Hypericum patulum as broader phloem, partially hollow pith and the presence of calcium oxalate crystals.

E. The similarity in Color:

It is well known that with the course of time, drug materials get changed to or substituted with other plant species. „Ratanjot‟ is a recent day example. In the past, roots of Ventilago madraspatana were collected from the Western Ghats, as the only source of „Ratanjot‟. However, that has not been practiced now. It is clearly known that Arnebia euchroma var. euchromais the present source. The similarity is in yielding a red dye, Arnebia euchroma substitutes Ventilago madraspatana. Recently Ventilago madraspatana is not found in the market. Whatever is available in the market, in the name of Ratanjot is originated from Arnebia euchroma.

F. Careless Collections

Some of the herbal adulterations are due to the carelessness of herbal collectors and suppliers.Parmelia perlata is used in Ayurveda, Unani, and Siddha. It is also used as grocery. Market samples showed it to be admixed with other species (Parmelia perforated and Parmelia cirrhata). Sometimes, Usnea sp. is also mixed with them. **[8]**

TYPES OF ADULTERATION

A. Substitution with inferior commercial verities

It is the use of morphologically resemble, different inferior commercial verities (may or may not have any chemical or therapeutic potential as that of original natural drug). Example are

- Arabian senna (Cassia angustifolia), dog senna (Cassia obovata) and ovaram senna

(Cassia auriculata) have been used to adulterate Senna (Cassia senna).

- Japanese ginger (Zingiber mioga) has been used to adulterate medicinal ginger (Zingiber officinale).
- Capsicum annum have been used to adulterate Capsicum minimum.
- Piper nigrum fruit is adulterated by Carica papaya seeds.

B. Substitution with artificially manufactured drug

Artificially manufactured substances use as a substitute of the original drug. Artificial sugar for honey, yellow colored paraffin wax for beeswax, compressed Chicory in place of coffee and properly cut and shaved basswood for nutmeg (Jaifal) are examples.

C. Substitution by exhausted drugs

Same plant material is mixed with a drug having no active medicinal components as they have already been extracted out. Examples

- Volatile oil containing drugs: Foeniculum vulgare (fruit / fennel) , Syzygium aromaticum (flowering buds / clove) , Coriandrum sativum (fruit / coriander) , Carum carvi (fruit / caraway / siahjeera) , Cascara sagrada(Sacred Bark / jamal gota) and Zingiber officinale (roots / ginger).
- Coloring matter containing drugs: In the case of loss of coloring material during exhaustion, the residue is recolored with artificial dye. Examples: Rosa macdub (Red rose petal) and Crocus sativus (stigma of flowers/saffron), Camellia sinensis (leaves/tea).

D. Substitution by superficially similar but cheaper natural substances

The adulterated product has no relation to genuine material, may or may not have any therapeutic or chemical component. As Ailanthus altissima (Ailanthus) are substituted for Atropa belladonna (Belladonna), Cassia acutifolia (senna) , Mentha longifolia (mint) etc.; Leaves of Phytolacca Americana (pokeweed) and Scopolia japonica, (Japanese belladonna) for Atropa belladonna (Belladonna); Leaves of Xanthium strumarium for stramonium and dandelion Anethum sowa (Indian dill) with Anethum graveolens (European dill) or Carum carvi (caraway).

E. Substitution by addition of worthless or heavy materials

Examples

- Large mass of stone mixed with Glycyrrhiza glabra (liquorice root).
- Pieces of limestone mixed with Ferula assafoetida (Asafoetida).
- Lead shot mixed with pieces of Papaver somniferum (opium).

F. Addition of synthetic principles

It is the use of synthetic chemicals to enhance the natural character. The addition of benzyl benzoate to Peru balsam, citral to citrus oils and lemon oil to orange oil are examples. Many herbal products contain undisclosed prescription or over-the-counter drugs and heavy metals. In 1998, the California Department of Health reported that 32 percent of Asian patent medicines sold in that state contained undeclared pharmaceuticals or heavy metals. The drugs most frequently found were ephedrine, chlorpheniramine, methyltestosterone, and phenacetin; 10 to 15 percent contained lead, mercury, or arsenic. The FDA and other investigators have also reported the presence of prescription drugs, including glyburide, sildenafil, colchicine, adrenal steroids, alprazolam, phenylbutazone, and fenfluramine, in products claiming to contain only natural ingredients. For example, PC-SPES is a patented herbal preparation marketed to "enhance prostate health," but commonly used to treat prostate cancer. Reports of its effectiveness have appeared in major medical journals. After a chemical analysis of PC-SPES revealed the presence of diethylstilbestrol, indomethacin, warfarin, or a combination of these drugs, the product was removed from the market. In 2002, the Japanese Ministry of Health, Labor and Welfare reported that the use of certain imported Chinese dietary supplements was associated with hepatic failure and hyperthyroidism. These products proved to be adulterated with N-nitroso-fenfluramine, fenfluramine, and thyroid extracts. As of September 2002, a total of 622 patients were known to have become ill, with 148 requiring hospitalization; 3 deaths have occurred. The offending products were recalled, and the ministry required manufacturers to perform chemical analyses on all imported dietary supplements.**[9]**

MISBRANDING

Section 502 of the Federal Food, Drug and Cosmetic Act (FFDCA) contains provisions on misbranding including some that relate to false or misleading labeling. A device's labeling misbrands the product if:

- Its labeling is false or misleading in any particular.
- It is in package form and its label fails to contain the name and place of business of the manufacturer, packer, or distributor and an accurate statement of the quantity of the contents in terms of weight, measure, or numerical count.
- Any required wording is not prominently displayed as compared with other wording on the device or is not clearly stated.
- Its label does not bear adequate directions for use including warnings against use in certain pathological conditions or by children where its use may be dangerous in health or against unsafe dosage, or methods, or duration of administration or application.
- It is dangerous to health when used in the dosage or manner or with the frequency or duration prescribed, recommended or suggested in the
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- labeling.
- It does not comply with the color additives provisions listed under Section 706 of the FFDCA.
- The device's established name (if it has one), its name in an official compendium, or any common or usual name is not prominently printed in type at least half as large as that used for any proprietary name.
- The establishment is not registered with FDA as required by Section 510 of the FFDCA and has not listed the device as required by Section 510(j) of the FFDCA or obtained applicable premarket notification clearance as required by Section 510(k) of the FFDCA.
- The device is subject to a performance standard and it does not bear the labeling prescribed in that standard.
- There is a failure or refusal to comply with any requirement related to Notification and other remedies prescribed under Section 518 of the FFDCA, if there is a failure to furnish any materials or information required by, or requested by the Secretary pursuant to, Section 519 of the FFDCA, or if there is a failure to furnish materials or information relating to reports and records required by Section 522 of the FFDCA.
- There is any representation that creates an impression of official approval because of the possession by the firm of an FDA registration number.

Note: Previously, it was a prohibited act to have the premarket approval application (PMA) number on the device labeling. The FDA Modernization Act of 1997 (FDAMA) repealed the restriction in Section 301(l) of the FFDCA, which prohibited reference to FDA approval in the labeling or advertising of medical devices that have an approved PMA or IDE.**[10]**

Spurious drugs

The Drug and Cosmetic Act 1940 and Rules 1945, a central legislation regulating the manufacture, sale, and quality of drugs and formulations in India provide a definition of 'Spurious Drug' under its section 17-B.

- If it is manufactured under a name which belongs to another drug; or
- 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 lacks of identity with such other drug; or
- 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
- It has been substituted wholly or in part by another drug or substance or
- If it purports to be the product of the manufacturer of whom it is not truly a product.

Counterfeit drugs

According to WHO estimates about 25% of the medicines consumed in developing countries are believed to be counterfeit. However, no systematical and scientifically study data is available on the extent of this menace. 'Counterfeit drug' is one which is deliberately and fraudulently mislabeled with respect to identity and/or source, as per WHO. Counterfeiting can apply to both branded and generic drug products and counterfeit medicines may include products with the correct therapeutically active ingredients but fake packaging; with the wrong ingredients; without active ingredients or with insufficient active ingredients. In developed countries, counterfeiters generally target newer, costly and top-selling drugs like hormones, steroids, antihistamines, psychiatric medicines and anticancer drugs. In developing countries, drugs used to treat life - threatening conditions such as malaria, tuberculosis and HIV / AIDS are generally counterfeited.**[11]**

SFFC drugs

In general poor quality drug are the spurious/falsely-labelled/falsified/counterfeit (SFFC) drugs that can cause treatment failure or even death Accordingly, International medical products anti counterfeiting Taskforce (IMPACT) of World Health Organization (WHO) defines SFFC medicines as “medicines which are deliberately and fraudulently mislabelled with respect to identity and/or source, and also which may include products with correct ingredients or with the wrong ingredients, without active ingredients, with insufficient or too much active ingredient, or with fake packaging”.**[12]** Poor quality drug or substandard product encounters a major stringent issue for the global health system and it cannot be ignored. In most streamlined regions of the globe like Japan, Canada, Australia, New Zealand, the United States of America and most of the European Union, hardly 1% of the market value products are counterfeit, developing countries like Africa, Latin America and many parts of Asia may markedly be the seller and producer of SFFC medicines.**[13]** Russia, China, India, Brazil, Mexico, Pakistan, Southeast Asian and Middle Eastern countries are considered as the chief operators in distribution and manufacturing of counterfeit drugs.**[14]** A decade ago, it was examined by WHO that 10% of the global medicines were counterfeit. However, contrary to its previous communicated data WHO-IMPACT pointed out that data was not much authentic.**[15]** It means no absolute extent is reported. Now, it is questionable that what are the causes and influences of this problem. In turn, one reason is poverty and other is ignorance and these could contribute to the demand for counterfeit and substandard drugs. Moreover, ignorance of poor quality, unregistered medicines, lenient penalties, inadequate enforcement of laws are some of the significant causes which provoke the situation.**[16]**

SFFC or NSQ drugs in India

India is the largest manufacturer of generic drugs and probably 12-25% of the medicines supplied globally are contaminated, substandard and counterfeit.**[17]** Being the world's largest manufacturers of active pharmaceutical ingredients and finished products, it is likely that India along with China could be the major contributors to spurious medications as per Patrick Lukulay, vice president of US Pharmacopoeial Convention's global health programs. In a report, it has been declared by the European Commission that 75% of the global cases of SFFC medicines originate from India.**[18]** Indian Government officials initiated an investigation to scrutinize the drug's product which is supplying by India to Nigeria when India was accused along with other 29 Asian countries as the main originator of counterfeit drugs.**[19]** On one side, India extensively interacts with the African countries in providing quality medicine at affordable prices, while on another side predictive blames were imposed on India and China for exporting the fake or substandard quality of antimalarial, antibiotics and contraceptives drug product to Uganda and Tanzania. In turn, India and China are denying for such blames. At present, Indian drug regulatory authority has taken various steps against the causes and they have put all their efforts to improve the drug regulation in the country.**[20]**

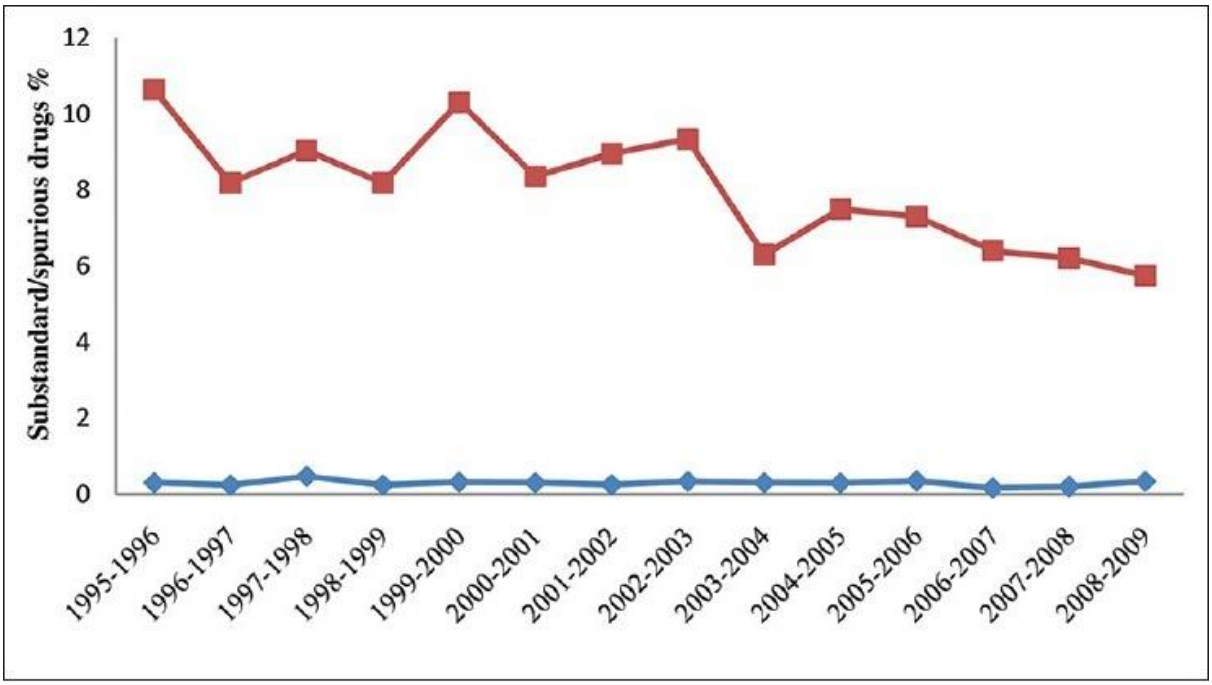

Fig. 1: Decline in substandard and spurious drugs cases from 1995 to 2009. Substandard drugs (−■−) and spurious drugs (−◆−).

Preventive measures for SFFC or NSQ drugs

To scrutinize the complications of the SFFC or NSQ drug in India, Government has acquired numerous steps which are,

1. Amendment of Drug and Cosmetic Act, 1940 in 2008 for making penal provisions and reset certain offenses as perceptible and non-bailable. When adulterated or spurious drug cause death then imprisonment imposed for not less than ten years or for a lifetime with a penalty of not less than one million Indian Rupees (INR) or three times the value of the drugs confiscated whichever is more; in order to make restraint for illegal practices.

2. Since 2008, on various levels, 216 additional posts generated to strengthen the regulatory mechanism. In 2008, there were 111 sanctioned posts and 64 officers in position while in 2012 there were 310 posts and 121 officers in position, which included 65 drug inspectors.

3. For the trial of offenses related to adulterated and spurious drugs product, Drug and Cosmetic (Amendment) Act, 2008 accredited establishment of specially designated courts, and nationally 14 states/Union territories already introduced such courts.

4. For effective regulatory surveillance throughout the country, Hyderabad and Ahmadabad have upgraded from subzone to full zone while Bangalore, Chandigarh, and Jammu have established as new subzones under the direction of CDSCO.

5. CDSCO publishes monthly a list of drugs, medical devices, and cosmetics that are evaluated and declared as not of standard quality/spurious/adulterated/misbranded.

6. Enhancement of Central Drug Laboratories with new sophisticated testing equipment set up and the creation of a new testing laboratory at Hyderabad.

7. To ensure proper traceability of those manufacturing units, which are situated abroad, from where drugs product are imported in India, a new scheme for regular overseas inspection has been introduced. For instance, two such inspections have formerly done in China.

8. To encourage attentive public participation in exploring the detection of the spurious drug product, a 'Whistle Blower' scheme is initiated. Under this scheme, if accurate information on the movement of spurious drugs product provided to the regulatory authorities, informers is suitably rewarded and 9. At the state level, Tamil Nadu and Kerala Government undertake drug quality evaluation services by Tamil Nadu Medical Service Corporation Limited and Kerala Medical Service Corporation Limited, respectively; and regularly report the NSQ products, which they fetched from government hospitals.

For minimizing SFFC or NSQ drugs at national or states level, still, there is an urgent requirement of more rigid and stringent regulations, policies and legal actions against the problem.

Guidelines for taking action on samples of drugs declared Spurious or not of standard quality in the light of enhanced Penalties under the drugs and cosmetics (amendment) act

The Drugs and Cosmetics (Amendment) Act, 2008 passed by the Parliament on 5th December 2008 provides deterrent penalties for offenses relating to manufacturing of spurious or adulterated drugs which have serious implications on public health. It will help regulatory authorities to handle anti-social elements involved in the manufacture of such drugs and playing with human safety. The penalty for manufacture of spurious or adulterated drugs has been enhanced to an imprisonment for a term which shall not be less than 10 years but which may extend to imprisonment for life and shall also be liable to fine which shall not be less than ten lakh rupees or three times value of the drug confiscated, whichever is more. In certain cases offenses have been made cognizable and non-bailable. It also provides a tool of compounding of offenses for dealing with certain minor offenses. Under the Drugs and

Cosmetics Act, 1940 control over manufacture and sale of drugs is exercised by the State Licensing Authorities. Licenses for drug manufacturing establishments and sale premises are granted by the said authorities. Inspections/raids are carried out by the Drug Inspectors appointed by the States to ensure compliance with the conditions of licenses. Samples are drawn by Drug Inspectors to check the quality of drugs marketed in the country. Legal/administrative actions as required under the said Act and Rules for the violation of the provisions of the Act are taken by the State Licensing Authorities. The actions are normally initiated on the basis of test reports of Government analysts declaring the drug samples as not of standard quality. The major categorization of not of standard quality reports could be as under:

Category A
(Spurious and Adulterated Drugs)

Spurious or imitation drug products are drug formulations manufactured concealing the true identity of the product and made to resemble another drug, especially some popular brand, to deceive the buyer and cash on the popularity of the original product. The product may or may not contain the active ingredients. Spurious drugs are usually manufactured by unlicensed anti-social elements but sometimes licensed manufacturers may also be involved. The adulterated drugs are those drugs which are found to contain an adulterant/substituted product or contaminated with filth rendering it injurious to health. Reports of availability of spurious drugs in the country shake the confidence of indigenous as well as foreign buyers. As the problem is an emotive issue also, it is required to be handled with a firm hand and in coordination with other agencies.

Category B
(Grossly sub-standard drugs)

Drugs manufactured by licensed manufacturers and reported to have defects of serious nature to affect the quality of the drug. Such defects may arise out of gross negligence or non-conformance to GMPs during manufacture. These defects may broadly be as under:

(i) Active ingredient contents below 70% for thermolabile products and below 5 % of the permitted limits for thermostable products.
(ii) Tablets/Capsules failing in disintegration tests wherever prescribed.
(iii) Tablets/Capsules failing in dissolution test and active contents found less than 70% for thermolabile products and below 5 % of the prescribed limits for thermostable products.
(iv) Liquid preparations showing the presence of the fungus.
(v) Parental preparations failing in sterility, pyrogen/endotoxin test or undue toxicity.
(vi) Vaccines failing in potency, sterility, toxicity or moisture content.
(vii) Presence of any adulterant which renders the product injurious to health.

Category C
(Minor defects)

Drugs manufactured by the licensed manufacturers found not of standard quality because of defects arising out of minor variations in quality. Such defects may arise because of inadequate pre-formulation development studies, lack of in-process controls exercised by the manufacturer or unsuitable conditions under which drugs are stored or transported. Examples of some such the defects are as under:

(i) Broken or chipped tablets.
(ii) Presence of spot/discolouration/uneven coating.
(iii) Cracking of emulsions.
(iv) Clear liquid preparations showing sedimentation.
(v) Change in colour of the formulation.
(vi) Slight variation in net content.
(vii) Formulations failing in weight variation.
(viii) Formulations failing to respond to the colour test.
(ix) Isolated cases of presences of foreign matter.
(x) Labeling error including nomenclature mistake, Rx, NRx, XRx, Red Line, Schedule H. Caution, Colour etc.

ACTION TO BE TAKEN ON CATEGORY A DEFECTS

1. To enquire into the matter immediately.
2. Issue instructions for immediate recall of batch from the market and to stop the further sale.
3. To ask for particulars of stock, distribution and production and test records.
4. Calling of explanation from the manufacturer by issuing a show-cause notice as to why license for the product/entire license should not be suspended/canceled.
5. After receipt of explanation and/or investigation report, the further appropriate action may be taken.

ACTION TO BE TAKEN ON CATEGORY B DEFECTS

1. Stoppage of further sale and recall of a batch of the drugs from the market.
2. Manufacturer to be asked to intimate stock and distribution details etc. of the particular batch.
3. Calling of explanation from the manufacturer.
4. After receipt of explanation or investigation report, if any carried out, the further appropriate action may be taken by issuing show cause notice etc. if so required.

GUIDELINES

The following guidelines should be adopted as model guidelines by the State Drug Control Organizations for uniform implementation of the provision of the Drugs and Cosmetics Act and rules made thereunder. While implementing the new provisions, the State Regulatory Authorities should ensure that the law is implemented in a comprehensive way. In order to effectively use the said instrument of law, it is necessary to have Standard Operative Procedures set in each State to examine and process various violations of the provision of the Act. The State Drug Control Organizations should have an internal mechanism of checks and balances to ensure that law-abiding manufacturers and sellers of drugs are not harassed or put in a disadvantageous position. Care should be taken that while violations with criminal intent or gross negligence leading to serious defects are dealt with heavy hand, the violations involving minor variations in quality by licensed manufacturers are resolved through administrative measures.

1. In the case of detection of manufacture and/or sale etc. of spurious or imitation drug products by the unlicensed manufacturers or sellers, the case shall be investigated on top priority and provisions of section 36 AC of the Act invoked under which these offenses are considered cognizable and non-bailable. Necessary help from the enforcement agencies like police etc. should also be obtained, wherever required, so that the brackets are busted and culprits booked in time for taking legal action. The investigations in such cases should be expedited and prosecutions launched at the earliest. The quick and timely investigations would have a deterrent effect on the unscrupulous persons involved in the nefarious trade of spurious drugs.
2. In the case of detection of a case of manufacture, and/or sale etc. of spurious drugs by a licensed manufacturer i.e. use of licensed premises for manufacture of spurious drugs and the criminal intent is apparent, the case is required to be pursued with equal vigour as in the case of the unlicensed manufacturer. The investigations should also include the other activities carried out by the manufacturer on the premises.
3. In the case of drugs manufactured by a licensed manufacturer under a valid manufacturing licence has been found grossly sub-standard, the matter may be investigated at the manufacturer's end, and where criminal intent or gross negligence has been established and if the merits of the case so demand, and where it is felt that administrative measures would not be sufficient to meet the ends of justice, the recourse to prosecution should be resorted to,
4. In the case of drugs manufactured by a licensed manufacturer under a valid manufacturing licence and found grossly sub-standard and where criminal intent or gross negligence is not established, weapon of prosecution should be used judiciously, where it is felt that administrative measures like suspension or cancellation of licenses or compounding of offences would not meet the ends of justice.
5. In the case of not of standard quality reports because of minor defects arising out of variations from the prescribed standards or contraventions of other provisions of chapter IV of the Act, administrative measures including suspension/cancellation or compounding of offenses may be resorted to. The prosecution may only be launched where it is justifiably felt that above measures would not meet the ends of justice.
6. Section 36 AC which makes certain offenses under the Act cognizable and non-bailable has been inserted to facilitate the arrest of anti-social elements involved in the manufacture of spurious or adulterated drugs. The section should, therefore, be invoked with utmost care and only in cases where it is justifiably felt that it is essential to book the culprits for proper investigations in the case
7. The State Drug Control Departments shall constitute screening committees comprising of at least three senior officers, not below the level of Assistant Drugs Controllers or equivalent to examine the investigation reports of the cases where prosecutions are proposed to be launched. The committee may submit written an opinion on the investigation reports regarding their feasibility of taking legal action. The criminal intent or gross negligence should be taken into consideration while recommending actions like prosecution etc. Care should be taken that charges framed are not based on inappropriate provisions which may be difficult to prove in the court of law in the absence of proper justification or evidence. Cases of failing in assay, brand name disputes and non-renewal of manufacturing license in time should be examined on their merits before recommending prosecution in such cases.
8. Prosecutions by the Inspectors shall be launched on the basis of written permissions of the controlling authority and this authority, in turn, shall consider the recommendations of the screening committee while taking a final decision in the matter.
9. The Patent and Proprietary formulations should be tested by the Govt. analysts as provided under rule 46 of the Drugs and Cosmetics Rules. In the case of non-Pharmacopeia or modified formulations, the samples may be tested as per procedure provided by the manufacturer, which has been duly approved by the licensing authority. In the case of non-receipt of such procedure on request, the sample may be tested as per the method of analysis available with the Government analyst.

PRINCIPLES FOR INSTITUTION OF PROSECUTION UNDER DRUGS&COSMETICS ACT

The weapon for prosecution should be used sparingly and judiciously but a due regard to merits of the case be given as a prudent measure. Prosecution should be launched where administrative measures have failed to have desired effects. However, while deciding to prosecute, due regard should be given to the nature of contraventions.

The persistent defaulter should be prosecuted but minor omissions may not form the basis of a prosecution. Administrative action should be initiated wherever possible to ensure preventive measures to safeguard public health. A broad classification of cases where prosecutions should be launched is given below:

1. Manufactured, sold or stocked or exhibited for sale or is distributed.
2. Cosmetic falling within the meaning of spurious cosmetics under Section 17(D) and misbranded under Section 17(C).
3. Where drugs/Cosmetics are manufactured without a license.
4. Where a parenteral preparation is reported by the Government Analyst to be non-sterile, pyrogenic or toxic and provided on the investigation is found to be substandard due to lack of adequate quality control and adherence to the provisions of GMP in the manufacturing processes.

5. Where a drug is found grossly sub-standard repeatedly where a spurious drug of drug falling within the meaning of adulterated/spurious/misbranded under Section 17(A), 17(B) and 17 of Drugs and Cosmetics Act is.

CONCLUSION

Adulterating and misbranding drugs are the severe effect on public health. Spurious or counterfeit drugs are involved in both generic and branded products of every category throughout the world, which is growing and expanding its roots and thus emerging as a menace. Responding to the spreading public health crisis of spurious or substandard drugs has led to the creation of transnational regulatory dimension. India is improving and achieving its mission in drug regulation process on account of decline in the number of SFFC or NSQ drugs cases and by taking several important initiatives and preventive steps in the country and stringent penalties as well to fight against the poor quality drugs for protecting and promoting the public health. It is now the time to explore this matter more vigorously in the times to come in order to safeguard the interests of the patient at large.

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