FEDERAL REPUBLIC OF NIGERIA

"COUNTERFEIT DRUGS AND PHARMACOVIGILANCE".

BY

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AT

THE 10TH PHARMACOVIGILANCE – THE STUDY OF ADVERSE DRUG REACTIONS TRAINING COURSE HELD AT UPPSALA MONITORING CENTRE, SWEDEN

ON

25th MAY 2005.

- **The National Agency for Food and Drug Administration and Control (NAFDAC), regulates and controls the manufacture, importation, exportation, distribution, advertisement, sale and use of**
- **Food**
- **Drugs**
- **Cosmetics**
- **Chemicals/detergents**
- **Medical devices**
- **All drinks including packaged and bottled water**

(All the above are referred to as regulated products). Worldwide, not just in Nigeria, all these regulated products are faked or counterfeited.

INTRODUCTION

- In pharmacovigilance (PV) it is often assumed that drug quality and efficacy are assured therefore safety monitoring does not take into consideration the quality of drugs being monitored.
- For many countries where counterfeit drugs have been reported, it is no longer safe to make this assumption while monitoring safety of medicines.
- Pharmacovigilance therefore must be on the alert for counterfeit medicines because with counterfeits, one may not be dealing with the medicine one presumes to be monitoring.
- There is fortunately a growing awareness that the scope of PV should be expanded beyond signal detection to other safety concerns.
- Counterfeit medicines constitute one of those yet to be integrated safety issues.

WHAT IS A COUNTERFEIT MEDICINE?

- **Despite the global nature of fake/counterfeit drugs, the International Community does not have a harmonized definition of fake/counterfeit drugs to reflect its global nature and capture its entire essence.**
- **There are different definitions by different countries according to their perception of the problem.**
- **However, the WHO defines a counterfeit medicine as“ one, which is deliberately and fraudulently mislabelled 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”.**

In Nigeria, the National Agency for Food and Drug Administration and Control (NAFDAC) has identified various forms of fake/counterfeit drugs, which include:

- **Drugs with no active ingredient(s)**
- **Drugs with insufficient active ingredients**
- **Drugs with active ingredient(s) different from what is stated on the packages**
- **Clones of fast moving drugs - these are drugs with the same quantity of active ingredients as the genuine original brand.**
- **Drugs without full name and address of the manufacturer.**
- **Herbal Preparations that are toxic, harmful, ineffective or mixed with orthodox medicine.**
- **Expired drugs or drugs without expiry date, or expired and re-labelled with the intention of extending their shelf-life.**
- **Drugs not certified and registered by NAFDAC**

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IMPLICATIONS OF COUNTERFEIT DRUGS

Counterfeiting of medicines is the greatest evil of our time and the highest weapon of terrorism against public health, as well as an act of economic sabotage. It is an ill wind that blows nobody good.

- **The evil of fake drugs is worse than the combined scourge of malaria, HIV/AIDS and armed robbery put together. This is because malaria can be prevented, HIV/AIDS can be avoided and armed robbery may kill a few at a time, but counterfeit/fake drugs kill en mass.**
- **The social problem posed by hard drugs, cocaine, heroine etc. cannot also be compared with the damage done by fake drugs, because illicit drugs are taken out of choice, and by those that can afford them, but fake drugs are taken by all and anybody can be a victim.**

- **Fake drugs have embarrassed our healthcare providers and eroded the confidence of the public on our healthcare delivery system. This development has led to treatment failures, organ dysfunction/damage, worsening of chronic disease conditions and the death of many Nigerians. The situation became so bad that even when patients were treated with genuine antibiotics, they no longer respond positively due to resistance induced by previous intake of fake/counterfeit antibiotics.**
- **Most of our local pharmaceutical industries that are producing genuine drugs, employing labour and boosting our economy, could not break even because of unfair competition with drug fakers, who are only paying for packaging and probably freighting without spending on active ingredients, which are the most expensive components of any drug.**

Difficult to export

SCOPE OF THE PROBLEM

- **Counterfeit pharmaceutical products were previously thought to be a substantial and increasing problem of low-income countries, most of the time dealing with weak administrative systems. Reports from different countries show that the problem is now widespread and increasing.**
- **The following review of some reports of counterfeit medicines from countries around the world will depict the global nature of drug counterfeiting.**

GLOBAL TRENDS IN DRUG COUNTERFEITING

ASIA

- Counterfeiting of drugs especially antimalarial drugs has been in existence in Asia since at least the 17th Century when cinchona bark, from which quinine is derived, was faked.
- A WHO report showed that in Vietnam, counterfeit drugs prevail nationwide, including the rural areas.
- Reports indicate that many of the masterminds of counterfeiting of medicines are based in Asia and are believed to be at the center of a complex global network that is manufacturing and distributing fake medicines all over the world. It is believed that in some extreme cases in countries within Asia, which have little regard for Patent Protection, companies may be producing legitimate goods at one end of the factory and counterfeits at the other.
- Another report from WHO has indicated that India is responsible for about 35% of the world fake drugs. The report noted that the illicit business is worth about two hundred million US dollars (US$200m) representing 20% of the World's total drugs market.

- **660kg of fake drugs, 1000kg of raw materials and boxes bearing the logo of another company were found in a counterfeiting factory in India (2001).**
- **The state Drug Administration of China seized counterfeit drugs valued at US$57 million. They also closed 1,300 illegal factories. (2002)**
- **The State Drug Administration of China in a nationwide survey of the quality of medicines, carried out in the last quarter of 1998, found that 13.1% of the 20 000 batches tested were either counterfeit or fell below minimal pharmaceutical standards.**
- **A five country survey of Southeast Asia, (Cambodia, Thailand, Myanmar, Vietnam, and Lao) in 2001 revealed that 38% of 104 samples of Artesunate on sale in pharmacies and shops were counterfeits**.

- **A total of 5,012,617 capsules of assorted counterfeit medicines including Amoxicillin, Ampicillin. Cloxacillin, Ampiclox and other products were seized in December 2003 in Myanmar. The seized counterfeits were smuggled in from India and China by unregistered and notorious counterfeiting companies.**
- **According to the WHO, counterfeit and substandard medicines that have failed quality testing circulating in some Asian countries are as follows: about 8.5% and 8% of medicines on the market in Thailand, and Vietnam respectively; 16% in Myanmar. Some of the highest drug failure rates of these tests included the tuberculosis drug Rifampicin, with 26 percent failure rate, and the antibiotic Cotrimoxazole, with a 24 percent failure rate (WHO release, Nov.11).**
- **Studies carried out on seven hundred samples in the Philippines, by the Pharmaceutical Security Institute showed that 7% of products marketed were definitely counterfeit.**

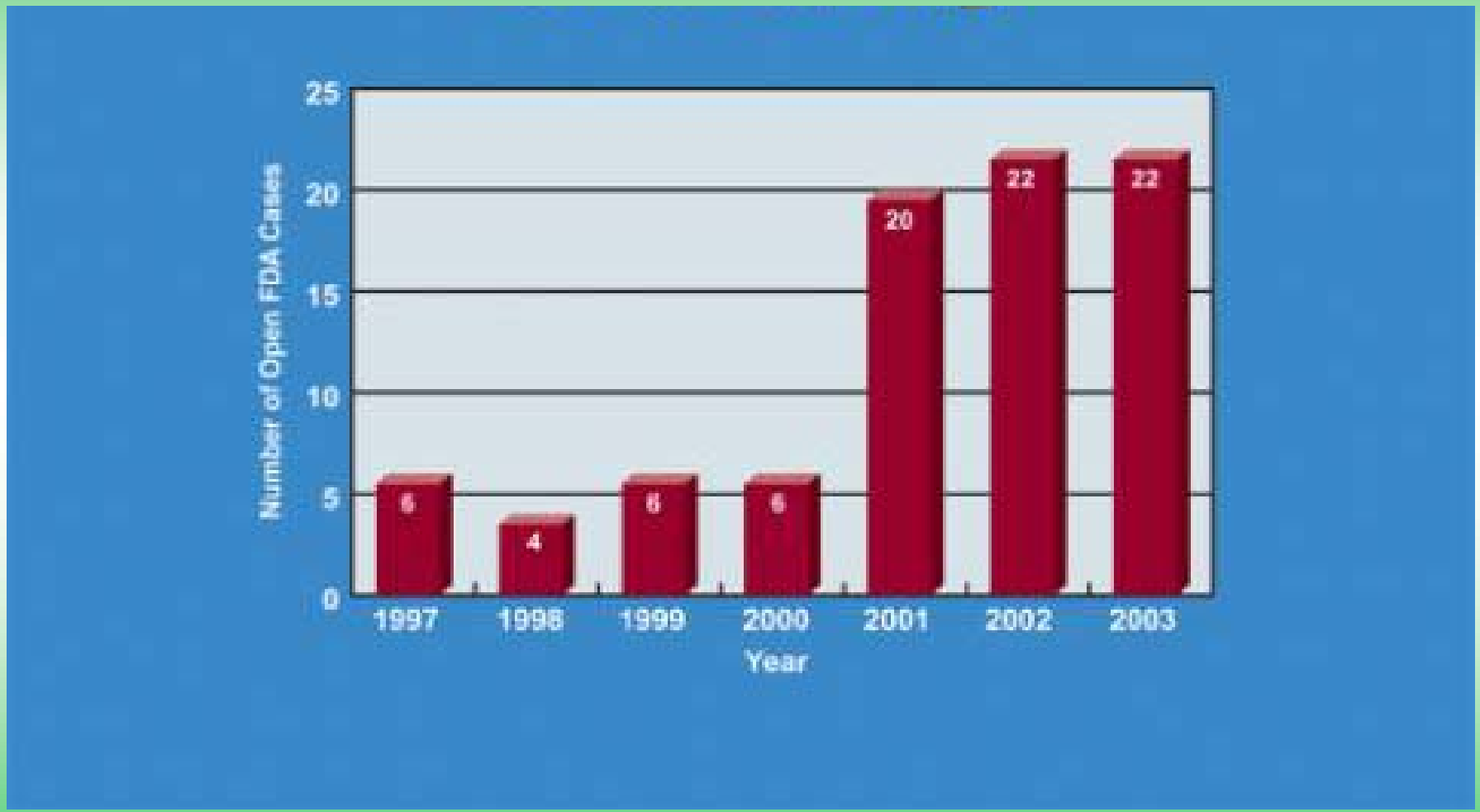
- **In Lebanon in 1982, due to the civil war and Israeli invasion, a lot of people needed drugs of which there was a dire shortage. Factories around Beirut were reported to be faking about 57 Western drugs. The Lebanese government despite being aware of this racket refused to do anything to stop these companies (criminals) or alert the public of the problem. These drugs were still killing people long after the guns had stopped.**
- **In countries such as Lebanon and Thailand, it appears that drug piracy was officially allowed to thrive, as governments in these countries refuse to go public with the knowledge of the counterfeiting problem.**
- **Even in Britain, with its wealth of copyright and drug laws, this silence prevailed**
- **The official reason for the silence is that patients run greater risks if the fear of fakes put them off taking the real product. However, a spokesman for the Association of the British Pharmaceutical Industry (ABPI) was reported to have stated the real reason for the silence as this; "it is difficult to declare a problem without damaging legitimate business" In other words, they believed there was more money to be made by keeping quiet.**

EUROPE

- **The Medical Control Agency (MCA) of the United Kingdom reported detection of many samples of counterfeit Viagra (Sildenafil Citrate), and other unapproved Sildenafil products (content vary between 40-100% of active ingredient).The government medicines safety agency seized £2.3 million worth of illegal and fake Viagra in 2003 and mounted numerous prosecutions.**
- **240,000 packs of counterfeit medicines and 2 tonnes of raw materials worth 1 million US$ seized in Italy (2000).**
- **A report from Russia showed that 12% of drugs in circulation are counterfeit**
- **In some countries of the former USSR, counterfeits account for up to 30% of drugs in circulation while in Ukraine this figure goes up to 40%, and in the case of certain pharmaceuticals it can be up to 80%.**

NORTH AMERICA

Increasing Trend of Counterfeit Drug Cases in USA



- **53 cases were detected in 2004**

In USA, with one of the most regulated and policed pharmaceutical markets, there had been reported cases of court actions resulting from patients treated with fake/counterfeit drugs. Two of the most outstanding reports of counterfeit drugs in the US are Lipitor and Serostim.

- **There are also increasing reports of counterfeit medicines in USA from 6 cases in 1997 to 22 in 2003, and 53 in 2004.**
- **There are reports by the US FDA of 3 lots of counterfeit Combivir and 3 lots of Lipitor preparations. About 200,000 bottles of Lipitor were recalled in 2003.**
- **Counterfeit alert from Solvay Pharmaceuticals, Inc. in response to the discovery of counterfeit ANADROL® Tablets. On analysis, the counterfeited Anadrol did not contain oxymethalone the active ingredient. Rather, it contained Androstenedione (December 2003).**
- **Counterfeit Serostim (Serono), Epogen, Gamimune(Bayer), Zyprexa (Eli Lily) reported in the USA in 2002.**
- **In USA (2002), Suspect bottles supposedly containing 60 tablets of Combivir (Lamivudine plus Zidovudine) which in reality contained Ziagen (Abacavir Sulfate).**

SOUTH AMERICA

- **In Argentina, counterfeit Voltaren, Tegretol, Hidergine and Reliveran (Novartis products) were detected in 1998. Novartis directed investigations which resulted in seizure of hundreds of USD worth of counterfeit and adulterated medicines, printing and packaging materials (both Novartis and other products).**
- **In 2000, 6 Million Ampoules of counterfeit Voltaren seized in Colombia.**

AFRICA

- In Africa, the level of incidence of fake/counterfeit drugs is difficult to estimate for many reasons, some of which include:
  - Poor communication within the continent.
  - Non-existence or ineffectiveness of drug regulatory authorities
  - Poor drug procurement practices.
  - Low literacy levels.
  - Low awareness of the existence of fake/counterfeit drugs.
  - Political instability.
  - High level of smuggling e.t.c.
- Perhaps, the Essential Drug Monitor (EDM) report on transforming drug supply in Dar es Salaam Tanzania, sums up the picture in most African countries as follows, “There was chronic shortage of drugs at health facilities, supplies were erratic, as was government funding, poor drug supply management and irrational use of drugs. Drug quality was questionable and pharmacy premises were often unsuitable, hot, humid and cluttered with piles of drugs, some of them expired. Pharmacists had low professional visibility.” This clearly mirrors the situation in many African countries with exception of a few such as South Africa, Ghana, Gambia, Egypt, e.t.c. with some level of systematic drug regulation, and drug distribution.

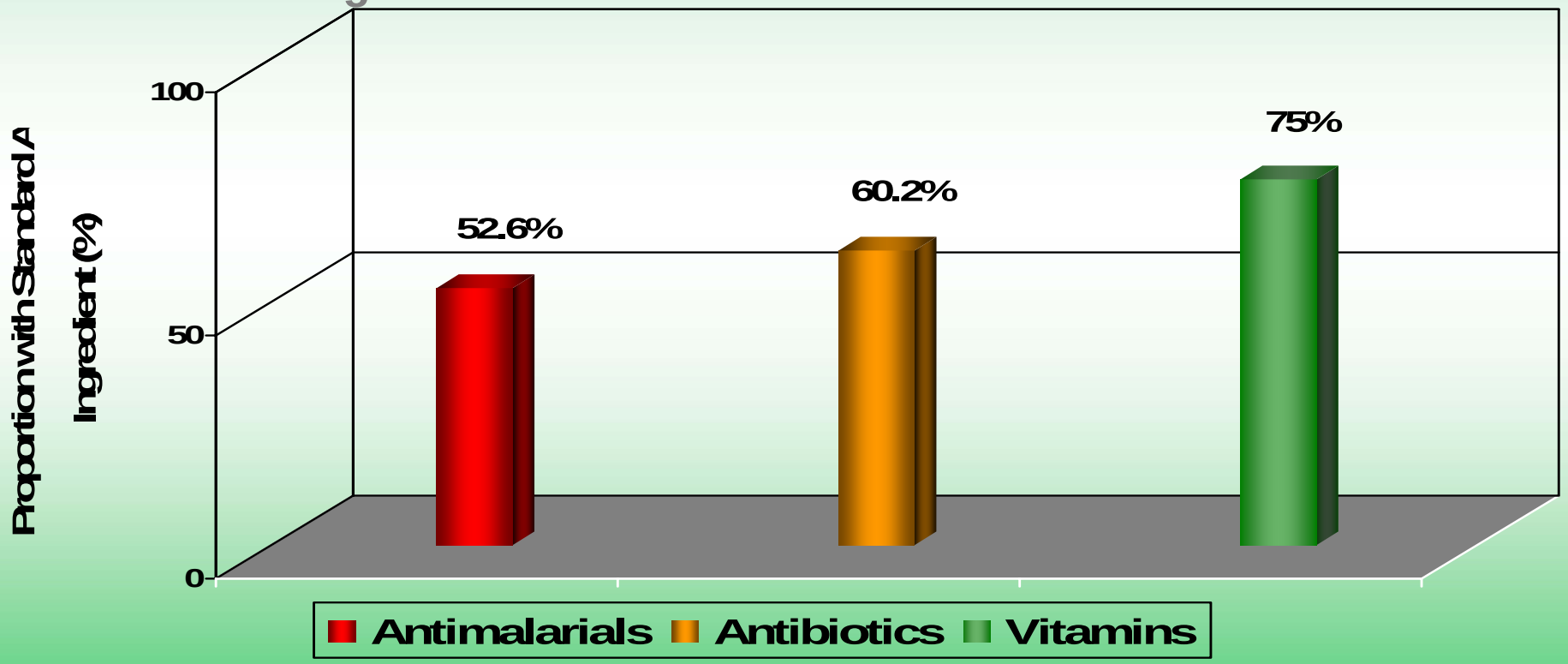
- **In a survey of 519 drugs in 3 African countries between 1991 and 1993, 77 drugs (18%) were found to be substandard. In Tanzania, counterfeit Ampicillin containing no active ingredient was found in 2000.**
- **In 2003, the Medicines Control Council (MCC) Of South Africa appealed to all members of the public, and health professionals not to sell or purchase counterfeits of the medicine Macrodantin 50mg (urinary tract antiseptic) on their market.**
- **In 2003, there were reports of counterfeit antiretroviral Ginovir 3D (Zidovudine 200mg, Lamivudine 150mg, Indinavir 40mg) capsules, in Cote d'Ivoire. On analysis, the capsules were found to contain, Zidovudine 201mg, Stavudine 40mg and some other unidentified substance.**
- **In the Republic of Benin, for instance, this inter-boundary trade is known as the "parallel market". An EDM report quotes the Benin's National office of Health Protection as estimating patronage of this parallel market to be around 85% of the population. These counterfeit and often under-strength drugs generally come from Gabon, Nigeria, and certain Asian, European and North American countries. This market is often controlled by travelling sales persons who have no training and lack all necessary skills to dispense drugs.**

- **Within the West African sub-region, there are very high activities in inter-boundary trade on pharmaceuticals. Most West African countries such as Togo, Benin, Chad, Niger and Cameroon buy their drugs from Nigeria, because Nigeria has the biggest drug markets in the Sub-region.**
- **In view of this flow of trade on pharmaceutical products between Nigeria and other neighbouring countries, the situation in Nigeria naturally reflects that of the West African sub region except for one or two countries.**
- **Even though faking/counterfeiting of pharmaceutical products is a global phenomenon, some countries are more affected, and to say that Nigeria is one of the most affected is not an exaggeration. Most West African countries are also badly affected, but the problem may not be highlighted in some of these countries, as they are in Nigeria, because of weak or non-existent drug regulatory authorities.**

- **Currently, there is no reliable statistics on the level of incidence of fake drugs in Nigeria.**
- **Estimates of the extent of counterfeit medicines in circulation in Nigeria ranged from 25% to 80% from various studies before 2001.**
- **A study by Poole in Nigeria in 1989 indicated that 25% of samples studied were fake, 25% genuine and 50% inconclusive.**
- **In 1990, Adeoye Lambo, a former WHO Deputy Director reported that 54% of drugs in every major pharmacy in Lagos were fake, and that the figure had risen to 80% in the subsequent year.**
- **Taylor et al reported that 48% of drugs tested were fake and substandard.**

- **Antimalarials, antibiotics, and vitamins are among the most used drugs in Nigeria. Out of the three, antimalarials as a group had the least proportion of products with standard active ingredients.**

Proportion of drugs with standard active ingredients.



Adapted from: Adenika FB. Pharmacy in Nigeria 1998

- **In 2001, NAFDAC carried a baseline study to ascertain the level of incidence of fake drugs in Nigeria. This study measured the level of compliance to drug registration, and we found that 67.95% of the drugs were unregistered and therefore unauthorised for use by NAFDAC.**

- **Repeats of this study revealed 67% and over 80% reduction in 2003 and 2004 respectively.**

- **The second phase of the study is being conducted in collaboration with WHO and DFID, and this involves laboratory testing.**

A few of the recorded cases are as follows:

- **In Niger Republic, the use of fake meningitis vaccine resulted in the death of about 2,500 persons.**
- **In 1989, poorly compounded Chloroquine syrup killed several children in U.N.T.H, Enugu in the early '80s of which there is no statistics, partly because many of the deaths were not even reported.**
- **In 1990, the "Paracetamol syrup disaster" occurred when 109 children died in Ibadan and Jos, after taking paracetamol syrup produced with the toxic ethylene glycol solvent instead of propylene glycol. This tragedy occurred more than fifty years after that of the U.S.A.**
- **In 2002, 3 patients reacted adversely to infusions manufactured by a Nigerian company. Some of the adverse reactions exhibited by the patients were severe rigor, vomiting, sweating, restlessness, seizure, impaired level of consciousness, etc. The reactions stopped immediately after the administration of the infusions were discontinued. Investigations by NAFDAC on the offensive infusions collected from the hospital revealed that three (3) batches were heavily contaminated.**

- **Fake Adrenaline reported to have contributed to the death of three children during open-heart surgery in Nigeria in 2003. Further investigations by NAFDAC revealed that the suxametonium used in the surgical procedure were also substandard.**
- **In 2004 three Nigerian hospitals reported cases of adverse reactions from the use of contaminated infusions produced by four Nigerian companies. Consequently we sampled infusions and water for injection from all over the country. Our results confirmed that some batches of infusions produced by the indicted companies were heavily contaminated with microorganisms. 147 of the 149 brands of water for injection screened were also not sterile.**
- **Counterfeit products, (drugs, food, cosmetics, medical devices, chemicals, and water including all drinks but mostly pharmaceuticals) valued at over N8.0b (US$60 million) were seized and destroyed in Nigeria by the National Agency for Food and Drug Administration and Control (NAFDAC) between April 2001 and December 2004.**

COUNTERFEITING-A REALITY!

CAUSES OF PHARMACEUTICAL COUNTERFEITING

Some of the following factors facilitate the existence of criminal networks that promote drug counterfeiting:

- **CORRUPTION AND CONFLICT OF INTERESTS.**

Chief among the factors that encourage drug faking worldwide is corruption and conflict of interests. Corruption is a driving force for poor regulation, which encourages drug faking/counterfeiting. "The efficiency of personnel is adversely affected by corruption and conflict of interests resulting in laws not being enforced and criminals not being arrested, prosecuted and convicted for crime".

Criminals in many parts of the world have discovered that the counterfeiting of medicines is financially lucrative and of relatively low risk. As a result, organized crime has shifted from the smuggling of narcotics and running of weapons to the counterfeiting of medicines.

At the inception of the present administration of NAFDAC, some NAFDAC Staff were not spared of this cankerworm called corruption that is endemic in our society. They indulged in over-sampling (collecting unreasonable large quantities of samples for analysis), willful delay in registration processes, etc.

Some local producers did not pay much attention to their Good Manufacturing Practice (GMP) and the quality of their products. This was partly as a result of inadequate supervision on the part of NAFDAC due to negative attitude to work and corruption.

On the part of the importers, dumping was business as usual as long as they could pay their way through the regulatory authorities.

Distributors were not spared of these corruptive practices because some of them were involved in re-labelling of drugs with the intention of extending their shelf lives.

We are happy that all these ugly practices have been drastically reduced to pave way for eradication of fake drugs, and creation of a strong regulatory environment.

➢ DISCRIMINATORY REGULATION BY EXPORTING COUNTRIES

Discriminatory regulation and control of drugs meant for export as against those for internal use in many countries have compromised the quality of drugs moving in international commerce. This practice has resulted in drugs labelled "for export only", not being subjected to the same strict regulation as those for internal use in the country of manufacture. There was a case of poorly packaged Paracetamol tablets in blisters labelled "Not for use in Southeast Asia", which is obviously fake. Poor regulation of exports from manufacturing countries exposes the countries with non-existent or weak regulation to dumping of fake drugs.

Presently, there are 86 pharmaceutical manufacturing companies, producing less than 30% of Nigeria's drug need while the rest are imported. It is noteworthy that most of the fake/counterfeit drugs in Nigeria are imported from Asia, particularly India and China. From 2001 till date, we blacklisted and banned thirty Indian and Chinese companies and one Pakistani company (confirmed to be fake drug producers) from exporting drugs into Nigeria. Discriminatory and poor regulation of exports by exporting countries informed the decision of the NAFDAC management to prohibit the importation into Nigeria of products marked "FOR EXPORT ONLY." Any product that cannot be used in the country of manufacture is officially unacceptable in Nigeria.

- **INSECURE AND UNFRIENDLY ENVIRONMENT**

  Insecure and unfriendly environment hamper the effort of regulatory authorities. I have experienced threats in the course of doing this job, for example;

- **In December 2003, an assassination attempt was made on my life. Gunmen fired at the vehicle I was travelling in, the back windscreen was shattered by bullets which pierced through my head scarf and burnt my scalp. During the shooting, a commercial bus was riddled with bullets and the driver died instantly.**

Car rear shattered wind shield. (26th Dec 2003)

Head Scarf showing bullet hole from attack of 26th Dec. 2003.

Front of car windscreen with bullet hole (26th Dec 2003)

- **In the past four years, drug counterfeiters also planned other attacks which by the grace of God did not succeed. In one of such instances, six (6) armed men invaded my residence in August 2001 but fortunately I was not available.**
- **There have been numerous other threats through mails, telephone calls, deposition of fetish objects in my office e.t.c. My family members and NAFDAC staff are also constantly under threat.**

- **The Agency's properties have not been spared either. On 29th August 2002, our laboratory in Oshodi was vandalized and most of our sensitive equipment were destroyed, while portable ones and samples for testing were carted away.**
- **On the 7th of March 2004, NAFDAC offices at the Federal Secretariat, Ikoyi, Lagos were set ablaze. The fire started at different floors simultaneously.**
- **Three days after, NAFDAC's Kaduna laboratory, which serves the Northern part of the country, was also set ablaze.**
- **In the same week these criminals broke into the premises of NAFDAC Maiduguri laboratory through a hole they bored on the fence but fortunately they were chased out by some alert security agents.**
- **In the same week, the building adjacent to our Benin office was burnt down as a mistaken identity.**
- **In July 2004, NAFDAC officers who confronted drug hawkers in Gombe state were severely beaten and their vehicle was destroyed.**

➢ CHAOTIC DRUG DISTRIBUTION SYSTEM

Drug distribution in Nigeria is very chaotic with drugs marketed like any other commodity of trade. Due to poor regulation over the years, drug markets evolved and got deeply established all over the country despite the illegality of such activities. Almost all drug manufacturers and importers supply to these drug markets. Drug sellers and even health professionals patronize the drug markets, which also service the hawkers that sell in streets and commercial buses.

Efforts made by NAFDAC to create an orderly Drug Distribution System so as to enable us phase out the existing disorganized Drug Markets, suffered a set back due to its unacceptability by some Pharmacists who are the major stakeholders in drug matters.

- **FALSE DECLARATION BY IMPORTERS**

This is a major constraint at the ports. Some drug importers, in order to evade inspection and detection, make false declarations about the nature/content of the products in their containers. They employ unimaginable concealment methods for their nefarious activities. In 2003, a large consignment of a controlled narcotic analgesic was concealed in T-shirts and imported from India via Lagos airport. Last year, 32 containers of various pharmaceuticals were imported and manifested as motor vehicle spare parts. They were moved to various locations within the ports to avoid detection, but were impounded by vigilant NAFDAC officials. NAFDAC inspectors have also found drugs concealed in the inner part of containers of textiles, candles, shoes, etc.

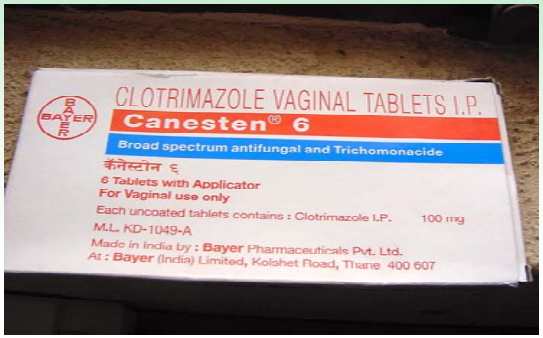
- **SOPHISTICATION IN CLANDESTINE DRUG MANUFACTURE.**

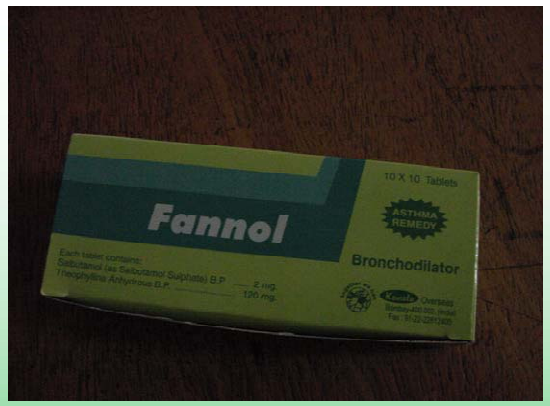
  Drug counterfeiting is made easier by increasing sophistication in technology of drug production. This is why cloning of fast moving drugs is so perfect that even the brand owners find it difficult to differentiate between fake and original.

Packs of counterfeit products detected by Pfizer[18]
(note wrongly spelt pfizer on left pack.)

18 Julian Mount Senior Director European Trade Group, Pfizer *"Supply Chain Integrity, Re-packaging and Counterfeits"* Paper presented at the 2nd Global forum on Pharmaceutical Anticounterfeiting, March 2005

Similar sounding names/look-alike counterfeits detected by NAFDAC.





- **LACK OF OR INADEQUATE LEGISLATION**

  Nigeria has a multiplicity of drug control laws that are unwieldy, overlapping and sometimes conflicting. Some of the laws were also old and needed to be amended or updated to meet the demands of present day realities for effective regulation.

  At the inception of the present administration of NAFDAC, we considered the review of the existing obsolete laws as an emergency, and within three months the draft was sent to the National Assembly for enactment.

- **INADEQUATE COOPERATION FROM GOVERNMENT AGENCIES**

  The absence of teamwork among the various sectors of government in Nigeria (NAFDAC, Customs, NDLEA, SON, NPA, Shipping Lines etc.) creates a fertile ground for counterfeiters to escape detection, arrest and sanctions. Some of the criminally minded importers take advantage of this lack of cooperation to propagate their illegal business.

COUNTERFEIT MEDICINES AND THEIR IMPLICATIONS ON PHARMACOVIGILANCE.

- With the increase in repored cases of counterfeit drugs globally, the effect of this phenomenon on pharmacovigilance becomes worrisome.
- It raises a pertinent question that must be answered for safety monitoring, especially in countries with high incidence of counterfeit medicines – is the drug being monitored what it purports to be, or should quality be first re-assured before safety can be monitored?

PRACTICAL CHALLENGES OF COUNTERFEIT DRUGS TO PHARMACOVIGILANCE.

1. Paracetamol/cough syrup formulated with toxic ethylene glycol solvent instead of propylene glycol present classical cases of uncertainty in safety monitoring. Such wrong use of excipeint occurs when counterfeiters mislabel one excipient for another to attract quick sales. In this case, pharmacovigilance activities will focus on the active ingredient (paracetamol) while in actual fact the cause of ADR is the wrong excipient (ethylene glycol). The implication of this is that time and resources which most developing countries can ill afford are wasted unless from the onset one is alert to the possibility of such counterfeits, and takes into consideration the quality and safety of both the actives And excipients
2. The case of counterfeit Ginovir 3D a triple antiretroviral combination product detected in Cote d'Ivoire in 2003 presents a serious challenge as indicated by the difference in content below.

Genuine Ginovir	Counterfeit Ginovir
Zidovudine 200mg(AZT)	Zidovudine (AZT) 201mg,
Lamivudine (3TC) 150mg	Stavudine (d4T) 40mg
Indinavir 40mg	unknown substance

Salient issues include:

1. **Possible lack of efficacy due to antagonistic effect.**
   - AZT and d4T are Nucleoside Reverse Transcriptase Inhibitor (NTRIs).
   - Both drugs, require the same cellular enzymes – thymidine kinase to become active and work against HIV, therefore they compete for the use of the enzyme. Consequently, neither of the two drugs is activated enough to fight HIV,
   - d4T antagonizes the effect of AZT (Merril et al 1996).
   - The counterfeit product may therefore be ineffective due to the antagonistic effect of AZT and d4T, patient on counterfeit Ginovir 3D may experience lack of efficacy

ii. **Increased risk of lactic acidosis**
    - **This is a side effect associated with the use of NRTIs due to their ability to damage or cause malfunctioning of the energy – producing part (mitochondria) of cells leading to build up of lactic acid in the blood.**
    - **Stavudine (d4T) (one of the components in the counterfeit Ginovir 3D) is more likely than other NRTIs to cause lactic acidosis.**
    - **"Results from at least one study suggest that people with HIV/AIDS who use d4T may be at increased risk for the development of lactic acidosis"**

iii. **Risk of peripheral neuropathy**
    - **A common side effect of d4T (contained in the counterfeit drug) is likely to be reported in a patient taking the counterfeit Ginovir 3D.**

iv. **Other unknown risks**
    - **The unidentified substance in the counterfeit may be toxic thereby presenting wrong signals in safety monitoring.**

These examples underscore the need for '*pharmaco-reassurance'* in pharmacovigilance. The question remains, 'are you sure that the medicine is really what it seems to be?'

EFFORTS BY NAFDAC TO COMBAT COUNTERFEITING OF MEDICINES IN NIGERIA

NAFDAC'S VISION, MISSION, GOAL AND STRATEGIES

The Management of NAFDAC has resolved that counterfeit medicines must be brought to the barest minimum in the shortest possible time. We have a clear vision, set goal and strategies.

Our VISION is to safeguard public health, while our MISSION is to safeguard public health by ensuring that only the right quality products are manufactured, imported, exported, advertised, distributed, sold and used in Nigeria.

Our current GOAL is to eradicate fake drugs and other substandard regulated products.

We have evolved some strategies to achieve our goal and create a strong regulatory environment some of which are:

- **Staff Re-Orientation and Motivation**
  - **At the inception of this administration, the inevitable need for staff re-orientation was glaring. We needed total change of mind-set and in fact, an organizational cultural revolution.**
  - **The following measures were undertaken to reposition staff for better effectiveness:**

    - Retrenchment of corrupt, redundant and incorrigible staff.

    - Staff training and re-training.

    - Effective delegation of duties and Staff empowerment.

    - To encourage staff, hard work, dedication and integrity are adequately compensated while any form of laxity or corruption is severely sanctioned. When hard work and integrity are not recognized and rewarded, corruption and ineptitude are promoted.

    - Leadership by example is highly emphasized.

- **Restructuring NAFDAC and Modernization of our Regulatory Processes**

NAFDAC was restructured into eight functional directorates as against the previous six. The two new directorates created, the Ports Inspection and Enforcement further positioned the agency to effectively tackle the problems emanating from inspection lapses and poor enforcement activities.

The other six Directorates are:-

1. **Laboratory Services**
2. **Narcotics and Controlled Substances**
3. **Establishment Inspection**
4. **Registration and Regulatory Affairs**
5. **Administration and Finance**
6. **Planning, Research and Statistics**

- **Ten new state offices were established and the existing twenty-seven were strengthened to cover the thirty-six states and Federal Capital Territory. Three special inspectorate offices were also established in the three towns with the biggest drug markets, Onitsha, Aba and Kano.**
- **NAFDAC has four laboratories, which are continuously upgraded, and two new ones are under construction.**
- **Constructed new warehouses and land border offices at some of our ports.**
- **New Standard Operating Procedures (SOPs) and guidelines were developed.**
- **Automation of all our regulatory processes.**

- **Public Enlightenment Campaign**

  Enlightenment campaign remains one of our most effective strategies in combating products' counterfeiting, and creating effective regulation.

  Our enlightenment programme involves dialogue, education and persuasion because this addresses the fundamental issue at stake, which is BEHAVIOURAL CHANGE. This has been sustained using print and electronic media such as jingles, alert notices, erection of billboards, publication of differences between identified fake and genuine products in the national dailies, etc. Workshops, seminars and meetings have been conducted for most stakeholders ranging from pharmacists, patent medicine dealers, traditional rulers, religious leaders, manufacturers, importers, transporters and even consumers. Grassroots mobilization campaign for the villages was launched in Kano in February 2005.

  We have produced many publications, fliers, leaflets, posters (both in English and vernacular languages).

The campaign has also been extended to Nigerian High schools in order to catch them young, by organizing annual competitions and prize giving ceremonies on their understanding of the ill effects of fake drugs on the society. We have also established NAFDAC Consumer Safety Clubs in most these schools. These activities are geared towards educating the young ones on the dangers of fake drugs, inculcating in them the value of quality and encouraging them to join NAFDAC in the fight against counterfeit medicines.

Enlightenment and the resultant voluntary change of heart are result-oriented and complimentary to confrontation and prosecution, which the Agency had used over the years with little or no success.

Our enlightenment campaigns have greatly empowered the public to recognize and reject expired, fake/substandard drugs and unwholesome food.

In any country we visit, we hold meetings with exporters of drugs, food, cosmetics and other NAFDAC regulated products. Through this, we have been able to convince many of them to set up drug industries in Nigeria.

- **Stopping the Importation of Counterfeit Medicines to Nigeria at Source**

  In a bid to stop the importation of fake drugs from the countries of production to Nigeria, NAFDAC has put in place some administrative guidelines which include the following:

  a) **A factory must be GMP certified before it can export drugs to Nigeria.**
  b) **NAFDAC officials must inspect factories anywhere in the world before we register or renew registration for their drugs, foods and other regulated products.**
  c) **NAFDAC has appointed analysts in India and China who re-certify any drug from the two countries before importation into Nigeria.**
  d) **For drugs imported from any country, NAFDAC requires mandatory pre-shipment information to be provided by all importers before the arrival of the drugs.**
  e) **Through advocacy and collaboration, we were able to convince Nigerian banks to assist us in the war against fake drugs. Since February 2003, the banks insist on NAFDAC clearance before processing financial documents for drug importers. This agreement is now a government policy because of its adoption by Central Bank of Nigeria. It is highly recommended that banks around the world should adopt this measure as it will go a long way to deter the activities of counterfeiters globally.**
  f) **Importation of drugs through land borders is banned, and there are only two designated airports and two seaports for drug importation into Nigeria.**

- **Beefing Up Of Surveillance At All Ports Of Entry**

  NAFDAC has re-enforced the two new directorates of Ports Inspection and Enforcement for more effective surveillance at all ports of entry, and better enforcement activities respectively. This has resulted in increased seizures of fake/counterfeit drugs and other substandard regulated products at the ports.

  Hitherto, land and sea borders were major routes of importation. The Agency, having considerably intensified surveillance at these borders, and the merchants of fake drugs resorted to the use of airlines. Consequently, NAFDAC issued a new guideline that any aircraft that lifts drugs to Nigeria without obtaining the Agency's authorization from their clients will be grounded.

  to NAFDAC's strong surveillance at the borders, and government's ban on importation of drugs and other regulated products through land borders, these criminals have resorted to the use of speedboats and other water transports.

- **Mopping Up Fake Drugs Already In Circulation**

  Cognizance of our many porous borders, NAFDAC embarks on planned, systematic, continuous and sustained surveillance at all markets and retail outlets for drugs in Nigeria. This has given rise to sealing of pharmacy retail outlets involved in selling counterfeit, unregistered or expired drugs, and also drug manufacturing factories, whose GMP status were found to be unsatisfactory. Another major drug market in Kano, Nigeria was closed for three months in 2004, besides the six months closure of Aba market in 2002.

  In order to achieve high level of success with our mopping up exercise, NAFDAC has put in place the following administrative guidelines:

  - **Confiscation and subsequent destruction of drugs of sellers who fail to provide a proper invoice of purchase with full name and address. This is to enable us trace the big time importers and distributors of fake drugs.**
  - **Faced with the frustrations of evacuating many lorry loads of fake drugs from warehouses on tip off without anybody accepting ownership, NAFDAC has notified the public that whenever the importer cannot be traced, the landlord of the premises used for the storage of fake drugs will be arrested, with a view to tracing the fake drug importer for necessary sanctions. In one occasion in Lagos, it was only after the landlord of the warehouse was arrested that the owner of the fake drugs gave himself up.**
  - **Raids are regularly carried out on drug hawkers, and their drugs are confiscated and destroyed.**
  - **Reported fake drugs manufacturing outfits are raided and dismantled.**

COUNTERFEITING-A REALITY!

- **Monitoring GMP of Local Manufacturers**

  NAFDAC monitors local manufacturers of drugs routinely. Compliance directives are issued and enforced to the letter when lapses are observed. Prosecution is carried out as a last resort when necessary.

- **Streamlining and Strict Enforcement of Registration Guidelines**

  NAFDAC has strengthened its registration processes with some administrative guidelines to ensure a strong and effective regulation, which is the most sustainable solution to dumping of fake products. These guidelines include:

  - **Renewal of registration of any drug every five years. Registration is automatically cancelled three months after expiration, if renewal is not commenced.**
  - **NAFDAC insists on fixing of NAFDAC registration number on the label of all regulated products to enable the public identify products certified by the Agency.**

  Also approved, is a policy that after the five years life of any drug registration, renewal of such registration is done to last for another five years giving a total of ten years. After ten years of importation of any drug that is not classified as an orphan drug, NAFDAC does not allow a second renewal. Consequently, drugs can be imported for only ten years, after which the importer must start producing locally.

OTHER MEASURES:

- **INTERNATIONAL:**
  - **We have established cooperation with food and drug regulators of almost all continents. We constantly dialogue with other West African countries' Food and Drug Regulatory Authorities with a view to sharing strategies and carrying them along, so that the counterfeiters will not find a safe haven any where in the sub region as we chase them out of Nigeria.**
  - **In 2002 in Hong Kong, NAFDAC originated the campaign for the setting up of an international convention on counterfeiting of pharmaceuticals just as we have for narcotics and psychotrophic substances. We have continued to aggressively pursue this campaign in all international meetings and it is catching on.**
- **DRUGS SAFETY MONITORING.**
  - **NAFDAC has established the National Pharmacovigilance Centre and was admitted as the 74th member of National Centres, participating in the WHO Drug Safety Monitoring Programme.**
- **ACCESS TO ETHICAL DRUGS STRICTLY ON PRESCRIPTION.**

  It has always been the practice in Nigeria for prescription drugs to be purchased without prescription and this fuels irrational drug use which sustains counterfeiting. NAFDAC will start enforcing that ethical products will be obtained strictly on prescription by July this year. We are currently holding meetings with all relevant stakeholders for smooth implementation.

- **REVIEW OF LAWS/RECONSTITUTION OF THE LEGAL UNIT**

Since 1902, the Nigerian government has enacted many laws and promulgated many decrees to ensure effective regulation and control of drugs, foods and other regulated products. These laws unfortunately are weak and non-deterrent, and some are unimplementable, but NAFDAC still derives its authority from them. The weaknesses in the laws are not as bad as the lack of will to enforce them.

The outdated laws were reviewed and have since been sent to the National Assembly in November 2001. Since then we have reviewed twice and again sent to the National Assembly.

In the interim we have strengthened our regulatory processes by putting in place some administrative guidelines within the law.

SOME OF THE ACHIEVEMENTS AND GAINS RECORDED SO FAR

i. Immense public awareness created by NAFDAC on its regulatory activities, especially on fake/counterfeit drugs resulted in the participation of the regulated industries, consumers and other stakeholders in the promotion of food and drug regulation in Nigeria. These achievements among many others have awakened the international consciousness that Nigeria is no longer a dumping ground for fake drugs.

ii. The level of incidence of fake drugs has been reduced by over 80% from what it was in 2001.

iii. The production capacities of our local pharmaceutical industries have increased tremendously according to reports by individual manufacturers and the Pharmaceutical Manufacturers Group of the Manufacturers Association of Nigeria (PMG-MAN).

iv. NAFDAC activities have reinforced the confidence of investors in the pharmaceutical industry, as evidenced in the continuous upward movement in the share prices of the pharmaceutical companies quoted in the Nigerian stock exchange.

v. The Agency's reforms have led to renewed confidence and increased patronage of drugs produced in Nigeria by other West African countries. This has resulted in the lifting of ban on made in Nigeria drugs by some West African countries.

vi. Many Multinational Drug Companies are coming back to Nigeria due to improved regulatory environment.

vii. Sixteen new drug manufacturing outfits were established in the last three years.

viii. There are cheering reports of declining number of kidney failure patients and death rates in our hospitals. We are working in concert with all Government hospitals in Nigeria, by compiling the number of renal failure patients and deaths on monthly basis in order to establish a trend.

ix. From April 2001 to December 2004; the Agency has carried out ninety destruction exercises of counterfeit and substandard products valued at over N8 billion (about US$60 million).

Over 1100 containers of regulated products were placed on 'Hold' at the Port Harcourt and Lagos ports, and most of the owners have absconded. From 2002 to July 2004 a total of 780 raids were carried out on distribution outlets of fake drugs.

x. Presently, we have secured 31 convictions in respect of counterfeit drugs related cases. Over forty cases against violators are still pending in various courts. Due to increased efficiency and transparency of NAFDAC staff, sanctions on erring manufacturers have increased. 2,226 sanctions were issued in 2002; 3,178 in 2003; and 3,460 in 2004.

CONCLUSION

- **Counterfeiting of pharmaceuticals is beginning to get the attention it deserves. This is evidenced by the number of anti-counterfeiting meetings organized by various interest groups around the world. It is further evidenced by the fact of my being here to speak on counterfeit medicines and how they affect pharmacovigilance.**
- **There is ample evidence to show that safety monitoring will need to pay more than passing attention to the threat counterfeits pose to safety monitoring.**
- **Perhaps we may be tempted to think that only developing countries that are experiencing counterfeit drugs on a large scale need to worry about it, but with the rapid globalization of the counterfeit problem, it will not be long before the problem spreads and worsens in developed countries.**
- **Persons, organizations and countries involved in pharmacovigilance will have to wake up to the maxim that "a stitch in time saves nine". Now is the time to combine *pharmaco-reassurance with pharmacovigilance* .**
- **Always ensure that the medicine is really what the label claims. Pharmaco-reassurance, i.e, ensuring that quality of medicine is assured is therefore imperative in pharmacovigilance because of the extra dimension from counterfeiting.**

Thank you for listening.

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