THALASSAEMIA INTERNATIONAL FEDERATION

In official relations with the World Health Organization

HEADQUARTERS:

PO Box 28807, 2083 Nicosia, 31 Ifigenias, 2007 Nicosia, Cyprus
Tel: +357 22 319129 Fax: +357 22 314552 Email: thalassaemia@cytanet.com.cy
Website: www.thalassaemia.org.cy

Position paper 5.3 **PP10/2012**

March 2012

Counterfeit Medicines & Patients' Safety
A global threat

The Thalassaemia International Federation (TIF) has focused attention for some time now and continues to do so, on the need for more strengthened and coordinated actions towards ensuring patients' safety by protecting them against what WHO[1] refers to as counterfeit/substandard/spurious/falsely labelled/falsified medicinal products *.

Introduction

A plethora of factors are known today to impact the safety of patients and a major one is related to the use of counterfeit medicines. It is useful for the objective of this position paper to start by making patients more aware and familiar with some relevant terminology such as: (i) branded, innovative, reference, new medicinal drugs, (ii) generic or copy drugs and (iii) bio-similar or biological drugs*.

Group (i) refers to those new drugs that have undergone extensive research, clinical trials in humans (in three or more phases) and have received authorisation or permission for being marketed, i.e. for being used by health professionals and patients. This is achieved after a long, cumbersome and extremely costly series of stringent procedures, set by official national and/or regional regulatory bodies such as FDA and EMA, in order to ensure that these medicinal products are safe and effective for the particular disease or group of diseases that were originally assigned to treat or diagnose.

On the other hand, a generic[2, 3, 4] or copy drug is a medicine similar to the 'reference' one, containing the same quantity of active**[5] substances and used at the same dose as that of the 'reference'. It is thus equally safe and effective. It has the same strength, it is taken in the same ways and works in the same way in the body as the 'reference' drug.

However, the name, appearance (colour or shape or flavour) and packaging differ and may also contain different inactive***[5]ingredients, which will be described both on the label and in the package leaflet of the generic medicine. In order though for generic or copy drugs to be safe and effective, they also need to receive marketing authorisation from an official regulatory body but the difference from the reference medicines is that, for the authorisation of a generic drug, clinical trials and studies essential in the case of the reference medicines, do not have to be duplicated. That is why generic drugs are cheaper than the innovative or reference drugs where considerable investments are made for their production.

**drug, medicinal product, medicines, pharmaceuticals*

*** Active Substance is any substance or mixture of substances intended to be used in the manufacture of a medicinal product and that, when used in its production, becomes an active*

ingredient of that product intended to exert a pharmacological, immunological or metabolic action with a view to restoring, correcting or modifying physiological functions or to make a medical diagnosis

****Excipient/Inactive substance is any constituent of a medical product other than the active substance and the packaging material*

That is also the reason why innovative medicines benefit from a period of data or patent's protection, allowing them to pay off the large costs of investment involved in the production of the new drug.

That is also why only after the expiry of this period (15-20 years), companies can apply for a marketing authorisation for a generic medicine.

Bio-similar or biological[6,7] medicines are a separate important and relatively new category and are defined as those medicines whose active substance is made by, or derived from, living organisms using biotechnology. Insulin, for example, can be produced by a bacterium or yeast (which is a living organism) which has been given the gene enabling it to produce insulin. As in the case of all medicines, innovative, generic or copy, European and international guidelines and regulations should be adhered to for the manufacture and distribution of bio-similar drugs used. Bio-similar, as well as generic medicines, provide today a major opportunity to help governments control the cost and availability of biopharmaceutical medicines, contributing thus to the sustainability of health care systems, particularly in the EU[7.]

Regulating medicines – An essential chain of procedures to ensure quality, safety and effectiveness of medicinal drugs for human use

Regulation has its roots in the industrialisation and modernisation of Western Europe and North America during the 19th and 20th centuries. US in 1906 passed the first Federation Food and Drugs act regulating interstate transportation of food and drugs[8.] In Europe, the British Medical Association began to express concerns over the safety of medicines during the 1980 and legislation followed through the Therapeutic Substances Act of 1925.

However, rigid systems of drug product authorisation were undertaken by authorities in Europe, USA and Japan, under the shadow of host national drug tragedies between 1930s and 1960s. In the US, mistakes in the formulation of a children's syrup that led to several deaths, prompted the necessity of setting up of a drug regulatory and safety system under the Food and Drug Administration (FDA)[9] while the thalidomide tragedies in Europe during the 1960s, prompted a similar reaction from European regulators. Since the 1960s and 1970s, there have been substantial increases in the number of regulations and rules guiding national drug authorisation processes. And due to the globalisation of the pharmaceutical market and the international interest in upholding the highest standards, there has been a push since the 1980s by governments and regulators from across the world, to engage international bodies such as the WHO and the pharmaceutical and medical industries to strengthen and harmonise drug regulations. Indeed, the contribution of the WHO has been pivotal in this work and a real effort in this direction has started from very early years. The launching in 1989 of the International Conference of Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) as an initiative of WHO, was a landmark in this field. In this conference, the EC, the European Federation of Pharmaceutical Industries and Associations, Ministries of Health, Ministries of Labour and Welfare, Japan Pharmaceutical Manufacturers Association,

FDA and the pharmaceutical Research and Manufacturers of America joined hands, while the European Free Trade Association and Health Canada participated as observers.

Since the 1990s, the ICH gave priority to harmonizing the regulating requirements to create global leading standards for the regulation and authorisation of drugs.

The International Medical Products Anti-Counterfeit Task Force (IMPACT) was another major contribution of WHO towards protecting patients' health. The development of principles and elements for national legislations against counterfeit medical products by IMPACT, endorsed in 2007 by the IMPACT General Meeting, where EU participated, was a real milestone in the development of regulations and measures against counterfeiting at the national, regional and international level.

In addition to ICH and WHO initiatives (see APPENDIX I), several important regional efforts took place including:

- The Collaborating Agreement of Drug Regulatory Authorities in EU Associated countries (CADREAC)

- The Association of SE Asian Nations (AESEAN) and Mercosur (the Southern Common Market)

More specifically in Europe, a Directive existed since 2001 (2001/83/EC), laying down the rules for, inter alia, manufacturing, importing and placing in the market and the wholesale distribution of medicinal products for human use in the EU, as well as rules relating to active substances.

Furthermore, other Directives and Regulations as well as their amended versions, strengthened the regulations for production and authorisation of medicinal products as well as the procedures ensuring their safety including

1. Directive 2010/84/EC amending Directive 2001/83/EC as regards Pharmacovigilance
2. Regulation (EU) No 1235/2010 amending Regulation No 726/2004 as regards pharmacovigilance of medicinal products for human use, laying down community procedures for the authorisation and supervision of medicinal products for human & veterinary use and establishing European Medicines Agency, and Regulation No 1394/2007 on advanced therapy medicinal products, and
3. Directive 2011/62/EU amending Directive 2001/83/EC relating to medical products for human use, as regards the prevention of the entry of falsified medical products into the legal supply chain – applicable as a new legal framework on Jan 2013. To this end, these new measures include:
    a. Amendments of guidelines of Good Manufacturing Practices (GMP) and Good Distribution Practices (GDP)
    b. An obligatory authenticity feature on the outer packaging of the medicines: this feature will be decided at a later stage
    c. A common, EU wide log to identify legal outline pharmacies, making it easier to distinguish between legal and illegal on line pharmacies throughout EU
    d. Tougher rules on the controls and inspections of procedures of active pharmaceutical ingredients and
    e. Strengthened record keeping requirements for wholesale distribution.

Good Manufacturing and Distribution practices should be ensured in the course of the whole process and in particular with regard to the manufacturing of active and inactive substances regardless of whether these are manufactured in EU or are imported from elsewhere. It should be ensured that legislative provisions are applicable to the manufacturing of particularly active substances in third countries as well as frequent inspections of facilities and sites of production.

For generic medicines, it is equally important for Health authorities and regulatory bodies to conduct stringent assessments when receiving applications for generic or copy drugs to determine their safety and effectiveness and the legislation of Europe, FDA but also other intentional standards, define clearly the procedures that must be carried out in the case of generic or copy drugs including:

1. Pharmaceutical equivalence[14]: Therapeutic equivalence requires that a copy product should show pharmaceutical equivalence, including the same active ingredient, dosage form, route of administration and strength or concentration, same conditions of use, and must meet compendia or other standards for purity, quality and identify as the innovator's reference drug.

2. Bioequivalence: To ensure clinical safety and efficacy, a copy drug must demonstrate bioequivalence to the reference drug. To do so, a copy manufacturer must conduct a bioequivalence study, a comparative pharmacodynamic study or a comparative clinical trial, and available when administered at the same dose under similar conditions.

   For solid oral forms, the sponsor of the copy drug is required to provide in vivo pharmacokinetic data to demonstrate bioequivalence to the innovator product. A two-treatment crossover study is required utilising the rate (Cmax) and extend (AUC) of drug absorption to measure parameters for both the copy and the innovator product. Products are considered bioequivalent if these properties fall within the range of 80-125% of the values of the innovator drug product

3. Product quality[15]: To ensure product quality, copy drug manufacturers must show evidence that they are using identical active ingredient with reliable, validated and reproducible processes to manufacture the drug substance and drug product. Analytical testing to compare the proposed product form to the innovator reference is necessary to guarantee that the active ingredients are indeed identical.

   It is important to note that the quality of the finished drug product can be significantly affected by the manufacturing process, including the choice of inactive, or otherwise referred to as Excipients, and materials used in chemical synthesis. Specifically, drug product purity may be compromised, resulting in an impurity profile which can lead to undesirable effects. These factors are covered under the new harmonised standards for GMP and have been widely and consistently observed. Adherence to GMPs as Assurance/Quality Control group and by Health Authorities, ensure consistent product quality and is designed to ensure that patient safety is not compromised.

The problem
Globalisation of the health care sector and the free movement of its goods and services has had enormous benefits including those for patients in accessing medicines that were in the past either not produced locally or far too expensive to import and access. The tremendous growth of generic medicines over the last two decades has greatly contributed to increase access. Indian generics for example make up a substantial part of the US generics market (26.5% in 2007, 30% in 2008 and 35% in 2009)11. At the same time, however, the globalisation of pharmaceutical markets and production has also increased the spread and prevalence of medicines which are unsafe, and/or ineffective. Although various names have been given (as mentioned above) to such drugs, for the purpose of a clearer understanding and consistency in the context of this text, these drugs can be broadly divided into two major categories:

Counterfeit and substandard
Counterfeit is defined by WHO as being "deliberately and fraudulently mislabelled with respect to identifying and/or sourcing". Counterfeit medicines are part of the broader phenomenon of substandard pharmaceuticals. Counterfeiting can apply to both branded/innovative/reference and generic products although originator pharmaceuticals with high added value are the main target of counterfeiters[4] and counterfeit medicines may include products with the: (i) right ingredients but fake packaging, (ii) with the wrong ingredients, (iii) without active ingredients or (iv) with insufficient active ingredients. Until recently, the most frequently counterfeit medicines in wealthy countries were new, expensive lifestyle medicines such as hormones, steroids and antihistamines, while in developing countries counterfeit medicines have been those used to treat life-threatening conditions such as malaria, tuberculosis and HIV/AIDS. Today more and more medicines are counterfeit, including expensive ones, such as anti-cancer drugs and many others highly in demand, such as antivirals.

Substandard on the other hand describes those pharmaceuticals which have been legally authorised for manufacturing and more often than not, approved for market and sale by a national or regional Drug Regulation Authority (DRA) but which do not meet the required quality or safety requirements for that particular drug or treatment.

Unfortunately to date slightly or significantly different definitions exist in different countries describing the terms 'Counterfeit' or 'Substandard' as below:

- The United States Federal Food, Drug and Cosmetic Act defines a counterfeit drug as, "...a drug which, or the containers or labelling of which, without authorization, bears the trademark, trade name, or other identifying mark, imprint, or device or any likeness thereof, of a drug manufacturer, processor, packer, or distributor other than the person or persons who in fact manufactured, processed, packed, or distributed such drug and which thereby falsely purports or is represented to be the product of, or to have been packed or distributed by, such other drug manufacturer, processor, packer, or distributor."

- The United States Pharmacopoeia (the USP) defined substandard drugs as being 'genuine' products that do not conform to the pharmacopoeia standards set for them[10]

- In the Nigerian Counterfeit and Fake Drugs and Unwholesome Processed Foods (Miscellaneous Provisions) Decree[11]; a fake drug is defined as: "...

    - any drug product which is not what it purports to be; or

- any drug or drug product which is so coloured, coated, powdered or polished that the damage is concealed or which is made to appear to be better or of greater therapeutic value than it really is, which is not labelled in the prescribed manner or which label or container, or anything accompanying the drug, bears any statement, design, or device which makes a false claim for the drug or which is false or misleading; or
- any drug or drug product whose container is so made, formed or filled as to be misleading; or
- any drug product whose label does not bear adequate directions for use and such adequate warning against use in those pathological conditions or by children where its use may be dangerous to health or against unsafe dosage or methods or duration of use; or
- any drug product which is not registered by the Agency in accordance with the provisions of the Food, Drugs and Related Products (Registration, etc.) Decree 1993, as amended."

- The Pakistan Manual of Drug Laws,[11] defines a counterfeit drug as:
  "...a drug, the label or outer packing of which is an imitation of, resembles or so resembles as to be calculated to deceive, the label or outer packing of a drug manufacturer."

- In the Philippines, the Republic Act No. 82036 refers to counterfeit drug/medicine to mean:

  "...medicinal products with correct ingredients but not in the amounts as provided there under, wrong ingredients, without active ingredients, with insufficient quantity of active ingredients, which results in the reduction of the drug's safety, efficacy, quality, strength or purity. It is a drug which is deliberately and fraudulently mislabelled with respect to identity and/or source or with fake packaging, and can apply to both branded and generic products. It shall also refer to:

  - the drug itself, or the container or labelling thereof or any part of such drug, container or labelling bearing without authorization the trademark, trade name or other identification mark or imprint or any likeness to that which is owned or registered in the Bureau of Patent, Trademark, and Technology Transfer in the name of another natural or juridical person;
  - a drug product refilled in containers by unauthorized persons if the legitimate labels or marks are used;
  - an unregistered imported drug product, except drugs brought in the country for personal use as confirmed and justified by accompanying medical records, and
  - a drug which contains no amount of or a different active ingredient, or less than 80% of the active ingredient it purports to possess, as distinguished from an adulterated drug including reduction or loss of efficacy due to expiration."

The most common reasons for substandard production include: poor manufacturing practices, use of impure formulation ingredients, inadequate quality of active ingredients (including decomposition of high temperature and humidity), addition of impure and toxic ingredients to the manufacturing process, issues that render medicines not only substandard but on occasions harmful. And crucially these are not detected in the drug regulating process and the drugs pass through the system undetected.

Current picture

Counterfeit and substandard drugs make up a growing share of the total drugs supply. WHO, FDA and others estimate that the number of counterfeit drugs is between 10-15% of the total drugs market, with some average in Asia and Africa reaching levels of almost 50%[12]. On the other hand and although estimation of the substandard market is very difficult to be made since so many substandard drugs are actually legitimately manufactured and regulatory approved medicines, the number from the few existing studies, estimate that these are as high as 40% of the total sample size[13].

In 1997 for example, 36.5% of the samples of anti-malaria drug (chloroquine) in Nigeria (36%) and Thailand (40%) were substandard and 6% had no active ingredient.

The growing prevalence of these medicines in both, developed and developing countries is a real threat to public health. Most of them however, emanate from, and are used in, the developing world although a considerable amount of substandard generic drugs manufactured in developing countries are exported and used in North America, EU and USA. Most of the international data come from five emerging countries where these drugs are a real and growing problem: China, India, Brazil, Argentina and Turkey, although many others are now entering or have already entered this chain (see APPENDIX II).

Between January 1999 and October 2000, 46 confidential reports from 20 countries reached WHO. About 60% from developing and 40% form developed countries. The counterfeit drugs included antibodies, hormones, analgesia, antihistamine and constituted 60% of the products reported. In terms of type and their magnitude, six categories can be described:

32.1%	Products without active ingredients
20.2%	Products with incorrect quantities of active ingredients
21.4%	Products with wrong ingredients
15%	Products with correct active ingredients but fake packaging
1%	Copies of original
8.5%	Products with high levels of impurities

In Europe, according to DG taxation and customs union in 2006, 2.7 million counterfeit medicines were seized at the EU's borders by Custom authorities representing a 38% and 628% increase as compared to 2005 and 2005-2007 respectively. Recently it has been estimated that Western European spends around 10.5 billion euros on legal medicines, many of which are counterfeit and that 50-90% medicines bought online are fake. These include products for life threatening diseases and contain substandard or falsified ingredients, or no ingredients at all, or ingredients in the wrong dosage, including active ingredients, representing a substantial risk for patients.

For the patients

In addition to regulations and measurements by authorities and in addition to the role of health professionals, it is ESSENTIAL that national, regional and international competent authorities develop communication strategies and campaigns to INFORM THE PATIENTS and the general public about the risks of counterfeit medicines. In the strategies, internet should also be addressed, as according to WHO more than 50% sales occur from illegal internet sites.

Any proposed safety measures should certainly not lead to more expensive medicines and serious consideration should be made to investigate in depth the factors that lead patients to bring medicines from unregulated sources such as unlicensed online pharmacies. Factors may

include costs, accessibility, convenience, strings attached to certain condition and, very importantly, lack of awareness of the dosages.

Patients and Patients' Organisations should be involved in global, regional and national initiatives to raise public and patients' awareness. Patients' Organisations should be in a position to provide relevant, accurate and accessible information to their patient members for their own country.

Patients are encouraged to know well their medicines, to access their quality, to be vigilant for signs that may indicate a counterfeit medicine.

Patients themselves and health professionals can play a valuable role in detecting and reporting counterfeit medical products, and thus protecting the public.

Patient organisations have the experience to provide relevant, accurate and accessible information for the communities that they know well. Patients should be encouraged to know their medicines – to access their quality and provenance, to be vigilant for sings that may indicate a counterfeit medicine, any differences in the medicine itself or its packaging, and to encourage them to go to a health professional if they have any concerns.

Attention should be paid on how patients are provided with information. This must be done with care and thought in order not to cause panic. Alarming people could result in patients stopping taking their medicines and thereby causing more harm, which we have seen can be a negative result of health services.

Anti-counterfeiting legislation and policy should reflect current moves towards a quality label for all health websites, to enable patients and citizens to discern between trustworthy websites and unlawful sites.

The development of the toolkit 'BE AWARE' by WHO, as well as other material by other NGOs such as the European Alliance for Access to Safe Medicines (EAASM) , have been great initiatives in promoting patients' knowledge and awareness in this subject and below is a summarised quotation from the 'BE AWARE' toolkit:

BE AWARE

Be observant and carefully inspect the packaging, the product and the information leaflet. Check the product's appearance against your usual medicine. Check the expiry dates and any other information on the packaging or on the leaflet inside. If there is anything unusual or different about the medicine, tell your health care professional, especially if you have bought your medicine from an unauthorised, unreliable or unknown source.

Evaluate your response to the medicine you are using. If your medicine has an unexpected effect or not effect at all, consider counterfeit medicine as a possible suspect.

Acknowledge to your health professional where you bought the medicines and what effects it had on you. Tell the full story so that the health professional can help you and others.

Where did you get your medicines? Tell your health professional where it was bought, particularly if it was not from a known and reliable source, such as a market over the internet or from an individual on the street.

Actively inform your health professional and other patients who might also have received the medicines about your experience to help keep others safe.

Remove any suspect medicine from your home, and take all the medicine – and its packaging- to your health professional so that it can be reported to the relevant authorities.

Educate your friends and family about the risk of fake medicines.

As patients, it is essential to be aware of OUR responsibilities in addition to those of the others such as health authorities/organisations and regulatory bodies. Patients should KNOW what to look for, what to ask for and what to expect with regard to medicinal products.

Patients' organisations at the European (European Patients Forum (EPF) http://www.eu-patient.eu/) and international level (International Alliance of Patient Organisations (IAPO) http://www.patientsorganizations.org/) as well as professional bodies including the World Medical Association, the International Council of Nurses, the International Pharmaceutical Federation, forming with some others the World Health Professions Alliance (WHPA) published and distributed position papers on this important threat to public health and patients. In addition, WHPA requested official bodies to support member states in the strengthening of regulations, monitoring of adherence to regulations and the commission of an expert group to report back to the next EB & WHA in 2013 on the feasibility of establishing a public health treaty on addressing counterfeit medicines and in raising funding for its implementation (similar to the Tobacco Control Framework Convention).

Conclusion
In conclusion, trade in counterfeit medicines is widespread and affects both developed and developing countries but is more prevalent in countries facing a variety of problems such as:

- weak drug regulatory control and enforcement
- scarcity and/or erratic supply of basic medicines
- unregulated markets and distribution chain
- high drug price
- significant price differentials.

In addition, lack of appropriate punishment in still many countries, encourages people to counterfeit for the sake of huge profits.

Cooperation between countries is extremely valuable and should include the timely and appropriate exchange of information at the harmonisation of measures to prevent the spread of counterfeit medicines through all channels, including internet.

Guidelines have been developed by WHO and many other initiatives have taken place at regional and national levels in USA, EU, Canada, Japan, Australia and other countries, with strong regulatory bodies present today in many countries. Nearly 100 countries globally have, for example, national systems in place to report Adverse Drug Reactions (ADR). All these should be taken advantage of by every country to build but very importantly for all to adhere to policies and regulations to combat this major threat.

Patients as well as consumers are the primary victims including those patients with thalassaemia – a great majority of who live in third world countries where weak drug regulations and the need for cheaper drugs contribute to the development of medicinal products that are unsafe and ineffective. Patients are on many occasions 'forced' in many countries, where reimbursement policies are not or are partly in place, to purchase the cheapest possible drug as their only option. It is thus necessary to provide patients globally with appropriate information and education on how to recognise, or on their right to enquire and ask for proof regarding the safety and efficacy of the drug that they will take and very importantly the consequences when this drug is 'fake' or substandard.

Ministries of Health, national medicinal regulations, health professionals and NGOs, have the responsibility to provide such information which should be frequently updated or upgraded. Health professionals need also to be aware and informed, in order to be able to detect anomalies and trigger investigation. They need, for example, to increasingly consider counterfeit medicines as a reason for non-response or unexpected response and it is thus essential to set up effective systems for collection of information. This global and deadly phenomenon will only be eradicated through an agreed framework of effective coordination, cooperation and action at the global level. Within the future role of WHO these three areas of focus are included:

- information and creation of awareness
- norms and standards and
- provision of technical support to countries

TIF Invites you ALL to join hands and fight against the spread of unsafe, substandard medicines. Patients' health and safety are pivotal issues to the mission and objectives of TIF and of every patients'-oriented organisation, but it should also be a priority in the activities of every National Health Authority.

APPENDIX I

WHO INITIATIVES

IMPACT GENERAL Meeting, Lisbon, 2007	Principles and Elements for National Legislation against counterfeit medicines endorsed.
61st WHA, 2008	Establishment of a programme to coordinate WHO work and the work of IMPACT
Group of Eight (G8) EU Summit, 124th Executive Board, Jan 2009	SUMMIT DECLARATION requested DG to revise the report on CMs before submission to WHA
62nd WHA 2009	Decided not to discuss and postpone the consideration of the matter
44th Meeting ECSPP, Oct 2009	Expert committee on specifications for pharmaceutical preparation recommended revision of Guidelines to include input from IMPACT work
March 2010	Revisit of the use of term 'counterfeit' and related definition
63rd WHO 11.20, 2010	Report discussed, progress noted and agreed on continuation of action
64th WHA 13.7, 2011	Subject revisited with patients' organisations involved, e.g. IAPO
WHO work	1951 WHO Executive Board Resolution EB7.R78 requested DG to consider advantages of uniform methods for the control of drugs in countries, for the interest of health and international trade
Nairobi, 1985	Conference of Experts on the Rational use of Drugs
WHA 41.16, 1988	Resolution – Prevention and detection of the export, import and smuggling of falsly labelled, counterfeited or substandard pharmaceutical preparations
Workshop, Geneva, 1992	Jointly with International Federation of Pharmaceutical Manufacturers and Associations in response to Resolution WHA 41.16 (Definition of counterfeit medicines agreed upon)
WHA 47.13, 1994	Support to MS to ensure good quality drugs and combat the use of counterfeit medicines
Project launched, 1995	With the financial support of Japanese Government
One of the outputs of this project	Assessing problem and designing measures to combat
Publication of the Guidelines on Good distribution practices for pharmaceutical products, 1999	INCREASED INTERNATIONAL TRADE AND SALES THROUGH INTERNET
2006	Launch of the International Medical Products Anti-Counterfeit Taskforce IMPACT

APPENDIX II [11]

General Policy Recommendations

- Recognise the problem. Governments in all countries (and across the world) must acknowledge the extent to which the production of substandard drugs and counterfeiting is a real threat to public heath and safety. This is the first step towards action.

- There must be a better understanding at the regulatory, policy and public level of the differences between substandard and counterfeiting drugs. While the effects of the two are often similar – detrimental and sometimes lethal health outcomes to patients – their causes are not always the same. Counterfeiting is the deliberate production of illegal, unsanctioned and mostly harmful medicines. Substandard drugs, by contrast, can be produced, sold and distributed by completely legitimate and authorised entities who are often unaware of their product being (or becoming) substandard.

Country-Specific Policy Recommendations

- **China**: China must do better at implementing its existing regulatory framework. While resources for the SFDA have been increased and there is improvement in national and international coordination, Chinese regulations and policymakers must make enforcement a greater priority.

- **India**: Indian drug regulations are highly disparate, inefficient and not well-enforced. Regulations should be streamlined and a clear regulatory framework and source or authority should be established. The current split between central and provincial functions does not foster efficiency or effectiveness. The resulting provincial and regional differences of rules, regulations and enforcement are at the heart of India's difficulties with substandard and counterfeit medicines.

- **Brazi**l: Like China, Brazil's enforcement mechanisms and authorities need to be strengthened. Legislation introduced in 2003 to effectively outlaw similars by 2015 is a step in the 'right' direction, but the long time-frame leaves many potential dangerous drugs in circulation.

- **Argentina**: Unlike Brazil, Argentina has not addressed the existence of non-bioequivalence tested similars and should do so. ANMAT should also introduce a more comprehensive system of pharmacovigilance which increases the burden of reporting onto health professionals.

- **Turkey**: Regulations of pharmacists and pharmacovigilance must be improved and implemented more effectively on the ground.

Comparison of Key Regulatory Capabilities of China, India, Brazil, Argentina and Turkey

	Comprehensive Legislative and Regulative Organisation	Pharmacovigilance Regulation and Implementation	GMP: Code in place and enforced	Overall Quality and Safety Control
China	High	Medium	Medium	Low-Medium
India	Low	Low	Low-Medium	Low
Brazil	Medium-High	Medium	Medium	Medium-High
Argentina	Medium-Low	Low-Medium	Medium	Low-Medium
Turkey	Medium	Medium-Low	Medium	Low-Medium

REFERENCES

1. WHO EB 130 R13, 2012-03-29
2. Facts and Myths about Generic Drugs WHO publ. 19/10/2009
3. Doc. Ref. EMEA/393905/2006
4. EGA position paper 2007
5. Directive 2011/62/EU June 2011 p.13
6. EMEA Doc. Ref. EMEA/74562/2006
7. EGA bio-similars handbook 2nd edition 2011
8. US Food and Drug Administration, FDA history – Part I http//: www.fda.gov/AboutFDA
9. International Conference on Harmonisation of Technical Requirements – 'History and Future' http://www.ich.org/cache/compo/276-254
10. United States Pharmacopoia – A review February 1997
11. Keeping Medicine Safe – David Tornsenson and Meir Pugatch, 2010
12. Roger Cockburn et al, 'The Global Thread of Counterfeit Medicines' PLOS Medicine, 2 (4), 2005
13. O. Shakoor, et al. Tropical Medicine and International Health p.842.3
14. Approved Drug Products with Therapeutic Equivalence Evaluations (orange books) 23rd ed 2003

Buehler. G. Regulatory Pathway: Abbreviated New Drug Application, 2007 http://www.fda.gov/cder/unapproved_drugs/presentation, (MAY 2