# **Substandard Drugs DA**

#### **Brink: 10% of all drugs in developing countries are substandard; Breman 19**

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**Each year, more than 250,000 children with malaria and pneumonia, common illnesses in poor countries, do not survive after treatment with fake and substandard drugs.** While poor quality drugs targeting older individuals are also entering global markets, the World Health Organization says “it is very difficult to quantify [their] impact.” Such useless or harmful drugs once went by the confusing designation “substandard/spurious/falsely labeled/falsified/counterfeit medical products.” A recent move by the WHO aims to simplify this by separating them into three categories: falsified medical products deliberately misrepresent their identity and are distributed with criminal intent substandard medical products fail to meet quality standards unregistered or unlicensed medical products have not been assessed or approved **According to the WHO, 1 in 10 medical products in developing countries is falsified or substandard. The personal and public health tolls are huge, as is the economic burden — up to $200 billion annually.** **Poor-quality antimicrobials are most often found in low-income countries.** In addition to failing to treat infection, **they also contribute to the evolution of antimicrobial resistance, which British researchers have estimated could kill up to 10 million people a year by 2050.** But counterfeit medications in virtually every therapeutic class, from blood pressure pills to treatments for cancer and vaccines, are made and distributed by unscrupulous criminals. **In countries with poor pharmaceutical control systems, such drugs can be made in illicit facilities inside or outside the country and enter the supply stream because no FDA-like system exists for inspection or approval. Expensive analytic equipment generally isn’t available, while simple, accurate, and inexpensive testing systems for use in the field, at pharmacies, and at the point of care remain out of reach in virtually all poor countries. To make matters worse, many countries do not have laws to define and enforce regulations addressing crimes related to counterfeit or substandard medicines, nor do the have well-defined judicial actions once criminals are suspected or identified.**

#### **Link: IP protections are a essential barrier to fight counterfeit medicine and substandard drugs; Lybecker, 16**

Lybecker, Kristina M (C. Dr. Kristina M. Lybecker is an Associate Professor of Economics at Colorado College in Colorado Springs, where she is also the Associate Chair of the Department of Economics and Business and the Gerald L. Schlessman Professor of Economics. She has testified numerous times on the economics of the importation of Canadian drugs and the risks of pharmaceutical counterfeiting. Dr. Lybecker has also worked with US Food and Drug Administration, PhRMA, and the World Bank, on a variety of issues relating to the economics of innovation and international trade policies.) “Counterfeit Medicines and the Role of IP in Patient Safety.” IPWatchdog.com | Patents &amp; Patent Law, IPWatchdog, 27 June 2016, [www.ipwatchdog.com/2016/06/27/counterfeit-medicines-ip-patient-safety/id=70397/](http://www.ipwatchdog.com/2016/06/27/counterfeit-medicines-ip-patient-safety/id=70397/).

As the author of the chapter on illicit trade in counterfeit medicines within the OECD report, I worry that global policymakers may be working against each other when it comes to battling counterfeit drugs, especially in the context of intellectual property rights. While the Senate Hearing and **the OECD report highlight the importance of strong IP protection in combating the growing threat of counterfeit goods, their efforts coincide with an initiative by the UN Secretary-General that has the potential to greatly worsen the problems of counterfeit pharmaceuticals.** UN Secretary General Ban Ki Moon’s High Level Panel on Access to Medicines proposes “to review and assess proposals and recommend solutions for remedying the policy incoherence between the justifiable rights of inventors, international human rights law, trade rules and public health in the context of health technologies.”[2] **The High Level Panel is a thinly veiled attempt to undermine the intellectual property rights architecture that incentivizes pharmaceutical innovation and protects patients from counterfeit medicines.** While **patents and other forms of intellectual property rights are widely recognized as fostering pharmaceutical innovation, they also serve to inhibit** **counterfeiting. The World Health Organization has determined that counterfeiting is facilitated where “there is weak drug regulatory control and enforcement; there is a scarcity and/or erratic supply of basic medicines; there are extended, relatively unregulated markets and distribution chains, both in developing and developed country systems; price differentials create an incentive for drug diversion within and between established channels; there is lack of effective intellectual property protection; due regard is not paid to quality assurance”.**

#### **Internal Link: Lack of IP floods markets with dangerous products; Mercurio, 21**

Mercurio, Bryan (C.Bryan Mercurio is the Simon F.S. Li Professor of Law at the Chinese University of Hong Kong (CUHK), having served as Associate Dean (Research) from 2010-14 and again from 2017-19. Professor Mercurio specialises in international economic law (IEL), with particular expertise in the intersection between trade law and intellectual property rights, free trade agreements, trade in services, dispute settlement and increasingly international investment law.) “The IP Waiver for COVID-19: Bad Policy, Bad Precedent.” *IIC; international review of industrial property and copyright law*, 1-6. 24 Jun. 2021, doi:10.1007/s40319-021-01083-5<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8223179/>

Alan Beattie, writing in the *Financial Times*, believes that even the proponents of the waiver desire this outcome: “having talked to the proponents, [the original proposal] was always a tactical position designed to start a debate, identify possible support and flush out opponents rather than a likely outcome. To that end, it seems to have worked rather well.”[19](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8223179/#Fn19) India’s negotiator to the TRIPS Agreement and longtime WTO staffer, Jayashree Watal, agrees, stating the proposal is an “indirect attempt to put pressure on the original manufacturers to cooperate [and license production to companies in their countries]”.[20](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8223179/#Fn20) This view makes sense, as the proponents (and their supporters) have not even pointed to one credible instance where IPRs have blocked the production of a COVID-19 vaccine. Moreover, it is well known that the **leading vaccines** using mRNA **are difficult to reproduce and having the “blueprints” does not guarantee safe and effective production.** Simply stated, if a pastry chef provides instructions on how to bake a cake, the cake they bake is still going to be better than cakes baked by novices using the exact same recipe. **The know-how** and trade secrets **are the key ingredient to the manufacture of quality, safe and effective pharmaceuticals** or vaccines, and not only is it not transferred through compulsory licenses but it is hard to imagine how any government would force the transfer of such information even under a waiver. For this reason, **instead of encouraging production everywhere – including in locations where safety and efficacy standards are virtually nonexistent – and accepting that there will be a flood of substandard vaccines coming onto the world market (with devastating effects) it is much more sensible to find out where potential manufacturing capabilities exist and find ways to exploit them and scale them up.**

#### **Impact: Increased presence of substandard drugs and falsified medicines endangers public health and strengthens antimicrobial resistance; Johnston and Holt, 14**

#### **Johnston, Atholl (C. Clinical Pharmacology, Barts and The London School of Medicine and Dentistry, Queen Mary, University of London, London, UK) and David W Holt (C. Professor David Holt has more than 47 years’ experience in the measurement of drugs as a guide to therapy, and has been responsible for the development of assays used to monitor a wide variety of therapeutic agents. For over 20 years he was the Director of the Analytical Unit at St George’s, University of London, where he was also responsible for the analysis of illicit and prescription drugs for the Unit’s Forensic Toxicology Services provided to HM Coroners, pathologists and law enforcement agencies. He now advises on proficiency testing schemes for the measurement of immunosuppressive drugs, and on problems associated with substandard pharmaceuticals.**

#### **Professor Holt is a frequent speaker on a broad range of issues relating to bioanalytics and clinical toxicology. He is the author of over 400 publications in peer reviewed journals and invited contributions to books. He is a past President of the International Association of Therapeutic Drug Monitoring and Clinical Toxicology and a recipient of the Charles E Pippenger Award for Outstanding Contributions to Therapeutic Drug Monitoring.. “Substandard drugs: a potential crisis for public health.” *British journal of clinical pharmacology* vol. 78,2 (2014): 218-43. doi:10.1111/bcp.12298** [**https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4137817/**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4137817/)

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#### **The WHO defines ‘counterfeit’ drugs as ‘medicines that are deliberately and fraudulently mislabelled with respect to identity and/or source’ [**[**8**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4137817/#b8)**]. It also states that both branded and generic products may be counterfeited and that ‘counterfeit medicines may include products with the correct ingredients or with the wrong ingredients, without active ingredients, with insufficient or too much active ingredient, or with fake packaging’. However, because of the potential misunderstanding of the term ‘counterfeit’ – which, in the context of intellectual property, refers specifically to trademark infringement – the phrase ‘falsified medicines’ is used by some authorities, particularly in Europe. The Commission of the European Communities defines these as ‘medicinal products which are falsified in relation to their identity, history or source. These products … usually contain sub-standard or false ingredients, or no ingredients or ingredients in the wrong dosage, including active ingredients’ [**[**9**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4137817/#b9)**].**

#### **Thus, falsified drugs are highly likely to be of substandard quality, possibly containing no API. However, only a small proportion of substandard drugs are falsified; the rest reach the market as a result of poor manufacturing practices, inadequate quality-control processes, incorrect storage or inappropriate packaging, or a combination of these factors. This can affect both branded and generic drugs. In many cases, the reason why a drug product is substandard (i.e. deliberate falsification or poor manufacturing practice) is not stated or is not known. Whether or not a drug product is substandard because of criminal intent or because of failures in manufacturing, storage, etc. is immaterial to the patient because the impact on their health will be the same, regardless of cause [**[**10**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4137817/#b10)**]. In this article, we consider the term ‘substandard’ to apply both to legally approved but poor-quality drugs and to falsified drugs, but we focus on the former with regard to reviewing potential solutions.**

#### **Substandard drugs pose a serious health concern from several perspectives (Table ​(Table44 [47,48,51,52,57,59,70,95–104]). Although falsified drugs have perhaps received most of the attention with respect to causing unnecessary deaths, substandard drug manufacture also leads to morbidity and mortality. A formulation with insufficient API may lead to a lack of clinical response, and possibly, death. For example, there are reports of patients failing to respond to antimalarial treatment [95,96] because the drugs contained less than the stated dose of API and, in one reported case, contained more paracetamol than antimalarial agent [95]. In other cases, a reduced therapeutic response has been associated with generic/copy versions of drugs compared with the originator drugs, including antibiotics, tacrolimus and imatinib [70,97,99–102].**

#### **Adverse events also occur due to drug–drug interactions with contaminants, the presence of excess API, contamination with poisonous substances, or allergic reactions to contaminants or substituted excipients. As mentioned above, some of the most extreme cases involve the (possibly deliberate) contamination of medicines with DEG [**[**47**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4137817/#b47)**,**[**48**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4137817/#b48)**]. In another case, heparin was found to be contaminated with oversulphated chondroitin sulphate, which was thought to be responsible for the allergic or hypersensitivity-type reactions experienced by a number of patients, some of which proved fatal [**[**51**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4137817/#b51)**]. At the time of the heparin incident, the oversulphated chondroitin sulphate could not be distinguished from heparin by the standard quality-control tests used. However, the FDA has since implemented changes to the USP standards for heparin, including a new test method that is able to detect such impurities [**[**105**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4137817/#b105)**].**

#### **There are also adverse societal effects arising from the use of substandard drugs. The inadvertent use of suboptimal doses of drugs is likely to be one of the key factors contributing to antimicrobial resistance and thereby leading to the wider spread of disease. This has been most widely discussed with regard to malaria [**[**106**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4137817/#b106)**–**[**108**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4137817/#b108)**]; the repeated administration of subtherapeutic doses of antimalarials will promote the selection and spread of resistant parasites [**[**95**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4137817/#b95)**,**[**106**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4137817/#b106)**]. Indeed, artemisinin-resistant malaria has been reported in Cambodia and Thailand [**[**109**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4137817/#b109)**,**[**110**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4137817/#b110)**], although the extent to which this can be attributed to the use of substandard drugs is unknown. Likewise, poor-quality antibiotics may contribute to the resistance and spread of diseases such as tuberculosis [**[**23**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4137817/#b23)**,**[**111**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4137817/#b111)**,**[**112**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4137817/#b112)**]. The use and subsequent failure of substandard narrow-spectrum antibiotics may lead to the unnecessary administration of broad-spectrum antibiotics, thus potentially creating further resistance [**[**113**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4137817/#b113)**]. Substandard antihelminthics have been implicated in the development of drug-resistant human helminths [**[**114**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4137817/#b114)**], and substandard antiviral drugs are likely to contribute to the evolution of drug-resistant viruses, including human immunodeficiency virus (HIV) [**[**115**](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4137817/#b115)**].**

# **Compulsory licensing**

#### **CP Text: The member nations of the WTO ought to agree on specific conditions under which they could issue a compulsory license.**

#### **Compulsory licensing increases access to essential medicine for developing countries**

**Ooms and Hanefield 19** (Department of Global Health and Development, Faculty of Public Health and Policy, London School of Hygiene and Tropical Medicine, London, UK. Gorik Ooms is a human rights lawyer and a global health scholar, Honorary Professor of Global Health Law & Governance at the London School of Hygiene & Tropical Medicine, Adjunct Professor at the Law Faculty of Georgetown University, and Visiting Professor at the Faculty of Medicine and Health Sciences of Ghent University. Johanna Hanefield is an Associate Professor in Health Policy and Systems Research at The London School of Hygiene and Tropical Medicine.), “Threat of compulsory licences could increase access to essential medicines”, BMJ 2019;365:l2098, 5-28-19, doi: <https://doi.org/10.1136/bmj.l2098>, <https://www.bmj.com/content/365/bmj.l2098> NT

The power of compulsory licences is most obvious when governments use them effectively. However, compulsory licences also have power when governments warn patent owners that they will use them if necessary. For example, when the US faced the threat of terrorists using anthrax in October 2001, the US secretary of health and social services wanted to stockpile ciprofloxacin, which was the best available treatment for anthrax. Bayer, the patent owner, demanded the usual price for ciprofloxacin, but when the US and Canada declared they might issue a compulsory licence, Bayer reduced the price.22 Neither Canada nor the US needed the Doha declaration to threaten Bayer as there was sufficient manufacturing capacity in both countries (and the Doha declaration came a month later). Thus threatening to use a compulsory licence may be as effective as formally issuing one**. The Doha declaration** solution is cumbersome to apply effectively, but it does **give countries**— even those without domestic manufacturing capacity— **the power to threaten to use a compulsory licence.** This may have an influence on prices. For example, sofosbuvir is a relatively new and highly effective treatment for hepatitis C, but its high price in some countries has proved controversial. Sofosbuvir came to the market in 2007. According to Iyengar and colleagues, the price of sofosbuvir was $64 680 per treatment in the US and $539 in India in 2015.23 In 2015, no country had issued a compulsory licence for sofosbuvir. The first such licence was issued by the Malaysian government in September 2017.24 Why the disparity in the price of sofosbuvir in the US compared with India? The prices were set by the originator, or by generic manufacturers working with a voluntary licence given by the patent owner. Thus, the “discount” for India, given or allowed by the patent owner, was 99% before any compulsory licence was issued. This is similar to the price reduction of the classic combination antiretroviral therapy, attributed to generic competition.25 We cannot be certain that the risk of a compulsory licence was the main reason for the patent owner of sofosbuvir allowing a 99% discount, but there is no other obvious explanation. India has manufacturers that can produce generic equivalents of sofosbuvir, as does Malaysia. Can countries without manufacturing capacity use the same strategy? Before the Doha declaration, **patent owners would not have been impressed by a threat to issue a compulsory licence from a country without domestic manufacturing capacity.** Since the declaration, such a threat would be credible. Although the Doha Declaration solution has been used only once, this was enough to show that it can be done, as long as countries with manufacturing capacity are willing to cooperate. Low and middle income countries would be in a stronger position if they declared their commitment to cooperate to make the Doha Declaration solution work. One option might be for them to agree on specific conditions under which they would issue compulsory licences for export based on the Doha declaration, if required by another member of the alliance.26 This would increase the credibility of threats to issue a compulsory licence by countries without manufacturing capacity. It would also give a signal to generic manufacturers of the potential size of the market, if all countries participating in this alliance would buy from the cheapest provider within the alliance. We should not be naive. As Sell points out, “there is a dizzying array of extra intellectual property protection that is being imposed on developing countries, such as TRIPS Plus agreements, in the form of bilateral agreements, free trade agreements, and plurilateral negotiations such as anti-counterfeiting trade agreements.”27 The political pressure used by rich countries against poorer countries to dissuade them from using their rights under the TRIPS agreement and the Doha declaration has increased. However, the governments of **low and middle income countries** with manufacturing capacity are not as powerless as before the Doha declaration. **They can issue compulsory licences for all medicines needed to protect public health without violating the TRIPS agreement. They can declare their intention to help low and middle income countries without manufacturing capacity and, by doing so, empower these other countries.** Whether they have the will to confront the likely political pressure is a different matter.