Medical Product Quality Report – COVID-19 Issues

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MORU Tropical Health Network

UNIVERSITY OF OXFORD

IDDO INFECTIOUS DISEASES DATA OBSERVATORY

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Contents

1. Summary of findings

The COVID-19 pandemic does not show signs of abating anytime soon. It continues to be a significant market force not only for good quality but more worryingly for substandard and falsified (SF) medical products. Reports on SF COVID-19 supplies range from personal protective equipment and diagnostic tests to vaccines and medicines.

During the month of September substandard remdesivir and falsified COVID-19 vaccines were reported in India. In the United States the Do-Not-Use-List of hand sanitizers kept on growing, albeit at a slower rate compared to the previous months. SF hand sanitizers were reported in Nepal and diverse other countries. The August issue of the medical product quality report reported problems of SF masks in Taiwan and in September additional articles reported on issues of falsified masks with forged labels in Taiwan. Other worrying phenomena are reflected by alerts on used medical gloves and masks that are repacked and sold. The articles discussed in the medical product quality reports are early warnings of potential problems with COVID-19 supplies. For all these products vigilance is needed considering the relentless risk of substandard or falsified versions.

2. Introduction

During the COVID-19 pandemic, the demand for COVID-19 related medical supplies has inevitably ballooned with an increased demand for personal protective equipment (PPE), diagnostics and preventive & curative pharmaceuticals. The high demand and related shortages of genuine products contributes to an increased global risk of substandard and falsified (SF) medical products, for COVID-19 and for many other essential medicines. The media have been reporting diverse examples of SF products flooding the market.

This report aims to collate information and reports in the public domain on the quality of medicinal products that are currently in use, or that are being trialled for COVID-19's prevention or treatment. We also include reports on key subjects such as access, affordability or off label use for COVID-19 if they mention concern of the quality of the products. We do not aim to include discussion of the multiple fraudulent claims and quackery.

We use the terminology for different types of poor quality medical products as defined by the World Health Organisation (WHO, 2017)[1]:

[1]Source: World Health Organisation. Appendix 3 WHO MEMBER STATE MECHANISM ON SUBSTANDARD/SPURIOUS/FALSELY-LABELLED/FALSIFIED/COUNTERFEIT (SSFFC) MEDICAL PRODUCTS WORKING DEFINITIONS. In: *Seventieth World Health Assembly*. ; 2017. Accessed August 14, 2020. https://www.who.int/medicines/regulation/ssffc/A70_23-en1.pdf?ua=1

- **Substandard medical products**
  Also called “out of specification”, these are authorized medical products that fail to meet either their quality standards or their specifications, or both.
- **Unregistered/unlicensed medical products**
  Medical products that have not undergone evaluation and/or approval by the national or regional regulatory authority for the market in which they are marketed/distributed or used, subject to permitted conditions under national or regional regulation and legislation.
- **Falsified medical products**
  Medical products that deliberately/fraudulently misrepresent their identity, composition or source.

We emphasise the difference between the use of the terms ‘falsified’ and ‘counterfeit’ medical products. ‘Falsified’ is a broad term including all the various types of deliberate misrepresentation of a medical product from a public health perspective. The term ‘counterfeit’ is specifically linked to intellectual property rights, ‘trademark counterfeit goods’[2] and ‘pirated copyright goods’[3] as used in the Trade-Related Aspects of Intellectual Property Rights (TRIPS) agreement.

The reports presented were mostly extracted from the Medicines Quality Monitoring Globe (the MQM Globe is accessible on the IDDO website[4]), a system that scrapes online newspapers (referenced in Google News) for early warnings of substandard and falsified medical products. In addition, alerts and reports by national and international organisations are included when captured by the members of the team or shared by colleagues. This report also includes scientific literature and policy documents related to COVID-19 medical products quality identified by manual searches in Pubmed and Google Scholar. These will be displayed on the Medicine Quality COVID-19 Surveyor to be released in the coming months. We also include preprint of articles. Please note that preprints should be viewed with additional caution as they have not been peer-reviewed. They should not be relied on to guide clinical practice or health-related behaviour and should not be reported in news media as established information.

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[2]*Trademark counterfeit goods*: any goods, including packaging, bearing without authorization a trademark which is identical to the trademark validly registered in respect of such goods, or which cannot be distinguished in its essential aspects from such a trademark, and which thereby infringes the rights of the owner of the trademark in question under the law of the country of importation.
Source: World Trade Organization. Part III — Enforcement of Intellectual Property Rights. Accessed August 14, 2020. https://www.wto.org/english/docs_e/legal_e/27-trips_05_e.htm#fnt-14

[3]*Pirated copyright goods*: any goods that are copies made without the consent of the right holder or person duly authorized by the right holder in the country of production, and which are made directly or indirectly from an article where the making of that copy would have constituted an infringement of a copyright or a related right under the law of the country of importation.
Source: World Trade Organization. Part III — Enforcement of Intellectual Property Rights. Accessed August 14, 2020. https://www.wto.org/english/docs_e/legal_e/27-trips_05_e.htm#fnt-14

[4]Infectious Diseases Data Observatory. Medicine Quality Monitoring Globe. Web Page. Published 2020. Accessed October 16, 2020. https://www.iddo.org/medicine-quality-monitoring-globe

Please note the caveats for the lay literature (MQM Globe disclaimer and caveats are accessible on the IDDO website[5]); we include abstracts and extracts from articles that are subject to a take down policy. If we are contacted by a potential rights-holder who objects to the presence of material, we will remove the material in question from the report and Globe until we have been able to assess the case. Where material is removed for valid reasons of copyright, its removal will be considered as lasting until copyright in the material expires, or until the rights-holder agrees that the material can be reinstated.

This fourth issue of the monthly report 'Medical Product Quality Report – COVID-19 Issues' covers information published during the month of September. The previous issues covered publications from January 1st to August 31th 2020 and are available on the IDDO website[6]. We also include publications and reports published prior to August 2020 that were missed in the previous issues of the report. We are developing a system for scraping regulatory authority and international organisation websites for alerts. Any remarks or additions to content are greatly appreciated (please write to medicinequality@iddo.org).

3. Scientific literature

3.1. General

Aseffa A, Lulseged S, Makonnen E. **Mitigating the impact of COVID-19 on pharmacovigilance.** *Ethiop Med J*. 2020;58(4). doi:10.1007/s40264-020-00965

> Extract of the editorial. *« Regulatory systems need to rise up to the challenges posed by COVID-19 to ensure that pharmacovigilance plays its essential role in the COVID-19 response. In Ethiopia, where the COVID 19 pandemic is on the rise, it is necessary to prevent public health damage from this complex pandemic as early as possible. Pharmacovigilance should be one of the priority interventions to this end. It is important that regulatory bodies ensure manufacturers and importers fulfil the required documentations and put in place efficient authorization processes to meet urgent public health needs, while protecting the public from unsafe and poor-quality medical products related to the diagnosis and prevention of COVID-19. The directive recently issued by the Ethiopian Food and Drug Authority (EFDA) (9), which provides directions for COVID-19 medical products conditional approval and import permit authorization is a useful step in the country's effort to guide and monitor the national response to the pandemic. Further measures need to be taken to strengthen pharmacovigilance in the broader sense, while keeping efficiency in perspective. »*

Belayneh A. **Off-Label Use of Chloroquine and Hydroxychloroquine for COVID-19 Treatment in Africa Against WHO Recommendation.** *Res Rep Trop Med*. 2020;Volume 11:61-72. doi:10.2147/rrtm.s269936.

> *Abstract.* « *COVID-19 is continuing as a big challenge for the globe and several types of research are continued to find safe and effective treatment and preventive options. Although there is a lack*

[5]Infectious Diseases Data Observatory. Medicine Quality Monitoring Globe disclaimer and caveats. Web Page. Published 2020. Accessed October 19, 2020. https://www.iddo.org/medicine-quality-monitoring-globe-disclaimer-and-caveats

[6]Infectious Diseases Data Observatory. Medical Product Quality Reports. News. Published 2020. Accessed October 10, 2020. https://www.iddo.org/mq/research/medical-product-quality-report

of conclusive evidence of their benefit, there is worldwide controversy to use anti-malarial drugs, hydroxychloroquine and chloroquine, for the treatment of COVID-19. FDA issued an emergency use authorization to the use of these drugs for the treatment of COVID-19. On the contrary to the FDA, the European Medicines Agency has warned against the widespread use of these drugs to treat COVID-19. Finally, the WHO declared that clinical trials on these drugs are halted after the devastating findings of the study published in the medical journal called The Lancet. Against this fact, there are several rumors about the irresponsible use of these drugs in Africa for the treatment of COVID19. This work aimed to review the off-label use of these drugs for the treatment of COVID19 in African countries against WHO recommendation. Data on the use of these drugs for the treatment of COVID-19 in African countries were searched from credible sources including Scopus, PubMed, Hindawi, Google Scholar, and from local and international media. The study showed that many African countries have already approved at the national level to use these drugs to treat COVID-19 by opposing WHO warnings. In addition to this, falsified and substandard chloroquine products started to emerge in some African countries. The health sectors of the African government should critically compare the risks and benefits before using these drugs. The WHO and African drug regulatory organizations should intervene to stop the off-label use practice of these drugs against the licensed purpose and distribution of falsified and substandard products in the continent. »

Forouzandeh P, O'Dowd K, Pillai SC. **Face masks and respirators in the fight against the COVID-19 pandemic: An overview of the standards and testing methods.** *Saf Sci*. 2020;133:104995. doi:10.1016/j.ssci.2020.104995.

Abstract. « *The COVID-19 outbreak has resulted in a shortage of personal protective equipment (PPE) throughout the world. This shortage has resulted in an increase in production of PPE to meet the demand, and as a result, several substandard equipment has entered the market. With face masks and respirators now beginning to see widespread use throughout the world, the standards and test with which they are required to undertake have become points of interest. The filtration efficiency of the masks is a key testing element that examines its ability to filter particles, bacteria and viruses; this examines the penetration efficiency percentage of each with lower results being preferable. Masks are also subjected to NaCl testing method, which allows a range of particle sizes to be examined and their penetration to be observed. The masks must also show considerable resistance to fluids and flames, to prevent the penetration of liquids and to be non-flammable. Various PPE testing protocols such as biological, chemical, fluid and flame resistances, protective ensemble, facepiece fit testing, NIOSH NaCl method and impact protection have been discussed. In addition, various tests involving bacterial and viral filtration efficiencies are also discussed. Differential pressure is examined to ascertain the comfort, airflow and breathability of the masks, whilst fit testing is examined to ensure a correct fit of the mask.* »

Jefferson M. **COVID-19: The Lessons We Should Have Learned from Existing Literature.** *Biophys Econ Sustain*. 2020;5(3):3. doi:10.1007/s41247-020-00079-y

Abstract. *« The linkages between natural resources and human well-being lie at the heart of biophysical economics. Huge disruptions to human well-being which can occur as a result of the impact of particular natural resources or species are, or should be, an obvious focus of interest for the biophysical economist whose focus is on flows between the natural world and human society. The causes and consequences of such disruptions, such as emanate from pandemics and epidemics, are a clear example of this. There is a need for better understanding of these causes and consequences. As an example, twelve books on epidemics and pandemics are considered here as providing the core for what guidance they might, and should, have provided on the sources, spreaders, and responses to COVID-19. A substantial amount of guidance is given in these and other sources referenced, which if followed would have reduced spread and mortality, but in far too many countries preparedness and speed of responses were inadequate. An effective global network and funding are required, as long advocated, but still not implemented. The economic and resource costs of this failure are huge. »*

Kalidoss VK, Bakshi SS. **Has the use of hand sanitiser substituted hand hygiene in the current COVID-19 pandemic?** A perilous path. *J R Coll Physicians Edinb*. 2020;50(3):343-350. doi:10.4997/JRCPE.2020.330

Extract of the text. *« There are other issues too, like the availability of substandard sanitisers on the market. This is of particular concern as the FDA recommends 60–95% of ethanol or isopropyl alcohol for a hand sanitiser to be effective, but there are many sanitisers available online which have a much lower concentration or the concentration information is not available. We would like to conclude that although hand sanitisers are a very effective measure of hand hygiene, their blind promotion should be avoided. The public should be educated in hand hygiene measures and should be made aware that hand sanitisers are not a substitute for the age-old, time-tested technique of hand washing with soap and water. Judicious use of standardised hand sanitisers is the need of the hour and we as healthcare workers should take the front line in educating the public about the same. »*

Kohler JC, Wright T. **The Urgent Need for Transparent and Accountable Procurement of Medicine and Medical Supplies in Times of COVID-19 Pandemic.** *J Pharm Policy Pract*. 2020;13(1). doi:10.1186/s40545-020-00256-w

Abstract. « *The COVID-19 pandemic has unleashed unprecedented and complex public policy issues. One that has emerged as a challenge for many countries globally is how to ensure the efficient and effective procurement of quality medical supplies. Existing corruption pressures on procurement—everything from undue influence to the outright bribery of public officials—has been amplified by the pandemic, and thus demands commensurate policy responses. We argue that transparency and accountability in procurement are essential to preventing the corruption risks that threaten the health and well-being of populations.* »

Mennechet FJD, Dzomo GRT. **Coping with COVID-19 in Sub-Saharan Africa: What Might the Future Hold?** *Virol Sin*. Published online 2020:1. doi:10.1007/s12250-020-00279-2

Extract of the text. « *Despite the enormous and global controversy over the use of hydroxychloroquine that has lasted for months, and against the WHO recommendations, many African countries are still refusing to abandon hydroxychloroquine or chloroquine for the treatment of COVID-19. Since the beginning of the epidemic, people infected with COVID-19 in the Republic of Chad are treated with chloroquine and azithromycin. In addition to the elements that call into question the therapeutic use of this drug for the treatment of COVID-19, there is also the very real threat of self-medication and the risk of the use of counterfeit drugs that are already flooding markets in Africa.* »

[Preprint] Novotny T. **Chloroquine and Hydroxychloroquine: how about switching?** *Authorea Prepr*. Published online September 11, 2020. doi:10.22541/AU.159986538.81056460

Abstract. *« Early studies suggesting that chloroquine (CQ) and hydroxychloroquine (HCQ) could benefit coronavirus patients brought these old medicines back to the spotlight. This led to an increase in demand and price, turning their counterfeiting a pharmacovigilance issue worldwide. Meanwhile, lack of evidence on effectiveness and safety concerns have reduced their clinical trials in severe COVID-19 cases. Despite the knowledge that CQ and HCQ toxic effects are stereo specific rather than their therapeutic effects, these drugs are available only as racemates. In this context, this work brings a discussion about chiral switching to their eutomers so that CQ and HCQ distomers would become impurities, what may be a viable alternative to test new dose-response curves. Even if it is proven that the use of pure CQ and HCQ enantiomers are useless against COVID-19, chiral switching would certainly improve safety and efficacy in the treatment of many autoimmune inflammatory diseases, benefiting chronic users of these drugs. »*

[Preprint] Nyamweya NN, Abuga KO. **Alcohol-Based Hand Sanitizers-A Multidimensional Perspective.** Published online September 15, 2020. doi:10.20944/preprints202009.0337.v1

Abstract. « *The global use of alcohol based hand sanitizers (ABHS) as a means of controlling the transmission of infectious disease increased dramatically in 2020 as governments and public health agencies across the world advocated hand hygiene as a preventative measure during the COVID-19 pandemic. Although the performance of these products is most commonly defined as a function of their alcohol concentration, they are multifaceted products in which an interplay of several factors is important in determining efficacy. The hand sanitizer tetrahedron, is a novel concept that considers both ABHS formulation factors and product performance factors from a multi-dimensional perspective. The four faces of the tetrahedron represent input/formulation factors: 1) the type and amount of alcohol, 2) inactive ingredients, 3) the type of formulation/delivery system and 4) manufacturing practices. The four corners of the tetrahedron represent output/product performance factors: 1) efficacy, 2) sensory characteristics, 3) usage, usability and compliance and 4) product safety/adverse effects. All factors are of importance to ensuring the effectiveness and utility of these products.* »

Proffitt E. **The dangers of fake PPE.** *BDJ Team*. 2020;7(8):20-21. doi:10.1038/s41407-020-0399-5

Extract from the text. « *The COVID-19 pandemic has shone a spotlight on some of the amazing selfless and caring aspects of human nature. However, it has also highlighted some more unsavoury aspects, a key one being the manufacture and supply of fake and non-compliant personal protective equipment (PPE). Unfortunately, it does not come as a great surprise that in these very challenging times when there is unprecedented global demand for face masks and PPE, millions of counterfeit products are appearing on the market, largely on sale from online vendors and linked to resourceful and adaptive criminal gangs.*
The British Dental Industry Association (BDIA) has been operating its Counterfeit and Sub-standard Instruments and Devices Initiative (CSIDI) awareness campaign in the dental press for several years now and is delighted with the significant increase in the dental profession's knowledge and understanding of the dangers of counterfeit and non-compliant dental devices. There is now significantly greater awareness of the issues and dangers associated with fake and non-compliant devices, the implications for users and patients and, very importantly, an understanding of the importance of purchasing from reputable suppliers, such as BDIA members, and being incredibly wary of 'too good to be true' online offers from unfamiliar suppliers. »

White NJ, Watson JA, Hoglund RM, Chan XHS, Cheah PY, Tarning J. **COVID-19 prevention and treatment: A critical analysis of chloroquine and hydroxychloroquine clinical pharmacology.** *PLoS Med*. 2020;17(9):e1003252. doi:10.1371/journal.pmed.1003252

Extract of the text. *« Diversion. Recommending valuable drugs for unproven indications wastes valuable resources, damages health, and compromises finding effective medicines. People are likely to assume that recommended drugs do work and, in the context of preventive use, will believe they are protected and therefore may not take other necessary precautions or adhere to other public health measures. Taking drugs is easier than complying with public health measures such as physical distancing and wearing protective equipment. In addition, the high demand for these currently unproven drugs has put patients at risk who legitimately need them for treatment for other conditions such as SLE and rheumatoid arthritis. Shortages have already occurred and prices have risen markedly, leaving these vulnerable groups to suffer unnecessarily. It could also encourage unscrupulous manufacturers to make falsified chloroquine and hydroxychloroquine.»*

3.2. Seizures/Surveys/Case Reports/Reviews

Mwema FM, Nyika JM. **Challenges in facemasks use and potential solutions: The case study of Kenya.** *Sci African*. 2020;10:e00563. doi:10.1016/j.sciaf.2020.e00563

> Abstract. « *The emergence of the novel Coronavirus has forced most governments across the world to enact stringent public laws to curb its transmission among the populations. The requirement to wear a facemask whenever in public places is one of such laws. As such, the demand for such masks has escalated across the world and this predisposition has presented a manufacturing challenge to the developing countries, which have limited capacity to meet the demand for their large populations. In developing countries such as Kenya, the citizens are now required to wear facemasks when in public places such as markets, streets, shopping malls, etc. With limited supply of the proper facemasks in the developing countries, the public is left to improvise them from the available resources. Alternatively, they purchase substandard facemasks from uncertified suppliers and sellers. The purchased masks do not meet the required health standards in most cases. In Kenya, for example, the government has been discouraging citizens from using N95 respirators and instead preserve them for medical practitioners due to their rarity and incapacity to manufacture them. The government has certified several textile industries to produce facemasks for the public from non-woven fabric materials. The challenge with such a move is that there has been an influx of an assortment of facemasks in the Kenyan market and it is not possible for the citizens to identify the safe ones. In this short communication, a brief description of the challenges facing the citizens in terms of access to and quality of face masks in developing countries, with a case study of Kenya is provided. Furthermore, a proposed design solution and a proof of concept of a low-cost and reusable 3D printed facemask for developing economies is herein presented. The adoption of such a design by the governments and manufacturers would solve the challenges of access and quality of the respirators to lower the transmissions of the Coronavirus.* »

Additional publications prior to September 2020

Fonseca Jr. F, Brito L, Pimentel MF, Leal L. **Determination of Ethanol in Gel Hand Sanitizers Using Mid and Near Infrared Spectroscopy.** *J Braz Chem Soc*. 2020;31(9):1759-1763. doi:10.21577/0103-5053.20200115

> Abstract. « *Alcohol-based gel hand sanitizers became very popular during the COVID-19 (coronavirus disease 2019) pandemic. In Brazil, several irregular factories emerged requiring an efficient control by the police and regulatory agencies to guarantee product quality. This problem required a method to determine ethanol content, which led to the development of two methods employing mid and near infrared spectroscopy associated with chemometrics. Partial least squares (PLS) models were built and presented satisfactory results with mean absolute percentage error of prediction and root mean square error of prediction (RMSEP) of 1.12 and 0.76% (m/m), respectively, for mid-infrared (MIR) and 1.83 and 1.18% (m/m) for near-infrared (NIR). The analysis of commercial and seized samples of hand sanitizers showed that only 7 out of 34 samples had an ethanol content of 70% (m/m) or higher. This result reinforces the need for constant vigilance by authorities to ensure that the products have the required specifications.* »

Schilling K, Gentner DR, Wilen L, et al. **An accessible method for screening aerosol filtration identifies poor-performing commercial masks and respirators.** *J Expo Sci Environ Epidemiol*. Published online 2020. doi:10.1038/s41370-020-0258-7

> Abstract. « *Background: The COVID-19 pandemic has presented an acute shortage of regulation-tested masks. Many of the alternatives available to hospitals have not been certified, leaving uncertainty about their ability to properly protect healthcare workers from SARS-CoV-2 transmission.*
> *Objective: For situations where regulatory methods are not accessible, we present experimental methods to evaluate mask filtration and breathability quickly via cost-effective approaches (e.g.,*

~$2000 USD) that could be replicated in communities of need without extensive infrastructure. We demonstrate the need for screening by evaluating an existing diverse inventory of masks/respirators from a local hospital.
Methods: Two experimental approaches are presented to examine both aerosol filtration and flow impedance (i.e., breathability). For one of the approaches ("quick assessment"), screening for appropriate filtration could be performed under 10 min per mask, on average. Mask fit tests were conducted in tandem but are not the focus of this study.
Results: Tests conducted of 47 nonregulation masks reveal variable performance. A number of commercially available masks in hospital inventories perform similarly to N95 masks for aerosol filtration of 0.2 µm and above, but there is a range of masks with relatively lower filtration efficiencies (e.g., <90%) and a subset with poorer filtration (e.g., <70%). All masks functioned acceptably for breathability, and impedance was not correlated with filtration efficiency. »

4. International organisations

Centers for Disease Control and prevention. Yip L, Bixler D, Brooks DE, et al. **Serious Adverse Health Events, Including Death, Associated with Ingesting Alcohol-Based Hand Sanitizers Containing Methanol — Arizona and New Mexico, May–June 2020.** *MMWR Morb Mortal Wkly Rep*. 2020;69(32):1070-1073. doi:10.15585/mmwr.mm6932e1

Summary. *« What is already known about this topic? Alcohol-based hand sanitizers should only contain ethanol or isopropanol, but some products imported into the United States have been found to contain methanol.*
What is added by this report? From May 1 through June 30, 2020, 15 cases of methanol poisoning were reported in Arizona and New Mexico, associated with swallowing alcohol-based hand sanitizers. Four patients died, and three were discharged with visual impairment.
What are the implications for public health practice? Alcohol-based hand sanitizer products should never be ingested. In patients with compatible signs and symptoms or after having swallowed hand sanitizer, prompt evaluation for methanol poisoning is required. Health departments in all states should coordinate with poison centers to identify cases of methanol poisoning. »

Europol. **No safe market for fakes: 21 countries target illegal goods in Europe-wide sting | Europol.** Press Release. Published September 25, 2020. Accessed October 16, 2020. https://www.europol.europa.eu/newsroom/news/no-safe-market-for-fakes-21-countries-target-illegal-goods-in-europe-wide-sting

Extract from the text. *« Europe-wide operation Aphrodite has brought together 21 countries* to target counterfeit goods trafficking. The eight-month operation was co-led by the Italian Finance Corps (Guardia di Finanza) and the Irish National Police (An Garda Síochána) with support from Europol. From December 2019 to July 2020, law enforcement authorities tracked online sales of a large variety of counterfeit items, culminating in checks in warehouses, shops and marketplaces in Belgium, Cyprus, Greece, Ireland, Italy, Portugal, Romania and Spain.*
Law enforcement find fake COVID-19 medical equipment among the seizures. The operation led to 123 social media accounts and 36 websites selling counterfeit products to be taken down. During the operation, law enforcement authorities seized nearly 28 million illegal and counterfeit goods among which were 800 000 counterfeit items of clothing, sportswear, footwear, personal accessories, IPTV set-top boxes and toys. Ten people were arrested in Greece and 37 others were reported to the judicial authorities in Greece, Italy and Portugal. More than €700 000 was also seized. The COVID-19 outbreak led the involved authorities to adapt the initial scope of the operation to focus on issues triggered by the pandemic. As a result, counterfeit and not compliant medical equipment was also seized, including 27 million medical facemasks, by the Italian Finance Corps (Guarda di Finanza).»

5. Miscellaneous

GS1. Jonasson P, Board E, Clemens R, Van Der Wilden E, Voorspuij J. **Sustainable post-COVID-19 supply chain recovery through global data standards: Building a resilient supply chain through product identification and data sharing A contribution to the Policy Hackathon on Model Provisions for Trade in Times of Crisis and Pan.** 2020. Accessed October 8, 2020. https://www.unescap.org/sites/default/files/113%20Final-Team%20Patrik%20Jonasson-GS1.pdf

> Extract of the text. *« Comprehensive product quality and supply chain security requires a multilayer approach that includes prevention, detection, and response strategies and actions. To address the issue of substandard and falsified medical products, regulators, industry stakeholders, representatives from non-governmental organizations, international organizations, and academics came together to create the "APEC Roadmap to Promote Global Medical Product Quality and Supply Chain Security: Supply Chain Security Toolkit"."*

Published in August

Aidspan. Boulanger C, Amendah D. **Corruption, fraud and disinformation during the Coronavirus disease 2019: heightened vigilance is necessary.** 2020 August 26. Accessed October 8, 2020. https://www.aidspan.org/en/c/article/5264

> Abstract. *International donors, including the Global Fund to Fight AIDS, Tuberculosis and Malaria, promptly made funds available to assist the fight of the COVID-19 pandemic. It is important to assess whether existing mechanisms, including the Global Fund's "three-line defense model," can be used to manage risk in the context of the COVID-19 crisis. Allegations of fraud and corruption are multiplying across countries. Aidspan relies on civil society organizations to help maintain accountability in this COVID-19 pandemic.*

6. Lay literature

6.1 Disclaimer & Notes

The information included below is based on the data used to create the Medicine Quality Monitoring Globe[7] (MQM Globe). It contains publicly available information on the quality of medical products from non-peer-reviewed lay literature. We report the information as it is stated in the articles and can thus be biased towards the authors perspective. It does not necessarily reflect our vision or judgment on the issue. Also, this information usually will not have scientific confirmation. Therefore, the information needs to be interpreted with the greatest caution. We regard the reports as early warnings of potential problems. No or few articles from a region does not imply that the medical product quality there is good, but probably reflects a lack of accessible information. Full disclaimer and caveats can be found at MQM Globe disclaimer and caveats[8].

The Google News search tool is used to capture data from online news sources. Articles matching the search terms are loaded into a database and curated by trained analysts. Because the Globe system extracts newspaper articles from journals referenced in Google News only, reports not referenced in Google News would not be captured. Please consult the IDDO website for full methodology[9]. On the 20th of March, the search terms were adapted to capture more papers on substandard and falsified (SF) medical supplies for COVID-19.

The news articles discussed in the sections below are available in the Globe-reports, in this report's annexes, or on the online MQM Globe using the report ID (six digits code). The MQM Globe-reports are generated with pre-defined search terms, which enable quick access to reports of (a) COVID diagnostics, (b) Personal protective equipment, (c) COVID medicines, and (d) Ventilators and Positive end-expiratory pressure.

In this report we share articles captured by the MQM Globe that are linked to medical products potentially used in the context of COVID-19 or to active pharmaceutical ingredients (APIs) that are being trialled for COVID-19 treatment and/or prevention. In theory there is a distinction between (a) SF incidents that are due to or increased by the COVID-19 epidemic; and (b) incidents that would have happened in any case. It can be difficult to make the distinction between the two types of incidents and some reports cited below are not directly linked to the treatment of COVID-19. Nevertheless we have included them as crossover risks and to assess the evolution of the alerts on

[7]Infectious Diseases Data Observatory. Medicine Quality Monitoring Globe. Web Page. Published 2020. Accessed October 16, 2020. https://www.iddo.org/medicine-quality-monitoring-globe

[8] Infectious Diseases Data Observatory. Medicine Quality Monitoring Globe disclaimer and caveats. Web Page. Published 2020. Accessed October 19, 2020. https://www.iddo.org/medicine-quality-monitoring-globe-disclaimer-and-caveats

[9]Infectious Diseases Data Observatory. Medicine Quality Monitoring Globe methodology. Web Page. Published 2020. Accessed October 19, 2020. https://www.iddo.org/medicine-quality-monitoring-globe-methodology

these medical products over time. Although oxycodone is trialled in two studies[10,11], we do not include issues related to oxycodone as the system would become swamped by reports on its inappropriate use and cases of pills laced with fentanyl due to its wide occurrence on the black market.

For this report, we only included data that were published in English. For articles in French, Spanish, Mandarin, and Vietnamese; please consult the online MQM Globe. We will continuously work to improve the MQM Globe and plan to add in articles in other languages to this report. Any remarks or additions to content are encouraged (please write to medicinequality@iddo.org).

6.2 Articles on SF medical products for COVID-19 – main characteristics

Since the beginning of the pandemic we have identified 380 relevant articles on quality problems of COVID-19 medical products. For the month of September we report on 53 articles linked to SF COVID-19 supplies alerted through the MQM Globe database (see table 1). Within those articles, 2 alerted on vaccines, 8 on diagnostics, 16 on COVID-19 related treatments and 33 are linked to personal protective equipment (PPE) (see figure 1). Similar to July and August, the MQM Globe did not identify any report linked to ventilation equipment in September.

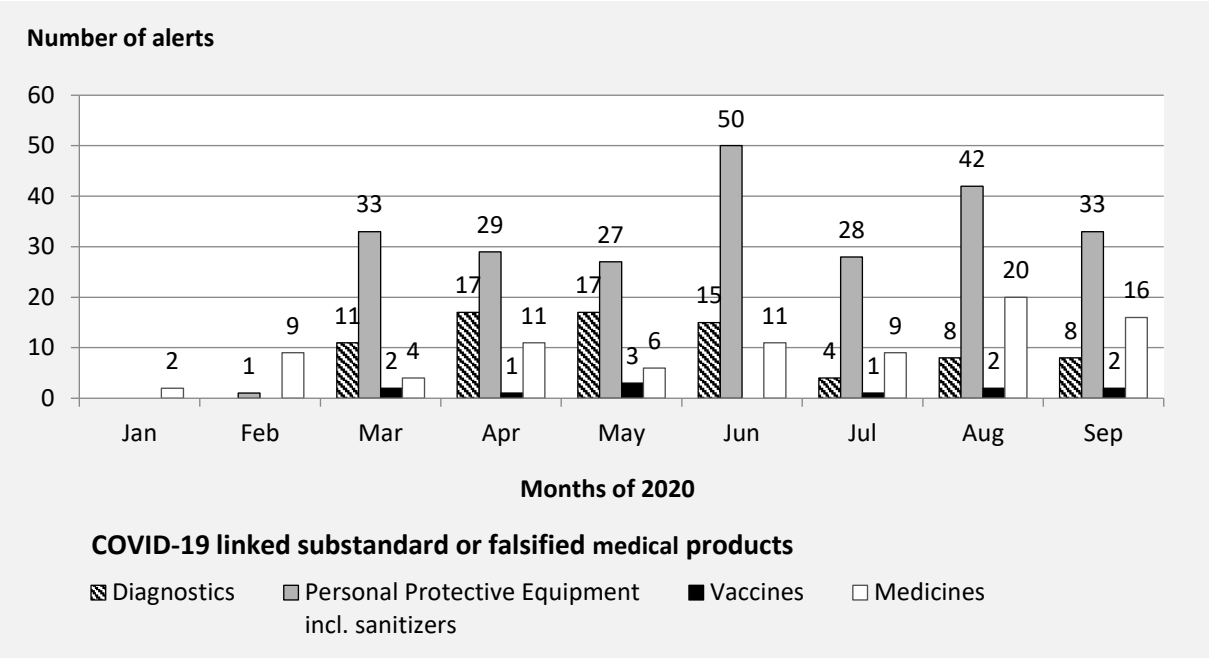

Figure 1. Number of alerts on the Medicines Quality Monitoring Globe by category of products and by month.
ALERTS ARE FOR SUBSTANDARD OR FALSIFIED PRODUCTS LINKED TO COVID-19. AS SOME ARTICLES DESCRIBE MORE THAN ONE CATEGORY OF PRODUCTS, THE SUM OF ALERTS PER MONTH MAY EXCEED THE SUM OF ARTICLES PER MONTH REPORTED IN TABLE 1.

[10]Ghanei M. Safety and Efficacy of Hydroxychloroquine + Favipiravir Drug Regimen in Comparison With Hydroxychloroquine + Kaletra on the Need for Intensive Care Unit Treatment in Patients With COVID-19. Iranian Registry of Clinical Trials. Published April 8, 2020. Accessed October 9, 2020. https://en.irct.ir/trial/46968
[11]Hashemian SRM. Evaluation the effects of Oxycodone administration on pain control in patients with COVID-19. Iranian Registry of Clinical Trials. Published June 8, 2020. Accessed October 9, 2020. https://en.irct.ir/trial/48534

Table 1. Number of articles on the Medicines Quality Monitoring Globe linked to substandard or falsified COVID-19 supplies by month. AS SOME ARTICLES DESCRIBE MORE THAN ONE CATEGORY OF PRODUCTS, THE SUM OF ALERTS PER MONTH AS SHOWN IN FIGURES 1 AND 2 MAY EXCEED THE SUM OF ARTICLES PER MONTH OF TABLE 1.

Month	Number of articles
January	2
February	10
March	49
April	50
May	47
June	64
July	42
August	62
September	**53**

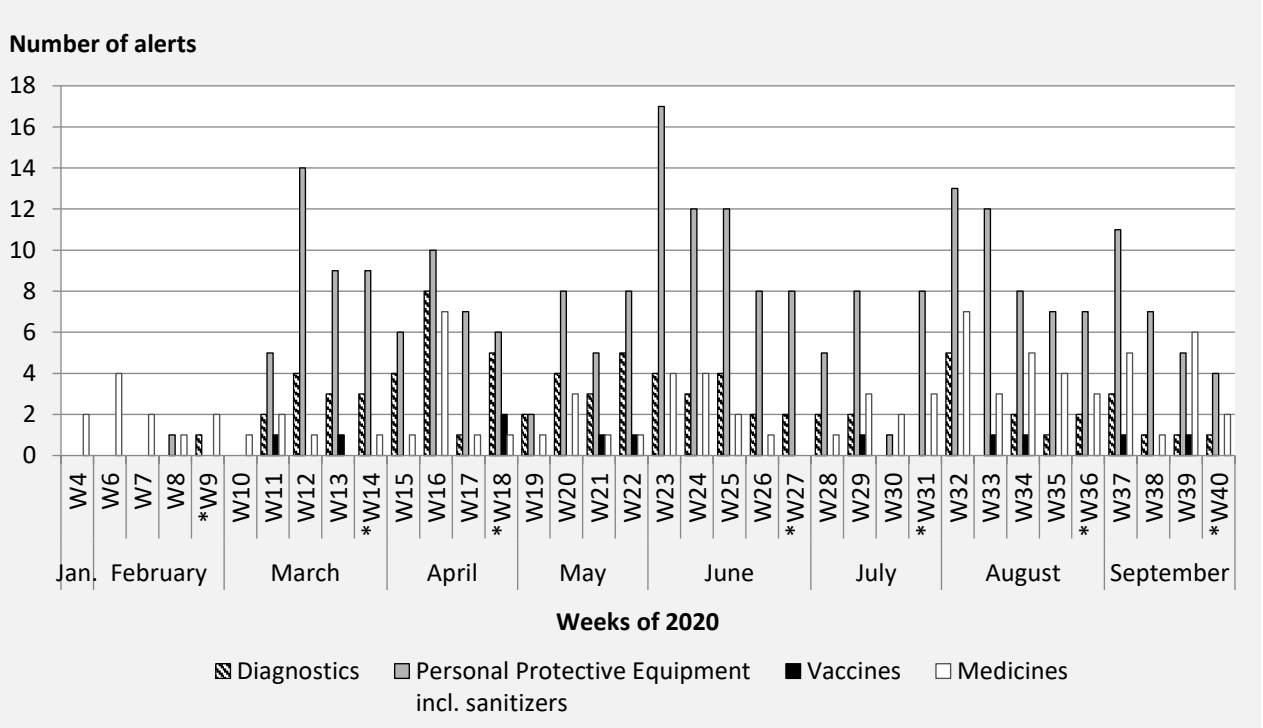

Figure 2. Number of alerts on the Medicines Quality Monitoring Globe by category and by week. ALERTS ARE FOR SUBSTANDARD OR FALSIFIED PRODUCTS LINKED TO COVID-19. WEEK 4 STARTS ON MONDAY 20TH OF JANUARY 2020 AND WEEK 40 ENDS ON WEDNESDAY 30TH OF SEPTEMBER 2020. WEEKS WITH AN ASTERISK ARE OVERLAPPING 2 MONTHS, EACH TIME THE WEEK IS ATTRIBUTED TO THE EARLIEST MONTH. AS SOME ARTICLES DESCRIBE MORE THAN ONE CATEGORY OF PRODUCTS, THE SUM OF ALERTS PER MONTH MAY EXCEED THE SUM OF ARTICLES PER MONTH REPORTED IN TABLE 1.

Online substandard and falsified products

An abundant presence of COVID-19 related SF products continues to be available online. The articles addressing all types of online COVID-19 products are discussed in this section. One article goes deeper into the sales of online COVID-19 products on the darknet: COVID-19 testing kits, vaccines, hydroxychloroquine pills and used facemasks (report ID 723812). It displays how darknet sellers found a way to make money during the pandemic by diversifying their portfolio. An interviewed darknet

vendor however claims not only to have financial motives for its business but really wants to save lives.

In the August report, we shared the study published by Mackey et al. 2020 on COVID-19 products offered on Twitter and Instagram during the months March to May[12]. An article in the lay press picked up on the paper explaining that there are waves of products on offer on social media platforms as demand and supply of these products change in the market (report ID 713833). For example, a first wave of preventive treatments was followed by a second wave of unapproved diagnostics products and PPE. With increased testing capacity the offer of COVID-19 testing kits went down on social media. The growing third wave consists of falsified pharmaceutical treatments.

The United States (US) Food and Drug Administration (FDA) has repeated its warning for consumers to raise awareness for (online) misleading COVID-19 products (report ID 722073). They have seen unauthorised COVID-19 testing kits and medicines, and they warn of other fraudulent products such as medical devices and vaccines. The article mentions several actions taken by the FDA to protect consumers from SF products: removing misleading products from the physical and online market, actively monitoring the sales (of online platforms), issuing warning letters to companies (examples of warning letters are report ID 723098 and 723165), increasing enforcement at ports of entry, and performing seizures (examples of seizures at ports of entry are report ID 727707 and 732067).

6.3 Vaccines

Dozens of coronavirus vaccines are sold online according to an article in the USA (report ID 723812). In India several media reported on a falsified COVID-19 vaccine in Odisha state (report ID 742841). Authorities raided a manufacturing unit and seized vials labelled as “COVID-19 vaccine”. Allegedly the product had not been sold yet. The owner was arrested but refused to reveal the composition of the falsified product, and further inspection is continuing. Interestingly our system also highlighted an article discussing the introduction of blockchain technology in Telangana State to combat against substandard and falsified COVID-19 vaccines[13]. UNICEF uses blockchain technology, Vaccine Ledger, that would provide information on the product while moving through the supply chain.

[12] Mackey TK, Li J, Purushothaman V, et al. Big Data, Natural Language Processing, and Deep Learning to Detect and Characterize Illicit COVID-19 Product Sales: Infoveillance Study on Twitter and Instagram. JMIR Public Heal Surveill. 2020;6(3):e20794. doi:10.2196/20794

[13] Sur A. Telangana to combat black marketing of COVID-19 vaccine via blockchain. The New Indian Express. Published September 28, 2020. Accessed October 15, 2020. https://www.newindianexpress.com/states/telangana/2020/sep/28/telanganato-combat-black-marketing-of-COVID-19-vaccine-via-blockchain-2202846.html

6.4 COVID-19 diagnostics

The police arrested the head of a manufacturing unit in the Indian state of Uttar Pradesh for producing falsified COVID-19 antibodies rapid test kits with forged labels (report ID 746390). Poor quality tests are used at the parliament according to one of the members of the Indian Parliament, Lok Sabha (report ID 729474). There is no indication in the article if the tests were falsified or substandard.

In the USA the FBI warned for falsified COVID-19 test kits sold door-to-door, via telemarketing calls and via social media platforms (report ID 719163). The FDA confirmed that unauthorized COVID-19 testing kits are sold online (report ID 722073). A darknet dealer allegedly sold IgM/IgG Rapid Tests to medical centres in Italy and the USA after buying them directly from manufacturers in Germany and Korea (report ID 723812). He also claims that some governments are buying COVID-19 testing kits on the darknet. Customs in the USA reported seizures of COVID-19 test cards, rapid kits and detection kits (report ID 740485).
Following online advertisement Kenyan authorities tracked down a shop that was allegedly selling falsified COVID-19 test kits (report ID 713707).

6.5 Personal protective equipment including sanitizers

Thirty-three articles are linked to SF equipment used in the protection against SARS-COV-2. Twenty articles report exclusively on SF personal protective equipment (PPE), out of which the majority discuss masks and respirators and two discuss gloves. Nine articles reported on problems with SF hand sanitizers. Other articles discuss a combination of products.

6.5.1 Personal Protective Equipment

Falsified nitrile gloves were sold to front-line workers in the USA (report ID 728784). The police raided an unlicensed factory and seized 900,000 pairs of ‘medical’ gloves in Thailand (report ID 723710). The gloves did not meet the national standards and allegedly it were used gloves repacked in boxes to make them look as new.

SF masks in Taiwan

In August problems of SF masks in Taiwan came to light. The Taiwanese authorities tightened inspections on import and sales to track falsified masks. In September several articles pointed on a growing number of SF mask issues. Problems occurred at suppliers that are part of the government’s mask rationing system and at entities that are not in the national team of suppliers.
Chinese masks labelled with the wrong origin: The Ministry of Economic Affairs tracked down two Taiwanese mask producing companies which were selling non-medical grade Chinese masks as “Made in Taiwan”. The first company was importing and repacking over 3 million Chinese masks as ‘Carry Mask’ to repurpose them for the Taiwan mask rationing system. The fraud was uncovered after complaints of pharmacies of labels in simplified Chinese script (report ID 714826). The second company was Haw Ping Co which allegedly imported over 7 million masks from China

selling them as “Made in Taiwan” (report ID 722442).
Falsified masks of unknown origin: Over 600,000 non-medical grade masks were packed to look like a genuine product from the official manufacturer Hung Wei Medical Consumable Co. of Taiwan (report ID 719567). The source of the masks is unknown. The owner of the company has been detained for allegedly supplying pharmacies with the falsified product.
Production of falsified masks: A clandestine Taiwanese mask factory was producing masks falsely labelled as manufactured by Taiwan Pro-Level Papers International Co and falsely using the companies medical device license number on the packaging (report ID 723919). During a raid 400,000 masks were seized together with raw materials to potentially produce over an additional 2.5 million masks. A suspect was detained for allegedly selling 750,000 falsified masks to pharmacies across the country.
Selling unapproved masks: A shop of the drugstore chain Great Tree Pharmacy has allegedly been selling masks made in Philippines as masks of the official Taiwanese mask rationing system (report ID 729679). A client noticed the masks were not “Made in Taiwan”, but were labelled as “Med Tecs” from the Philippines. Great Tree Pharmacy allegedly has bought the masks through qualified channels and claims it had no intention to act outside the frame of the mask rationing system.

Issues linked to importation

In the USA, the Customs and Border Protection (CBP) seized falsified N95 respirators: 20,400 coming from Hong Kong (report ID 732067) and 500,000 coming from China (report ID 727707). Analysis revealed that 10% of the tested respirators coming from China had a filter efficiency below 95%. Custom officers in Japan seized falsified masks of a Japanese brand (report ID 725140). In the Philippines the Department of Trade and Industry was urged to track down sellers of imported substandard masks (report ID 719408). Some imported masks allegedly do not comply with the Philippine standards. Another problem at the Philippine border involves a shipment that was coming from Singapore declared as PPE, which turned out to be undocumented medicines and ointments (report ID 737299).

Sourcing difficulties for governments and contractors

Articles continue to report on governments facing difficulties with the purchase of masks. In Bangladesh over 20,000 falsified N95 respirators were supplied to 10 health care institutes (report ID 746401). Six officials of the Central Medical Stores Depot and the supplier were held responsible. In India, in Tamil Nadu state, officials received substandard masks from a contractor (report ID 715991). Out of 1.2 million masks almost 600,000 were rejected following quality checks. In the USA, the government contractor MJL enterprise sued Eco Lighting USA Limited Liability Company (report ID 712513). Allegedly Eco Lighting supplied falsified N95 and KN95 respirators to MJL together with certificates falsely claiming the masks were FDA certified.

In the USA the National Institute for Occupational Safety and Health (NIOSH) shared a list of suspected brands of falsified N95 respirators, together with an update on their guidance with regards to falsified respirators and misrepresentation of NIOSH-

approvals (report ID 712648). The article encourages "*Contractors should carefully consider where they buy their masks*".

Miscellaneous

In South Africa four companies were charged and several companies investigated for supplying substandard PPE (report ID 716864). In Bangladesh an article reports on the lack of guidelines and monitoring of the quality of PPE in Bangladesh, creating a vacuum for fraudsters to sell 'substandard' products (report ID 743276). The ECRI, a non-profit patient safety organization, tested the quality of 200 KN95 masks from 15 different manufacturers imported from China into the US (report ID 761005). Result show that 70% did not meet the filtration standards of KN95 masks.

In Morocco a man was arrested for repacking and selling falsified masks and 121,600 masks were seized (report ID 736630). In India falsified N95 respirators are present in the market and clandestine manufacturers have been taken to court (report ID 748680). An article reported on operation Aphrodite, an operation supported by Europol targeting counterfeit goods trafficking that ran from December 2019 to July 2020 (report ID 745185). Due to the pandemic the initial scope was adapted which led, amongst others, to seizures of 27 million falsified and unregistered medical facemasks by the Italian Finance Corps. It is the first alert the MQM-Globe database holds on SF products in Italy.

6.5.2 Sanitizers and disinfectant

The MQM Globe alerted on the first articles on SF hand sanitizers in Nepal. Around 45 percent of hand sanitizers sold on the local market are substandard or falsified according to results published by the Nepal Academy of Science and Technology (report ID 730915). In September the Nepal Department of Drug Administration banned hand sanitizers from nine companies due to high amounts of methanol (report ID 725135, 730915). At least seven of the companies were based in Nepal and one in India.
The Indian Central Drugs Standard Control Organization (CDSCO) released the monthly routine quality tests on a range of pharmaceutical products results for August. Eight hand sanitizers were declared as "Not of Standard Quality", after failing the tests for the identification of isopropyl alcohol and/or assay of ethyl/isopropyl alcohol (report ID 727310).

During the month of September the US FDA continued to add hand sanitizers to their Do-Not-Use-List[14] (report ID 724196, 732787, 745249). Several retail chains, unknowingly selling methanol containing products, launched recalls. Although more than twenty products were added, the growth of the list slowed down compared to the previous months June, July and August. The vast majority of products on the FDA's Do-Not-Use-list are allegedly coming from Mexico. An article in the Mexico News Daily expressed the concern that several products that are banned in the USA, are still

[14]United States Food and Drug Administration. FDA updates on hand sanitizers consumers should not use. Drug Safety and Availability. Published June 19, 2020. Accessed October 19, 2020. https://www.fda.gov/drugs/drug-safety-and-availability/fda-updates-hand-sanitizers-consumers-should-not-use

available in Mexico (report ID 723274). For example the company 4E Global, which has 37 hand sanitizers on the Do-Not-Use-list, mentions on its English language website about some products containing methanol. Whereas the Spanish language website does not mention any problem of methanol or product recall.

On the British Virgin Islands the Ministry of Health warned about falsified hand sanitisers sold on their market (report ID 719716). The Nigerian National Agency for Food and Drugs Administration and Control (NAFDAC) seized 13 brands of falsified sanitizers in supermarkets and drug retail outlets (report ID 741664). All of them were stated as produced in Nigeria.

6.6 COVID-19 medicines

Remdesivir and corticosteroids have shown to be beneficial in the treatment of some well-defined subgroups of COVID-19 patients. For the month of September the MQM Globe does not hold reports of SF corticosteroids. In India a batch of Remdesivir was found to be substandard and has been withdrawn from the market (report ID 739155). Following the withdrawal there were concerns about supply shortages.

Many other repurposed and investigational antiviral and immune-based COVID-19 therapies are being trialled[15]. In addition patients turn to some medicines that are generally used for a cold, pain, fever or to boost the immunity. For all these medicines vigilance is needed considering the risk of substandard or falsified versions.

In September there was an article on falsified tocilizumab in India (report ID 748338). A medical store owner has been arrested for producing falsified tocilizumab using asthma medicines.
The Indian CDSCO released the results of their monthly routine quality tests. In August samples of prazosin, amoxicillin-clavulanic, and vitamin complexes containing vitamin C were reported as “Not Of Standard Quality” (report ID 727310).
In the USA there are litigations against some pharmacy stores for multiple reasons. One being that the “pharmacies failed to detect the sale of allegedly contaminated valsartan” (report ID 736772).
As in previous months SF sildenafil, a well-known medicine for erectile dysfunction, was reported. Studies for its use in the treatment of COVID-19 are ongoing[16]. A couple have been found guilty for importing sildenafil into the USA wrongly labelled as dietary supplements (report ID741030). In the UK a convenience store was allegedly illicitly selling this pharmacy controlled drug (report ID 746374). Two articles report on

[15]Infectious Diseases Data Observatory. COVID-19 Clinical Trials Interactive tool. Published 2020. Accessed October 19, 2020. https://www.iddo.org/tool/COVID-19-clinical-trials-interactive-tool

[16] Ning Q (Tongji Hospital). A Pilot Study of Sildenafil in COVID-19. U.S. National Library of Medicine - Clinical Trials. Published 2020. Accessed October 14, 2020.
https://clinicaltrials.gov/ct2/show/NCT04304313?term=sildenafil&cond=COVID19&draw=2&rank=2
Lomakin FM (Universidad NAB). Sildenafil in COVID-19. U.S. National Library of Medicine - Clinical Trials. Published 2020. Accessed October 14, 2020.
https://clinicaltrials.gov/ct2/show/NCT04489446?term=sildenafil&cond=COVID19&draw=2&rank=1

sildenafil as a hidden drug ingredient in sexual enhancement products in the USA (report ID 722151) and in Nigeria (report ID 739955).

Falsified Lian Hua Qing Weng capsules were seized by the Philippine FDA (report ID 741529). The traditional medicine is used in China for the treatment of COVID-19, however in Philippines this indication is not approved. The US FDA sent a warning letter to Extrapharma, a company offering arbidol and claiming that it has activity against coronavirus, whereas Extrapharma has no approved drug application for its arbidol product and the FDA has not approved its use in COVID-19 (report ID 723098). Pharmacy owners were fined for the production and distribution of “Anti-Coronavirus” medication in Ukraine (report ID 740873). A seizure of medicines smuggled from Guinea into Liberia contained painkillers, multi vitamins, and cold caps (report ID 711310).

7. Annexes

The annexes contain the reports generated by the MQM-Globe using pre-defined search terms. The report IDs (six digits code) discussed in section 6 ‘Lay literature’ are detailed in the annexes. To consult the annexes, please see the extended version of the report and/or consult the online MQM Globe[17], using the report ID in the search box.

[17]Infectious Diseases Data Observatory. Medicine Quality Monitoring Globe. Web Page. Published 2020. Accessed October 16, 2020. https://www.iddo.org/medicine-quality-monitoring-globe