Medical Product Quality Report – COVID-19 Issues

Issue 1. January to June 2020

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IDDO INFECTIOUS DISEASES DATA OBSERVATORY

Contents

1 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, 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. A group of 54 signatories from 20 different countries expressed their concerns on the negative effects of the pandemic on the quality of medicines and the integrity of the supply chain and argued for urgent planning to prevent, detect and respond to these issues[1].

We use the terminology for different types of poor quality medical products as defined by the World Health Organisation (WHO 2017)[2]:

> **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'[3] and 'pirated copyright goods'[4] as used in the Trade-Related Aspects of Intellectual Property Rights (TRIPS) agreement.

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[1] Newton PN, Bond KC. **COVID-19 and risks to the supply and quality of tests, drugs, and vaccines.** *Lancet Glob Health.* 2020 June; 8(6): e754–e755. doi: 10.1016/S2214-109X(20)30136-4. Epub 2020 Apr 9. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7158941/

[2] Source: Appendix 3 to Annex, World Health Assembly document A70/23, 2017: https://www.who.int/medicines/regulation/ssffc/A70_23-en1.pdf?ua=1

[3] '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: https://www.wto.org/english/docs_e/legal_e/27-trips_05_e.htm#fnt-14.

[4] '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: https://www.wto.org/english/docs_e/legal_e/27-trips_05_e.htm#fnt-14.

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 trialed for COVID-19's prevention or treatment. We do not aim to include discussion of the multiple fraudulent claims and quackery. 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.

The reports presented were mostly extracted from the Medicines Quality Monitoring Globe (MQM Globe)[5], 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.

Please note the caveats for the lay literature (https://www.iddo.org/medicine-quality-monitoring-globe-disclaimer-and-caveats); 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 first issue covers January 1st to June 30th 2020. We plan to issue further reports in the middle of every month detailing COVID-19 medical product SF medical product issues described in the previous month. We are developing a system for scraping regulatory authority and international organisation websites for alerts that we will also include. Any remarks or additions to content are greatly appreciated (please write to medicinequality@iddo.org).

2 Scientific literature

2.1 General

Newton PN, Bond KC. **COVID-19 and risks to the supply and quality of tests, drugs, and vaccines.** *Lancet Glob Health.* 2020 June;8(6): e754–e755. doi: 10.1016/S2214-109X(20)30136-4. Epub 2020 Apr 9. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7158941/

> A group of 54 signatories from 20 countries led by Paul Newton and Katherine Bond discussing reflections on the negative effects of the COVID-19 pandemic for quality of medical products, but also for the integrity of supply chains and argue for urgent planning to prevent, detect and respond to these issues.

[5] IDDO. **Medicine Quality Monitoring Globe**: https://www.iddo.org/mqmglobe/

Abena PM, Decloedt EH, Bottieau E, Suleman F, Adejumo P, Sam-Agudu NA, Muyembe TamFum JJ, Seydi M, Eholie SP, Mills EJ, Kallay O, Zumla A, Nachega JB. **Chloroquine and Hydroxychloroquine for the Prevention or Treatment of COVID-19 in Africa: Caution for Inappropriate Off-label Use in Healthcare Settings.** *Am J Trop Med Hyg*. 2020 June; 102(6):1184-1188. doi: 10.4269/ajtmh.20-0290. Epub 2020 Apr 22. https://pubmed.ncbi.nlm.nih.gov/32323646/

> Abstract. "*The novel severe acute respiratory syndrome-coronavirus-2 pandemic has spread to Africa, where nearly all countries have reported laboratory-confirmed cases of novel coronavirus disease (COVID-19). Although there are ongoing clinical trials of repurposed and investigational antiviral and immune-based therapies, there are as yet no scientifically proven, clinically effective pharmacological treatments for COVID-19. Among the repurposed drugs, the commonly used antimalarials chloroquine (CQ) and hydroxychloroquine (HCQ) have become the focus of global scientific, media, and political attention despite a lack of randomized clinical trials supporting their efficacy. Chloroquine has been used worldwide for about 75 years and is listed by the WHO as an essential medicine to treat malaria. Hydroxychloroquine is mainly used as a therapy for autoimmune diseases. However, the efficacy and safety of CQ/HCQ for the treatment of COVID-19 remains to be defined. Indiscriminate promotion and widespread use of CQ/HCQ have led to extensive shortages, self-treatment, and fatal overdoses. Shortages and increased market prices leave all countries vulnerable to substandard and falsified medical products, and safety issues are especially concerning for Africa because of its healthcare system limitations. Much needed in Africa is a cross-continental collaborative network for coordinated production, distribution, and post-marketing surveillance aligned to low-cost distribution of any approved COVID-19 drug; this would ideally be piggybacked on existing global aid efforts. Meanwhile, African countries should strongly consider implementing prescription monitoring schemes to ensure that any off-label CQ/HCQ use is appropriate and beneficial during this pandemic."*

Ippolito M, Gregoretti C, Cortegiani A, Iozzo P. **Counterfeit filtering facepiece respirators are posing an additional risk to health care workers during COVID-19 pandemic.** *Am J Infect Control*. 2020 Jul; 48(7):853-854. doi: 10.1016/j.ajic.2020.04.020. Epub 2020 Apr 29. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7189852/

> A reflection on the use and emergence of substandard and falsified filtering face piece respirators in the context of the current COVID-19 pandemic. They refer to the Centre for Disease Control and Prevention that listed out some characteristics that might point in the direction of falsified respirators (such as no name or altered name on the packing, no approval number, ear loops, decorative materials, etc).

Schneider M, Ho Tu Nam N. **Africa and counterfeit pharmaceuticals in the times of COVID-19.** *J. Intellect. Prop. Law & Practice.* Online ahead of print: jpaa073. doi: 10.1093/jiplp/jpaa073. Epub 2020 May 1. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7197578/

> Extract from the paper. *"At a time where counterfeit and substandard medications and critical medical supplies, such as hand sanitizers and face masks, are flooding the world market due to the COVID-19 pandemic, the 2020 report from the Organisation for Economic Co-operation and Development and the European Union Intellectual Property Office on 'Trade in Counterfeit Pharmaceutical Products' finding that trade in falsified medicine reached USD 4.4 billion in 2016, threatening public health and safety, while enriching criminals and organized crime, is very timely"*

Fairgrieve D, Feldschreiber P, Howells G, Pilgerstrofer M QC. **Products in a Pandemic: Liability for Medical Products and the Fight against COVID-19.** *Eur J Risk Regul*. 2020 May 20; doi: 10.1017/err.2020.54. Epub 2020 May 20. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7302949/

> Extract from the paper. *"A multitude of medical products are being developed and produced as part of efforts to tackle COVID-19. They are varied in nature and range from test kits to tracing apps, protective equipment, ventilators, medicines and, of course, vaccines. The design, testing and manufacture of many of these products differs from production in normal times due to the urgency of the situation and the rapid increase in demand created by the pandemic. This article considers the legal issues arising as a*

result of the production of emergency products, particularly from a products liability perspective. To what extent do existing concepts under the European Product Liability Directive, such as defect, causation and the various defences, permit the pandemic to be taken into account when a Court is considering issues of liability? What is the impact on liability of the modified regulatory regime? In light of that discussion, the case for alternative responses is examined from a comparative and European perspective, including the issue of Government indemnities for the manufacturers of products, legal exemptions from liability and alternative no-fault compensation schemes."

Gurvich VJ, Hussain AS. **In and Beyond COVID-19: US Academic Pharmaceutical Science and Engineering Community Must Engage to Meet Critical National Needs.** *AAPS PharmSciTech*. 2020 Jul; 21(5):153. doi: 10.1208/s12249-020-01718-9. Epub 2020 May 24. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7245992/

Abstract. "*The supply of affordable, high-quality pharmaceuticals to US patients has been on a critical path for decades. In and beyond the COVID-19 pandemic, this critical path has become tortuous. To regain reliability, reshoring of the pharmaceutical supply chain to the USA is now a vital national security need. Reshoring the pharmaceutical supply with old know-how and outdated technologies that cause inherent unpredictability and adverse environmental impact will neither provide the security we seek nor will it be competitive and affordable. The challenge at hand is complex akin to redesigning systems, including corporate and public research and development, manufacturing, regulatory, and education ones. The US academic community must be engaged in progressing solutions needed to counter emergencies in the COVID-19 pandemic and in building new methods to reshore the pharmaceutical supply chain beyond the pandemic."*

Ogar C, Mathenge W, Khaemba C, Ndagije H. **The challenging times and opportunities for pharmacovigilance in Africa during the COVID-19 pandemic.** *Drugs Ther Perspect*. Online ahead of print. doi: 10.1007/s40267-020-00748-4. Epub 2020 May 26. https://europepmc.org/article/pmc/pmc7249980

Extract from the paper. "*Hidden effects of irrational use of medicines and medical products; Whereas access to treatment is a major priority in any emergency health situation such as the COVID-19 pandemic, patient safety must not be compromised by the need for access. Access to the wrong, poor quality, or unsafe product might have worse consequences than lack of access. The past weeks of the global pandemic have seen reports of increased sales and perhaps hoarding of some medical products, such as chloroquine, hydroxychloroquine, and lopinavir/ritonavir, in some countries, as well as increased sales of fake medical products and medicines related to COVID-19, such as face masks, hand sanitizers, and antiviral medications."*
"In the absence of a scientifically verified treatment or vaccine, numerous remedies (conventional and non-conventional) have been touted for treating or preventing the disease. Given the relatively low literacy levels and poorly regulated healthcare practices in Africa, some of the 'remedies' pose potential risks to patient safety. Drug safety practitioners need to be vigilant about these risks and strengthen reporting systems to document, characterize, communicate, and minimize the risks of such remedies."

Climent-Ballester S., Selva-Otaolaurruchi J. **Hospital Pharmacy: Comprehensive Management of Medical Devices During SARS-CoV-2.** *Farm Hosp.* 2020 Jun 14; 44(7):21-23. doi: 10.7399/fh.11486. http://www.aulamedica.es/fh/pdf/11486.pdf

Abstract. *"Medical devices have become essential to the prevention and control of the COVID-19 pandemic, being crucial for health professionals and patients in particular, and the population in general. It is important to be aware of the laws that regulate the management, distribution, and control of medical devices. Article 82 of the Spanish Law 29/2006 on Guarantees and Rational Use of Medicines and Medical Devices establishes that it is the responsibility of Hospital Pharmacy Services "to participate in and coordinate the purchase of medicines and medical devices in the hospital to ensure an efficient acquisition and rational use of medical devices". For this reason, working groups of the Spanish Society of Hospital Pharmacy and other scientific societies have issued technical guidelines and consensus*

statements to provide technical support and updated information on the use of masks, individual protection equipments and other medical devices. In addition, the shortage of medical devices caused by the high demand has resulted in the uncontrolled production and distribution of medical devices. This phenomenon, added to the fraudulent selling of medical devices, highlights the need for a closer surveillance of the market to guarantee the efficacy and safety of available medical devices. A rational use of medical devices is necessary to ensure the availability and safety of these products, which requires the involvement of different stakeholders, including hospital pharmacists. Thus, it is essential that hospital pharmacists receive specific training in technical aspects concerning the possession and use of medical devices. This will help guarantee an effective and safe use of medical products. The acquisition and use of medical devices requires a keen understanding of the technical and legal aspects concerning these products, which makes hospital pharmacists essential for the integral management of medical devices."

Alan G Fraser AG, Szymański P, Macintyre E, Landraye M. **Regulating drugs, medical devices, and diagnostic tests in the European Union: early lessons from the COVID-19 pandemic?** *Eur Heart J*. 2020 Jun ; 41(23): 2140–2144. doi: 10.1093/eurheartj/ehaa506. Epub 2020 June 18. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7337778/

Extract from the paper. *"The COVID-19 pandemic has clearly reinforced the need for scientists and physicians collectively to engage with regulators to develop appropriate systems for evaluating and approving both laboratory tests and new medical devices, as well as with the European Medicines Agency for drugs. The Regulatory Affairs committees of the ESC and the Biomedical Alliance in Europe (representing 33 medical specialist associations) nominate colleagues to be stakeholder members of European regulators' committees."*

Moynihan R, Macdonald H, Bero L, Godlee F. **Commercial influence and covid-19.** *BMJ*. 2020 Jun 24; 369:m2456. doi: 10.1136/bmj.m2456. https://www.bmj.com/content/369/bmj.m2456

Extract from the paper. *"There are valid arguments for "regulatory agility" during emergencies such as covid-19, but speed should not undermine basic standards for trustworthy evidence. As a 2017 report on Ebola from the US National Academy of Sciences noted, "despite [the] sense of urgency, research during an epidemic is still subject to the same core scientific and ethical requirements that govern all research on human subjects." Clear evidence of the risk of bias in commercially funded research should drive efforts to develop a new, but equally agile, system of independent evaluation of all tests and treatments."*

Kohler JC, Mackey TK. **Why the COVID-19 pandemic should be a call for action to advance equitable access to medicines.** *BMC Med.* 2020 Jun 25; 18(1):193. doi: 10.1186/s12916-020-01661-3.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7315687/pdf/12916_2020_Article_1661.pdf

A call for action to reflect on existing frameworks which have proven to work in access to HIV, TB, Malaria etc and the current actions launched since the start of the pandemic. Using both as a catalyst for a global call to action to improve access to COVID-19 treatments and more widely to general improve the long-standing problem of access to essential medicines and other health commodities.

2.2 Seizures/Surveys/Case Reports/Reviews

Jairoun AA, Al-Hemyari SS, Shahwan M. **The pandemic of COVID-19 and its implications for the purity and authenticity of alcohol-based hand sanitizers: The health risks associated with falsified sanitizers and recommendations for regulatory and public health bodies.** *Res Social Adm Pharm*. Online ahead of print: S1551-7411(20)30393-4. doi: 10.1016/j.sapharm.2020.04.014. Epub 2020 Apr 20. https://pubmed.ncbi.nlm.nih.gov/32334979/

> Abstract. "*With the beginning of the pandemic of COVID-19 throughout the world, the demand and consumption of hand sanitizers has increased, which had led to a sharp crunch in these products at all levels. This shortage has led to an increase in the prevalence of falsified alcohol-based hand sanitizers, including the illegal addition of methanol to hand sanitizers and the production of hand sanitizers with an alcohol concentration of less than 60%. These findings indicate that regulatory and public health bodies should take an active role in ensuring the safety and quality of antimicrobial products such as alcohol-based hand sanitizers at every stage of the products' lifecycle, including distribution, manufacture and import.*"

Gnegel G, Hauk C, Neci R, Mutombo G, Nyaah F, Wistuba D, Häfele-Abah C, Heide L. **Identification of Falsified Chloroquine Tablets in Africa at the Time of the COVID-19 Pandemic.** *Am J Trop Med Hyg*. Online ahead of print: tpmd200363. doi: 10.4269/ajtmh.20-0363. Epub 2020 May 12. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7263564/

> Abstract. "*Reports that chloroquine and hydroxychloroquine may be effective against COVID-19 have received worldwide attention, increasing the risk of the introduction of falsified versions of these medicines. Five different types of falsified chloroquine tablets were discovered between March 31, 2020 and April 4, 2020, in Cameroon and the Democratic Republic of Congo by locally conducted thin layer chromatographic analysis. Subsequent investigation by liquid chromatography and mass spectrometry in Germany proved the absence of detectable amounts of chloroquine and the presence of undeclared active pharmaceutical ingredients, that is, paracetamol and metronidazole, in four of the samples. The fifth sample contained chloroquine, but only 22% of the declared amount. Such products represent a serious risk to patients. Their occurrence exemplifies that once medicines or vaccines against COVID-19 may be developed, falsified products will enter the market immediately, especially in low- and middle-income countries (LMICs). Timely preparations for the detection of such products are required, including the establishment of appropriate screening technologies in LMICs.*"

Lam SC, Suen LKP, Cheung TCC. **Global risk to the community and clinical setting: Flocking of fake masks and protective gears during the COVID-19 pandemic.** *Am J Infect Control.* Online ahead of print. doi: 10.1016/j.ajic.2020.05.008. Epub 2020 May 13. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7219383/

> Extract from the paper. *"We tested 160 brands of masks from different sources and countries. Results showed that low-quality face masks accounted for 48.8% (ie, 0.3 μm PFE, mean = 47%; 1 μm PFE, mean = 69%). Approximately 42.6% of face masks claimed to achieve ASTM level 1 standard (ie, PFE ≥95% on 0.1 μm, provided with certification or printed description on box) but demonstrated insufficient filtration performance at 0.3 μm (range = 6%-94%). Surprisingly, we extracted seven randomly selected boxes (out of 200 boxes) of the same brand (labelled with ASTM level 1 standard), the 0.3 μm PFE of 35 sampled face masks were highly inconsistent, ranging from 29.9% to 99.9%. Only 37.5% of the sampled face masks may potentially achieve the claimed standard. By inspecting the filter layer (melt-blown Polypropylene) through microscope (×1,000), a number of tiny holes and uneven distribution of fiber were observed on face masks with low 0.3 μm PFE. Several face masks (~3.1%) were the counterfeit sourced from internationally well-recognized brands of medical equipment manufacturers. Of which, the 0.3 μm PFE varied considerably from 38% (fake ones) to 99% (good-quality ones). Counterfeit and fake face masks are merely the tip of the iceberg in the personal protective equipment market. However, general public and even health care professionals may be unable to distinguish the counterfeit and fake face masks from those quality one. More importantly, most organizations and hospitals nationwide lack*

the appropriate equipment to initially examine the purchased face masks prior to distribution to different units. It is anticipated that they may face similar difficulty in examining their PPEs, N95 respirators, and surgical gown."

[MedRxiv preprint] Adams ER, Anand R, Andersson MI (and 63 more authors). **Evaluation of antibody testing for SARS-CoV-2 using ELISA and lateral flow immunoassays.** MedRxiv preprint. April 2020. doi: 10.1101/2020.04.15.20066407.
https://www.researchgate.net/publication/340797938_Evaluation_of_antibody_testing_for_SARS-Cov-2_using_ELISA_and_lateral_flow_immunoassays

Abstract. "*Background: The SARS-CoV-2 pandemic caused >1 million infections during January-March2020. There is an urgent need for robust antibody detection approaches to support diagnostics, vaccine development, safe individual release from quarantine and population lock-down exit strategies. The early promise of lateral flow immunoassay (LFIA) devices has been questioned following concerns about sensitivity and specificity. Methods: We used a panel of plasma samples designated SARS-CoV-2 positive (from SARSCoV-2 RT-PCR-positive individuals; n=40) and negative (samples banked in the UK prior to December-2019 (n=142)). We tested plasma for SARS-Cov-2 IgM and IgG antibodies by ELISA and using nine different commercially available LFIA devices. Results: ELISA detected SARS-CoV-2 IgM or IgG in 34/40 individuals with an RT-PCR-confirmed diagnosis of SARS-CoV-2 infection (sensitivity 85%, 95%CI 70-94%), vs 0/50 pre-pandemic controls (specificity 100% [95%CI 93-100%]). IgG levels were detected in 31/31 RT-PCRpositive individuals tested ≥10 days after symptom onset (sensitivity 100%, 95%CI 89-100%). IgG titres rose during the 3 weeks post symptom onset and began to fall by 8 weeks, but remained above the detection threshold. Point estimates for the sensitivity of LFIA devices ranged from 55-70% versus RT-PCR and 65-85% versus ELISA, with specificity 95-100% and 93-100% respectively. Within the limits of the study size, the performance of most LFIA devices was similar. Conclusions: The performance of current LFIA devices is inadequate for most individual patient applications. ELISA can be calibrated to be specific for detecting and quantifying SARSCoV-2 IgM and IgG and is highly sensitive for IgG from 10 days following symptoms onset"*

3 International organisations

3.1 WHO

Medical Product Alert	
N°3/2020: **Falsified medical products, including in vitro diagnostics, that claim to prevent, detect, treat or cure COVID-19** 2020 March 31	*"This Medical Product Alert warns consumers, healthcare professionals, and health authorities against a growing number of falsified medical products that claim to prevent, detect, treat or cure COVID-19. The Coronavirus disease (COVID-19) pandemic (caused by the virus SARS-CoV-2) has increased demand for medicines, vaccines, diagnostics and reagents, all related to COVID-19, creating an opportunity for ill-intended persons to distribute falsified medical products. Due diligence is required from all actors in the procurement, use and administration of medical products, in particular those affected by the current crisis of, or related to, COVID-19. 1. Falsified in vitro diagnostics and laboratory reagents, 2. Falsified medicines and vaccines."* https://www.who.int/news-room/detail/31-03-2020-medical-product-alert-n-3-2020
N°4/2020: **Falsified chloroquine products circulating in the WHO region of Africa.** April 9 (update June 9)	*"This Medical Product Alert relates to several confirmed falsified chloroquine products circulating in the WHO regions of Africa and Europe. New reports of falsified chloroquine which have been validated by WHO are included in this update. Between 31 March and 2 April 2020, the WHO global surveillance and monitoring system on substandard and falsified (SF) medical products received 14 reports of confirmed falsified chloroquine products from 5 countries: Burkina Faso, Cameroon, Democratic Republic of Congo, France, and Niger. All reported products were identified at patient level and all have been confirmed as falsified."* https://www.who.int/news-room/detail/09-04-2020-medical-product-alert-n4-2020
N°5/2020: **Falsified and contaminated Defibrotide identified in WHO regions of Western Pacific, Europe and Eastern Mediterranean** 2020 May 7	*"This Medical Product Alert relates to falsified DEFIBROTIDE 200MG VIALS OF 2.5ML (80MG/ML) CONCENTRATE FOR SOLUTION FOR INFUSION identified in Australia, Latvia and Saudi Arabia. This product is sold under the brand name Defitelio."* https://www.who.int/news-room/detail/07-05-2020-medical-product-alert-n-5-2020

3.2 Europol

Europol. **Viral marketing - counterfeits, substandard goods and intellectual property crime in the COVID-19 pandemic.** *Report*. 2020 April 17. https://www.europol.europa.eu/publications-documents/viral-marketing-counterfeits-substandard-goods-and-intellectual-property-crime-in-covid-19-pandemic

> Extract from the report. *"Counterfeit goods sold during the corona crisis do not meet the required quality standards and pose a real threat to public health and safety. People who buy these fake products have a false sense of security, while they are in fact left unprotected against the virus. Therefore, we should not only go after the criminals behind these scams but also, through prevention work, inform potential victims who are putting themselves and others at risk by using such fake goods."*

Europol. **Beyond the pandemic - how COVID-19 will shape the serious and organised crime landscape in the EU.** *Report*. 2020 April 30. https://www.europol.europa.eu/publications-documents/beyond-pandemic-how-covid-19-will-shape-serious-and-organised-crime-landscape-in-eu

> Extract from the report. *"Serious and organised crime is exploiting the changing circumstances during the pandemic. From the onset of this crisis, Europol monitored these developments to help Member States understand and tackle this emerging phenomena. The full impact of the pandemic – not only on crime but also more widely on society and the economy – is not yet apparent. However, law enforcement should be prepared to be able to respond to the warning signals as the world deals with the fallout of the COVID-19 pandemic. Now more than ever, international policing needs to work with the increased connectivity both in the physical and virtual worlds. This crisis again proves that exchanging criminal information is essential to fighting crime within the law enforcement community. Europol, as the criminal information hub for all law enforcement organisations, will continue to play its part."*

Europol. **EU drug markets: impact of COVID-19.** *Report*. 2020 May 29. https://www.europol.europa.eu/publications-documents/eu-drug-markets-impact-of-covid-19

> Extracts from the report. *"The two EU agencies have joined forces to improve understanding of drug market developments under COVID-19 and their impact on internal security and public health in the EU. The findings are based on opinions collected through a targeted EMCDDA online survey of drug experts in the EU Member States, Europol's operational intelligence gathering on organised crime and structured monitoring of open source information."*
> *"In Czechia, it was reported that a lack of precursors for the production of methamphetamine has led to an increase in the price and a reduction in the quality of methamphetamine in some places. Bulgaria reported a decrease in synthetic drug production combined with a decrease in the availability of drug precursors. Any shortages of precursors may prompt producers to use alternative substances, which may result in unexpected drug products that may present additional risks to consumers."*

3.3 Interpol

Interpol. **Global operation sees a rise in fake medical products related to COVID-19.** *News release.* 2020 March 19. https://www.interpol.int/en/News-and-Events/News/2020/Global-operation-sees-a-rise-in-fake-medical-products-related-to-COVID-19

> Extracts from the news. *"Coronavirus outbreak sparks a new trend in counterfeit medical items. Counterfeit facemasks, substandard hand sanitizers and unauthorized antiviral medication were all seized under Operation Pangea XIII, which saw police, customs and health regulatory authorities from 90 countries take part in collective action against the illicit online sale of medicines and medical*

products. The operation resulted in 121 arrests worldwide and the seizure of potentially dangerous pharmaceuticals worth more than USD 14 million."

Interpol. **COVID-19 pandemic: guidelines for Law enforcement.** *Guidelines*. 2020 March 26. https://www.interpol.int/content/download/15014/file/COVID19_LE_Guidelines_PUBLIC_26mar2020.pdf

Extracts from the report. *"The coronavirus outbreak that began in late 2019 (COVID-19) has evolved so rapidly and globally that it has been qualified as a Public Health Emergency of International Concern and a pandemic by the World Health Organization (WHO). The rapid spread of the disease worldwide, and uncertainties as to its evolution, demand a global response in which law enforcement services play a crucial role in contributing to the effort to control the disease, promoting safer communities, and fighting criminals who see the outbreak as an opportunity to increase or diversify their activities."*

Interpol. **COVID-19: the global threat of fake medicines.** *News release*. 2020 Mai. https://www.interpol.int/en/content/download/15305/file/20COM0356%20-%20IGGH_COVID-19%20threats%20to%20medicines_2020-05_EN.pdf

Extracts from the news. *"Since the outbreak of the COVID-19 pandemic, the threat posed by fake medicines and medical products has increased dramatically. Organized crime groups take advantage of the high market demand for medicines, personal protection and hygiene products and make lucrative profits from the sale of counterfeit items."*

3.4 Other

OECD. **COVID-19 crisis underscores need to address trade in fake pharmaceuticals, say OECD & EUIPO.** *Newsroom*. 2020 April 21. https://www.oecd.org/newsroom/covid-19-crisis-underscores-need-to-address-trade-in-fake-pharmaceuticals-say-oecd-and-euipo.htm

"Recent seizures of fake medical supplies being marketed as protection against COVID-19 underscore the need to address a growing international trade in counterfeit pharmaceuticals that is costing billions of euros a year and putting lives at risk, according to the OECD and the EU's Intellectual Property Office. A joint report, Trade in Counterfeit Pharmaceutical Products, and an accompanying brief on links with the COVID-19 crisis, says the trafficking and sale of fake or defective medicines is enriching criminal groups and endangering health while draining away vital industry and tax revenues. Analysis of customs seizures over 2014-16 finds that trade in counterfeit pharmaceuticals was worth EUR 4 billion in 2016. That figure excludes fake medicines produced and consumed domestically and shipments of pharmaceuticals that are stolen in transit and rerouted for sale in a different market or country."

UNAID. **The impact of the COVID-19 response on the supply chain, availability and cost of generic antiretroviral medicines for HIV in low- and middle-income countries.** *Survey.* 2020 June. https://www.unaids.org/sites/default/files/media_asset/covid19-supply-chain-availability-cost-generic-arv_en.pdf

Key points. *"(*) Lockdowns have impacted both the transport of goods across the value chain of production and the distribution of HIV medicines.f(*) Barriers to the supply chain and a forecasted economic shock indicate a possible fluctuation in the availability of antiretroviral medicines and anincrease in cost. f(*) Manufacturers are facing logistics issues that may indicate a potential disruption in the next few months. f(*) Countries should identify the risk level for the stock of all antiretroviral medicines. f(*) Coordinated action by governments is necessary to ease the supply chain and the distribution of medicines to facilities. f(*) Buyers (both donors and domestic governments) should enhance transparent and timely communication between countries and suppliers."*

4 Lay literature

4.1 Disclaimer & Notes

The information included below is based on the data used to create the Medicine Quality Monitoring Globe (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[6].

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 website for full methodology[7]. 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 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 trial medicines, and (d) Ventilators and Positive end-expiratory pressure (PEEP).

In this report we share articles captured by the MQM Globe that are linked to medical products that potentially are used in the context of Covid-19 or to active pharmaceutical ingredients (APIs) that are being trialed 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 here below are not directly linked to the treatment of COVID-19. Nevertheless we have included them as crossover risks and to see if the alerts on these medical products change over time.

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 add in articles in other languages to this report in time. Any remarks or additions to content are encouraged (please write to medicinequality@iddo.org)

[6] IDDO. **Medicine Quality Monitoring Globe disclaimer and caveats**: https://www.iddo.org/medicine-quality-monitoring-globe-disclaimer-and-caveats

[7] IDDO. **Medicine Quality Monitoring Globe methodology**: https://www.iddo.org/medicine-quality-monitoring-globe-methodology

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

From January 1st until June 30th 2020, we recorded at least 222 relevant articles linked to SF COVID-19 medical products alerted through the MQM Globe database (table 1). Within those articles 6 alerted on vaccines, 43 are linked to COVID trial medicines, 60 to COVID-19 diagnostics and 140 to personal protective equipment (PPE) including sanitizers (table 2; figure 1). The first article appeared on the 20th of January and the number of reports reached 64 in June alone. The first articles related directly to SF COVID-19 diagnostics, vaccines and trial medicines (i.e. chloroquine) were published on the 1st of March, 12th of March and 3rd of April, respectively.

Table 1. Number of articles on the Medicines Quality Monitoring Globe linked to substandard or falsified COVID-19 supplies by month.

Month	Number of articles
January	2
February	10
March	49
April	50
May	47
June	64
Total	**222**

Table 2. Number of alerts on the Medicines Quality Monitoring Globe by category of products.
As some alerts described more than one category of products the sum of alerts per category exceeds 222.

Month	Number of alerts			
	COVID-19 diagnostics	Personal Protective Equipment incl. sanitizers	COVID-19 trial medicines	COVID-19 purported vaccines
January	-	-	2	-
February	-	1	9	-
March	11	33	4	2
April	17	29	11	1
May	17	27	6	3
June	15	50	11	0
Total alerts per category	**60**	**140**	**43**	**6**

Of the 140 articles related to SF equipment used in the protection against SARS-COV-2, 68 were about SF hand sanitizers and products to disinfect surfaces. On the 11th of March the first article on falsified hand sanitizers was captured by the MQM Globe, which was about a plant allegedly producing falsified sanitizers in India (report ID: 482314). Sixty-seven articles reported specifically on SF masks and respirators. Other articles described incidents related to other PPE including gloves, gowns, aprons, visors and goggles. The first article on SF PPE (other than disinfectants and sanitizers) was captured by the MQM Globe on the 23th of March in Morocco, where 2 people were arrested for the distribution of gloves and masks without authorisation (report ID: 506341).

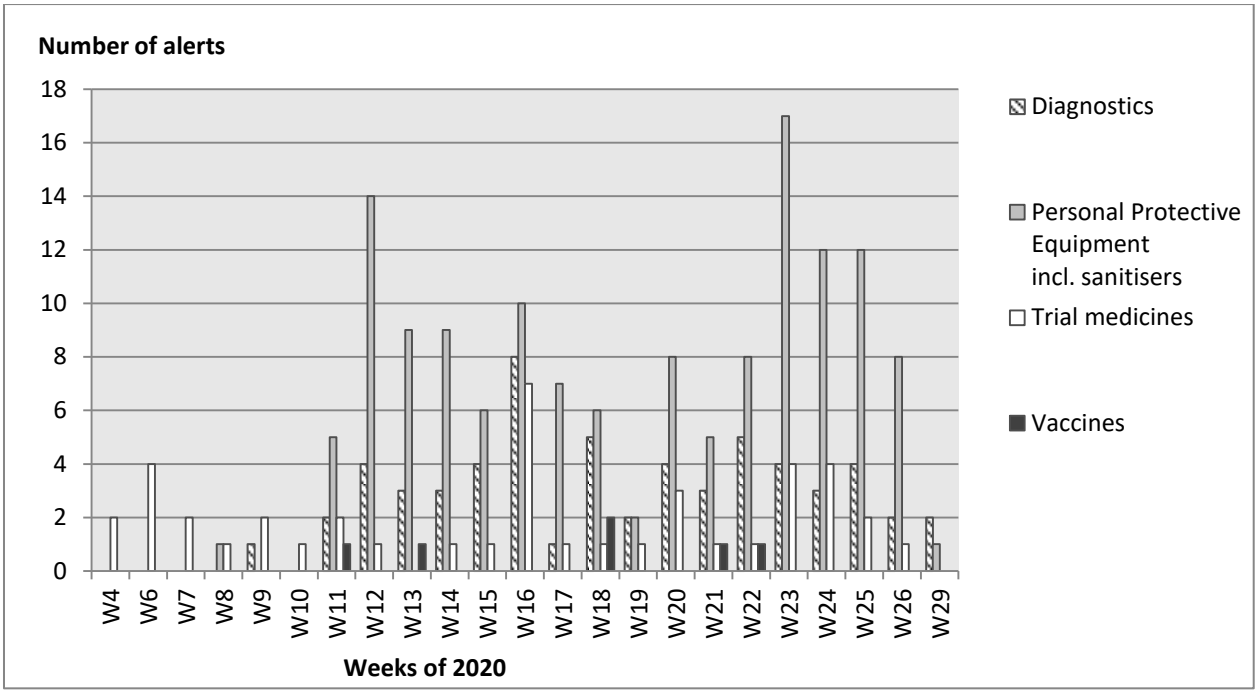

Figure 1. Number of alerts by category over time, on the Medicines Quality Monitoring Globe. Week 4 started Monday 20 January 2020 and week 29 ended on Tuesday 30th of Jun 2020.

Online substandard and falsified products

The high demand and shortage of COVID-19 products has led to an increase in reports of SF medical products from online 'pharmacies'. Criminals have been quick to fill the gap between demand and supply with falsified products (report ID: 527646, 533066, 550753). In early March 2020, Operation Pangea XIII was conducted, involving regulatory authorities from 90 countries (report ID: 491119, 491989, 503622, 507709, 581799)[8]. Every year Interpol leads this international effort to disrupt the illegal online sale of medicines and medical products. In 2020 the operation seized more than 34,000 unlicensed and fake products advertised as "corona spray", "corona virus medicines", or "corona viruses packages" and it identified 2,000 online COVID-19 related advertisements. Of these online advertisements the most commonly sold online medical devices were falsified surgical masks. But also SF testing kits (report ID: 555739, 589528, 591153) and hand sanitizers (report ID: 533104) have invaded the web market.

Europol reports that most of the SF COVID-19 products in Europe are distributed via e-commerce and social media platforms, rogue pharmacies, messaging applications, and the dark web[9]. Currently in the UK, most reports to Action Fraud are linked to online purchases of COVID-19 related products that never arrived or appeared substandard upon arrival (report ID: 596569).

[8] Interpol. **Global operation sees a rise in fake medical products related to COVID-19.** *News release.* 2020 March 19. https://www.interpol.int/en/News-and-Events/News/2020/Global-operation-sees-a-rise-in-fake-medical-products-related-to-COVID-19

[9] Europol. **Beyond the pandemic - how covid-19 will shape the serious and organised crime landscape in the EU.** *Report*. 2020 April 30. https://www.europol.europa.eu/publications-documents/beyond-pandemic-how-covid-19-will-shape-serious-and-organised-crime-landscape-in-eu.

On the dark web, there are advertisements for a wide range of COVID-19 related products: medicines such as hydroxychloroquine, masks and test kits (report ID: 573362). On the online dark website space 'ToRRez Market', Europol found a vender offering oxygen concentrator/ventilators. Often the products sold on the dark web are not approved, do not correspond to authentic medical products or are clearly scams (report ID: 573362, 588095). In early June an article reported that several dark web markets banned the sale of pandemic-related goods (report ID: 588095). 'Empire Market', one of the prominent dark web spaces, however apparently continues to sell illegal COVID-19 testing kits.

In mid-March, the European Anti-Fraud Office launched an inquiry to tackle the sale of falsified medical products on the continent, facilitating actions against online sources and products entering through land borders (report ID: 497265). Within the current context they especially target falsified masks, medical devices, disinfectants, sanitizers and test kits. By the beginning of June Malaysian authorities had arrested 181 individuals and 53 others had been charged in court as they were linked to the online sale of masks (report ID: 593100). In the United States the Environmental Protection Agency ordered Amazon and eBay to stop selling unapproved products with false claims of pesticide-containing products that would protect against coronavirus (report ID: 572257, 614836). Both companies say they are taking measure to keep SF-products from their marketplace but nevertheless, unregistered, misbranded, or restricted-use pesticides apparently continue to appear on their websites. In March, Vistalworks updated its online tool to pick up specifically falsified COVID-19 related products on sale on eBay[10]. The tool gives an indication to online shoppers on potential falsified testing kits, sanitizers and "miracle" corona virus cures.

Seizures of substandard and falsified COVID-19 products

Around the globe, seizures of SF products have been reported. The MQM Globe picked up many reports of interceptions by the US Customs and Border Protection. Compared to other countries it seems that US media (and US authorities) report more often on seizures performed on their territory.

In late June The US Partnership for Safe Medicines[11] reported that the Department of Homeland Security in the United States had seized over a 1 million fake COVID-19 products: fake and substandard personal protective equipment such as masks, falsified test kits, black market medicine, unapproved thermometers, and fake treatments such as colloidal silver or bleach. Indeed on the MQM Globe this is reflected by a wide range of reports on seizures by United States authorities (report ID: 530144, 551204, 551209, 551362, 556139, 563221, 566171, 581681, 584561, 585805, 593883, 593984, 602903, 624639, 628266). In these articles the products were stated as shipped from manufacturers and distributors from many countries (e.g. China, Hong Kong, Nigeria, the United Arab Emirates, Vietnam, the United Kingdom). Goods come in through different entry points. For example in March, the US authorities intercepted several packages containing suspected falsified COVID-19 test kits arriving from the United Kingdom at Los Angeles International Airport (report ID: 485819) and Chicago O'Hare International Airport facility (report ID:491485). At land entry points test kits were seized in May at Santa Teresa port, on the border with Mexico (report ID: 576192). In June falsified COVID-19 kits were seized at the port of Baltimore (report ID: 598640).

[10] BBC. **Corona virus: Online tool to target fake testing kits:** https://www.bbc.com/news/uk-scotland-scotland-business-51959570

[11] The US Partnership for Safe Medicines. **CBP Seizures Of Fake COVID-19 Products Top 1 Million**: https://www.safemedicines.org/2020/06/1mm-fake-covid-19-seized.html

4.3 Vaccines

No vaccine has completed clinical trials and is officially approved for the prevention of COVID-19 anywhere in the world. Nevertheless, the MQM Globe identified multiple purported COVID-19 vaccines, for example in the USA (report ID: 497263, 549794) and in India (report ID: 487568). The United States Food and Drug Administration (US FDA) issued warning letters to Apollo Holding LLC and North Coast Biologicals for selling fake vaccines containing cannabidiol oil (report ID: 578176). In Israel The Galilee Research institute MIGAL is working on developing a COVID-19 vaccine. However, in parallel a seller in Ecuador was already found selling boxes with MIGAL's Hebrew language logo on fake vaccines (report ID: 582392). On the dark web, several fake vaccines have been advertised when none have been approved (report ID: 497263, 550753). The Australian Institute of Criminology found a "makeshift vaccine", an injection of SARS-Cov-2 antibodies, extracted from blood plasma from recovered COVID-19 patients (report ID: 550753). Interpol[12] and Europol[13] (report ID: 551270) have warned of a wave of offers for falsified vaccines once a genuine approved vaccine for COVID-19 will be announced.

4.4 COVID-19 diagnostics

Two articles reported on the seizure of thermometers in the United States (report ID: 602903, 619366). The thermometers had US FDA markings but were not registered with the US FDA when the shipment arrived from Malaysia and China. One article reported on an order for test tubes used in laboratory analysis of COVID-19 test samples (report ID: 614170). Instead of standard vials, the company Fillakit LLC, was stated to have supplied plastic tubes made for bottling soda which were unusable. Former employees reported on the substandard conditions in which the test tubes were produced.

All the other reports were related to COVID-19 test kits, sometimes within the context of several other COVID-19 related supplies. The articles often do not contain information on the type of test kit they report on. For example the article does not state whether they detect SARS-CoV-2 virus components or if they are serological tests which detect antibodies to the SARS-CoV-2 virus. The distinction is however vitally important as WHO does not recommend antibody tests for diagnosis of current infection with COVID-19[14].

Contaminated test kits

Several countries encountered problems of contaminated COVID-19 test kits. In the United States, the first batch of COVID-19 test kits that were produced in the Centers for Disease Control and Prevention (CDC) laboratory in Atlanta, United States, were likely to have been contaminated.

[12] Interpol. **COVID-19: the global threat of fake medicines.** *News release*. 2020 Mai. https://www.interpol.int/en/content/download/15305/file/20COM0356%20-%20IGGH_COVID-19%20threats%20to%20medicines_2020-05_EN.pdf

[13] Europol. **Viral marketing - counterfeits, substandard goods and intellectual property crime in the COVID-19 pandemic.** *Report*. 2020 April 17. https://www.europol.europa.eu/publications-documents/viral-marketing-counterfeits-substandard-goods-and-intellectual-property-crime-in-covid-19-pandemic

[14] World Health Organisation. **Clinical management of COVID-19**. *Guidance.* 2020 May 27. https://www.who.int/publications/i/item/clinical-management-of-covid-19

Assembling the kits in the same room as corona virus material was thought to have made the test unusable (report ID: 471711, 614634). At the end of March, some laboratories in the United Kingdom were warned by their supplier, a Luxembourg based company Eurofins, that a delivery of 'probes and primers' had been contaminated with Sars-Cov-2 (report ID: 506213). In April the Canadian press reported thousands of kits from a supplier in China that were found to be contaminated with bacteria "*related to the packaging and the situation around the company*" and the tests were also stated as "defective" (report ID: 531737). In the Philippines, a batch recall was launched in May for locally manufactured COVID-19 test kits stated as from Manila HealthTek. A reagent used for the test was contaminated leading to 30% of the tests giving no result (report ID: 575821).

Governments facing problems with substandard or falsified test kits

Some test kits purchased by national governments have proven to be unreliable. In **Pakistan** test kits provided to the Sindh government were found to be substandard by medical experts (report ID: 549516).

In March the Ministry of Health (MoH) in **Nepal** bought COVID-19 rapid antibody test kits stated to be developed by Guangzhou Wondfo Biotech (report ID: 610542). In May the Nepal Health Research Council informed the MoH of the substandard performance of the test kits. Controversy arose when the MoH cancelled the procurement tender but used the tests that had already arrived nevertheless.

In March the government in **Spain** found its antibody testing kits were substandard with an accuracy of only 30% (report ID: 510935, 515255, 521647). Although the test was stated to be from Shenzen Bioeasy Biotechnology Company Limited were EU-certified, the Chinese authorities claim the supplier was not recommended by the Chinese state.

In the **USA** some public health departments were supplied with tests that were not approved by China's Centre for Medical Device Evaluation (report ID: 530299).

In the beginning of April the **UK** government, through evaluation conducted at the University of Oxford, found that the antibody tests bought from China had poor diagnostic accuracy but the paper did not state the manufacturers[15] (also report ID: 515255, 521647).

Similar issues were reported in the **Czech Republic, Slovakia and Turkey** on products made in China (report ID: 510935, 521647).

Substandard and falsified test kits stated as coming from China

Not only governments were facing problems with SF COVID-19 testing kits stated to be originally from China. They were also found (in other countries) at several levels of the supply chain. In April two US companies, Premier Biotech of Minneapolis and Aytu Bioscience of Colorado, were stated to have distributed tests from Chinese manufacturers which were not FDA approved (report ID: 530299). In Zimbabwe falsified test kits were sold in the street (report ID: 532443). At the end of May

[15] [MedRxiv preprint] Adams ER, Anand R, Andersson MI (and 63 more authors). **Evaluation of antibody testing for SARS-CoV-2 using ELISA and lateral flow immunoassays.** MedRxiv preprint. April 2020. doi: 10.1101/2020.04.15.20066407.https://www.researchgate.net/publication/340797938_Evaluation_of_antibody_testing_for_SARS-Cov-2_using_ELISA_and_lateral_flow_immunoassays

Chinese-labelled testing kits for COVID-19 were seized at a clandestine medical facility in the Philippines (report ID: 585953).

At the end of March after several quality problems with Chinese test kits, China tightened its export regulations. Previously China required only a foreign license of the medical product prior to export (report ID: 521647). However, apparently an European Union CE certification is easy to falsify. Now China requires a domestic registration certificate and additional quality checks are performed at customs. China also banned the export of medical equipment from some companies (report ID: 530299, 527963). For example Tus Data Asset in Beijing and AIPO International Co Ltd in Shenzhen are no longer authorised to export medical products for pandemic prevention due to quality issues. The United States' NBC news summarizes as follows: "*Many of the unapproved tests appear to have been shipped to the US after the FDA relaxed its guidelines for tests in mid-March and before the Chinese government banned their export just over two weeks later*" (report ID: 530299).

On the 1st of April, after several reports of SF COVID-19 testing kits, the European Commission announced that it will support laboratories by providing positive control SARS-CoV-2 material for evaluation of diagnostic tests (report ID: 510935)[16].

Unregistered test kits

Various regulatory authorities, such as the Philippines FDA (report ID: 486234) and the UK Medicines & Healthcare products Regulatory Agency (MHRA) (report ID: 530572), have warned the public about unregistered test kits and the risk of using poor quality test kits. In some countries, such as Canada[17] and the United States[18], national lists are developed specifically registering the approved (and banned) COVID-19 test kits.

Several countries do not approve the sale of rapid diagnostic tests since the results can be easily misinterpreted. Nigeria had not approved any rapid test kit by the end of May 2020: the Medical Laboratories Science Council of Nigeria assessed 11 rapid test kits for validation; only 4 of the rapid test kits met the validation inclusion criteria but all were found to be substandard (report ID: 585887). The government warned the public with regards to the use of non-validated rapid test kits.

Even when home testing kits have not yet been approved, such tests have been available on the market since the beginning of the pandemic. Several media reports are highlighting their non-approved status by the US FDA (report ID: 529643, 574088, 601700), Health Canada (report ID: 560379) and UK MHRA (report ID: 553784, 523694).

[16] European Commision. **A new control material developed by JRC scientists to help prevent coronavirus test failures**: https://ec.europa.eu/jrc/en/news/new-control-material-developed-jrc-scientists-help-prevent-coronavirus-test-failures

[17] Health Canada. **Authorized medical devices for uses related to COVID-19: List of authorized testing devices**: https://www.canada.ca/en/health-canada/services/drugs-health-products/covid19-industry/medical-devices/authorized/list.html

[18] United States Food and Drugs Administration. **In vitro Diagnostics Emergency Use authorizations**: https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas

Actions against substandard or falsified tests in the market

In the light of the SF products flooding the market, governments are taking action. Around the globe falsified or unlicensed tests have been seized, for example in Bangkok (report ID: 521980), Canada (report ID: 555739) and the Philippines (report ID: 585953). The US FDA issued warning letters to companies inappropriately marketing antibody tests (report ID: 609690): Medakit Ltd. of Sheung Wan (Hong Kong); Antibodiescheck.com and Yama Group; and Dr. Jason Korkus, DDS and Sonrisa Family Dental d/b/a My COVID19 Club of Chicago (Illinois). "*Violations outlined in the warning letters include: offering test kits for sale in the United States directly to consumers for at-home use without marketing approval, clearance, or authorization from the FDA; misbranding products with labelling that falsely claims products are 'FDA approved'; and labelling that bears the FDA logo, which is only for the official use by the FDA and not for use on private sector materials* (report ID: 609690)".

From March onwards several articles reported arrests and prosecutions. Ten people were arrested in Kenya for selling falsified COVID-19 testing kits (report ID: 487232). The USA was pursuing a person for selling non-FDA approved kits stated to be manufactured by the Chinese company Anhui Deep Blue Medical Technology Co (report ID: 529724) and several arrests were made for selling unapproved COVID test kits in a convenience store (report ID: 550482), on the street (report ID: 566076) or on the internet (report ID: 589528). In the UK a pharmacist has been arrested for false and misleading claims about tests' capabilities (report ID: 527188). Another man was arrested for online selling of falsified COVID-19 testing kits (report ID: 591153). Yet another man was arrested in the UK and charged for making and selling falsified corona virus treatment kits and sending them to the US (report ID: 524168). The kits were intercepted by the US customs and the FDA alerted the MHRA in the UK.

4.5 Personal protective equipment including sanitizers

The Cleaning & Hygiene Suppliers Association (CHSA) in the UK warned buyers of cleaning and hygiene products of SF products (report ID: 572120). Like other articles they warn about new companies that are set up to produce or buy and subsequently sell products without guarantee that they meet industry standards. The National Agency for Food and Drug Administration and Control (NAFDAC) in Nigeria said in June that before Covid-19 there were about 21 companies producing hand sanitizers after the pandemic started there are over 110 (report ID: 591853). The NAFDAC warned the manufacturers to adhere to global best practices, otherwise risking penalties (report ID: 626983). The FDA in Pune, India, said that there are new companies coming up with products for which the quality has not been verified, and they already cancelled several licences (report ID: 483978). Between the middle and the end of March, the Palestinian Authority closed several businesses that were manufacturing unlicensed face masks and hand sanitizers (report ID: 503801). Similar issues were encountered in Egypt (report ID: 503007) and Bangladesh (report ID: 624844).

4.5.1 Sanitizers and disinfectant

SF hand sanitizers were identified in Bangladesh (report ID: 621929, 622004), in different states of India (report ID: 482314, 488219, 489274, 493688, 504810, 505033, 506687, 593218, 611732, 615378), Ghana (report ID: 541805) and Pakistan (report ID: 591427). In Uganda a man was arrested for making falsified disinfectant and sanitizers at his home (report ID: 491075). Some reports

describe completely new units producing falsified or substandard products but some manufacturers are redirecting their business. For example in India one manufacturer normally produced chlorine liquid to disinfect swimming pools and water tanks (report ID: 517171), another company produced industrial oils (report ID: 483776), both shifted their production to SF hand sanitizers.

Several healthcare workers were also caught with SF products. In India, a pharmacist together with accomplices were arrested producing sanitizers without license and labelling them “made in Nepal/Taiwan” (report ID: 488498). Another pharmacy owner was preparing hand sanitizers without a valid license and with no quality control (report ID: 493218).

Production of these hand sanitizers led to a flood of SF products sold around the globe such as in Bangladesh (report ID: 573184), India (report ID: 492031, 493688, 607813, 621266), Kenya (report ID: 502766), Nigeria (report ID: 509876), Philippines (report ID: 533104), Thailand (report ID: 521980, 555122, 569519, 594232), Uganda (report ID: 510967, 601256) and the UK (report ID: 585527). One article quoted a note of the Kenya Bureau of Standards that explained the public how to step by step verify whether the sanitizer is genuine or not (report ID: 493734).

In the USA a man was detected selling and promoting a disinfectant for large scale disinfection incorrectly as approved by the Environmental Protection Agency (report ID: 601700). In Pakistan health authorities seized thousands of bottles of falsified Dettol (report ID: 601599). In India disinfectant for sanitation of electronic devices contained water and damaging the device display (report ID: 611732).

In April in India, the Central Drugs Standard Control Organisation (CDSCO) analysed 12 samples of hand sanitizers and all failed the tests (report ID: 575646, 609090). Two samples were falsified and ten were “Not of Standard Quality”. They compared according to the standards and guidelines provided by the World Health Organisation (WHO). According to the WHO hand sanitizers should consist of 80% v/v ethanol or 75%v/v isopropyl alcohol, and in addition contain 1.45% v/v glycerol and 0.125% v/v hydrogen peroxide. None of the products contained glycerol or hydrogen peroxide. The samples tested by the CDSCO contained methanol, denatured spirit and only low concentrations of ethanol (between 24% and 65% v/v).

The expiry date of genuine products manufactured by Eurolife Healthcare (India) were stated to be fraudulently extended from ‘2020’ to ‘2021’ by the company (report ID: 488219). Some hand sanitizers were imitations of the original product for example ’M/s Ron and Baker‘ (report ID: 607813, India), ’Semuns Cleansem‘ and ’Kausthuba Coclean 19‘ (report ID:489274, India), and ’Savelon‘ and ’Savalon‘ products were similar to genuine ’Savlon‘ products (report ID: 622004, Bangladesh). In Kenya several products such as ’0-Germs‘, ’San Gel‘and ’Pure Magic‘ were seized without the standardization mark from the Kenyan Bureau of Standards (report ID: 492098).

Raw ingredients quality issues

Health Canada launched a substantial recall of products containing industrial-grade ethanol (e.g. ’Eltraderm‘, ’Gel 700’, ’Sanilabs‘, ’Walker Emulsions’)(report ID: 595844). Industrial grade alcohol might contain impurities that are not found in pharmaceutical-grade ethanol causing dry skin, irritation or cracking. In Egypt the police raided a hand sanitizers manufacturer that was using ethyl alcohol which was undocumented and was from unknown origin (report ID: 503007). In the

Philippines a trader was arrested for selling adulterated alcohol (report ID: 567031). In Cambodia police officers raided a location storing and distributing methanol as ethanol for hand-sanitizer (report ID: 494898).

Wrong, low amount or absence of active ingredients

In Ghana a starch-made hand sanitizer was sold (report ID: 544618). In India a unit mixed petroleum gel along with rose water and labelled it as 'Germ X Hand Sanitizer' (report ID: 521193). In Bangladesh a unit only used colour, fragrance, gel and spirit to make their sanitizers, not including isopropyl alcohol nor ethyl alcohol (report ID: 621929). In Guyana the Food and Drug Administration found that 'Purcill' only contained 0.53% alcohol. Other products claimed to contain ethyl alcohol but were found to contain low dosages of isopropyl alcohol instead (report ID: 609090). For example products were reported to contain 54.5% isopropyl alcohol, instead of 75% ethyl alcohol claimed on its label (report ID: 616113).

In the USA a convenience store owner sold a self made hand sanitizer, mixing water and a foaming sanitizer (report ID: 482512). The mixture caused chemical burns on at least four children of which one was hospitalized.

A multitude of articles reported on hand sanitizers containing methanol such as in Thailand (report ID: 594232) and India (report ID: 616113, 621266, 622830). Methanol is extremely toxic at high doses (mainly affecting the central nervous system, eyes and kidneys) and can cause death. It can be absorbed through the skin. In India one sample contained 47.14% v/v methanol, whereas the label claimed 70% ethyl alcohol (report ID: 609090). In mid June the US FDA warned the public about nine hand sanitizers stated as produced by Eskbiochem SA (Mexico) that may have been contaminated with methanol (report ID: 617470).

4.5.2 Personal Protective Equipment

Most of the articles recovered from the MQM Globe on personal protective equipment (PPE) are related to masks and respirators, but some articles reported on other protective equipment. Falsified gloves were intercepted in Bangladesh (report ID: 624844) and by the New Zealand customs (report ID: 527646). The MQM Globe captured an article of a batch recall in January in the USA of 9 million level 3 Cardinal Health surgical gowns (report ID: 458225). The recall was launched voluntarily by Cardinal Health since the sterility of the gowns could not be ensured. In the United Arab Emirates the police arrested 3 men selling protective glasses, gloves and overall protective gear through WhatsApp (report ID: 525009). The products bore no label of the brand or the place of manufacture. In May there were alerts on gowns from Selegna Tekstil specially flown by the Royal Air Force from Turkey that were said to have failed the UK quality checks (report ID: 584212). The company reacted that all the goods they supplied were certified and that they had not received any quality complaint.

Producing and selling substandard and falsified PPE

Worldwide millions of SF masks have been seized. Production of falsified masks was reported in Bangladesh (report ID: 599566, 615643), India (report ID: 505932, 594003, 600447), Turkey (report ID: 503622), Ghana (report ID: 540250, 541805), United Arab Emirates (report ID: 506405), and Zimbabwe (report ID: 532443).

However, most substandard and falsified masks were reported to lead to manufacturers allegedly based in China. In the USA, masks were for sale on Amazon that claimed to be manufactured by a company "based in USA", when they were actually manufactured in Wuhan, China (report ID: 506891). Articles reported on SF Chinese PPE, especially masks, in Australia (report ID: 507627, 521647), Canada (report ID: 569809, 579488), Finland (report ID: 521647), India (report ID: 600447), Netherlands (report ID: 510935, 521647), New Zealand (report ID: 527646), the UK (report ID: 616236), and the USA (report ID: 530203, 539880, 554265, 594241, 624639). At the ports of New Orleans and Shreveport (USA), shipments from China and Vietnam containing falsified face masks with Burberry, Supreme, Gucci and Chanel logos were intercepted (report ID: 610906). In April, with complaints arriving from around the world, Chinese officials seized more than 89 million substandard face masks in China (report ID: 546665).

Several businesses were raided, fined or closed for selling low quality masks. Often these masks were falsely claimed as N95-certified respirators such as in Bangladesh (report ID: 539058, 573184, 614418), Portugal (report ID: 588476), the USA (report ID: 506815), Australia (report ID: 594855), and in Thailand (report ID: 521980, 555122). Also Health Canada has received reports of uncertified N95 respirators illegally sold with the claim to protect against COVID-19 (report ID: 528011). Online the sale of SF PPE has ballooned. Some examples were found in Malaysia (report ID: 593100), there were "virus protection" masks on eBay in the UK (report ID: 593479) and in South Africa clients realised that something was wrong when they could more easily breath through the online bought N95 respirator than through the homemade sewn masks (report ID: 613834).

As for diagnostic tests, several national authorities were victims of substandard or falsified respirators. For example the governments in Canada (report ID: 579488), Kenya (report ID: 578762), different states in the USA (report ID: 530203, 551277, 554265, 600120, 614954), the Netherlands and Belgium experienced problems (report ID: 510935).

SF masks and respirators reached frontline aid workers in police departments (report ID: 551277), regional transportation services (report ID: 584025) and medical workers (report ID: 506961, 582468) in the USA. Other articles also reported on SF masks and respirators reaching medical staff in hospitals in Bangladesh (report ID: 599566), India (report ID: 590876) and in Mexico (report ID: 600685). In the Netherlands a survey revealed that about half the masks used in care homes to protect staff and residents were substandard (report ID: 580095). Twelve out of 25 types of masks analysed were not compliant according to Greencycl, a company used to analyse masks for hospital use.

In March, the Australian Therapeutic Goods Administration (TGA) adapted the regulations for masks by no longer requiring testing prior to registration. This resulted in SF masks being used in some Australian hospitals (report ID: 580519, 594855). Since March 22, 774 masks had been registered with the TGA but after the concerns on SF masks in the market, 58 companies cancelled the TGA registration (report ID: 585316).

Quality problems encountered with respirators and surgical masks

The US CDC found that 60 percent of 67 different imported N95 and KN95 respirators did not meet the US standards (report ID: 582468). The US National Institute for Occupational Safety and Health

(NIOSH) tested 130 international respirator types, more than half were classified as substandard (report ID: 600120).

Falsified respirators. In Bangladesh the Central Medical Stores Depot supplied "ordinary face masks" in N95 packaging (report ID: 599566). The company and vendor said it was a packaging mistake but there were rumours that the supply was deliberately set up. In the USA a Chinese manufacturer was charged with producing misbranded and defective masks as KN95 respirators (report ID: 610033).

Filtration standards not met. A plethora of articles report on respirators that fail to meet the filtration standards for personal protective equipment (report ID: 569809, 579488, 585316), filtering 22.33% (on average, report ID: 610033), 28% (report ID: 551277), 62% (report ID: 585316) or 65% (report ID: 580095) of airborne particles instead of the required 95% required in a medical setting. The University of Oklahoma's Health Sciences Centre, USA, found that around one-third of the approximately 70 brands tested did not meet the 95% filtration standard. Some products fall short in layer specifications and the right materials are not used (report ID: 503007, 540250).

Lack of good seal. Apart from a good filtration, respirators need to achieve a good seal, which is often not the case (report ID: 585316). For safety of healthcare workers the respirator should be equipped with head bands that give tight fit, however alerts were published on respirators having ear loops instead (report ID: 564916, 567746, 582468, 614954).

Labelling and certification problems. SF products bearing no or falsified authorisation logos such as CE or FDA-logo (report ID: 503007, 572120, 582468, 600120) were reported. An article reported on stamps falsely indicating that the products were safe for health care workers by the US government (report ID: 567746). In the UK millions of seized masks labelled with false claims or with falsified safety certificates had to undergo label amendment before release (report ID: 585527).

Other encountered quality problems. In a care home in the Netherlands, masks were in use that were 10 years beyond their use-by date (report ID: 580095). Belgian media reported on masks coming from Colombia that contained "animal faeces" (report ID: 510935). An article discussed how in India fabric from discarded clothes was used to produce masks (report ID: 611732).

PPE stated as from the company 3M

Personal Protective Equipment from the company 3M has been in great demand for the prevention of the spread of SARS-COV-2. The MQM Globe alerted on several cases in which products stated as from 3M were involved. In China, a case dates back to January where a pharmacy chain sold more than 580,000 falsified masks advertised as being made by 3M (report ID: 615338). In June the head of the Chinese pharmacy chain was sentenced. In Thailand unlicensed 3M PPE suits were seized during a raid in April (report ID: 531196). In June falsified 3M masks were seized by the United States Customs and Border Protection (report ID: 617819).
3M works with a dedicated group of distributors and has not changed the prices of its respirators since the COVID-19 outbreak. The company states that it tries to fight against non-authorised wholesalers and distributors, of which some are selling falsified products, products at very high prices, or as a scam. In April the United States Attorney prevented a fake sale of 39 million 3M N95 respirators (report ID: 515936). 3M commented: "*there was no way someone has 39 million masks in a warehouse, because we only make 20 million a year*". In June 3M sued Preventative Wellness

Consultants LLC for representing themselves as authentic 3M distributors having access to 3M N95 respirators and for price gouging (report ID: 601877). 3M filed a lawsuit against an Amazon vendor for selling falsified versions of 3M N95 masks at grossly inflated prices[19]. Since January, 3M filed at least 12 lawsuits across the United States for falsified products and price gouging. Worldwide the company worked to remove more than 3,000 websites with unlicensed or falsified 3M products.

Public engagement with warnings

In Bangladesh public health experts rang the alarm bell because of high volumes of SF PPE in the market without proper monitoring and regulation by the authorities (report ID: 599392). In the UK retailers were warned to turn to trusted sources of supply (report ID: 588307). In the USA, it was warned that the authenticity of respirators should be checked against FDA's list of approved respirators (report ID: 533620). The US CDC released a warning for falsified products, highlighting how to identify an approved respirator and signs that a respirator may be falsified (report ID: 569358)(see figure below). They released some very practical 'Additional Tips for Spotting Counterfeit Respirators' specifically for third-party market places and websites[20].

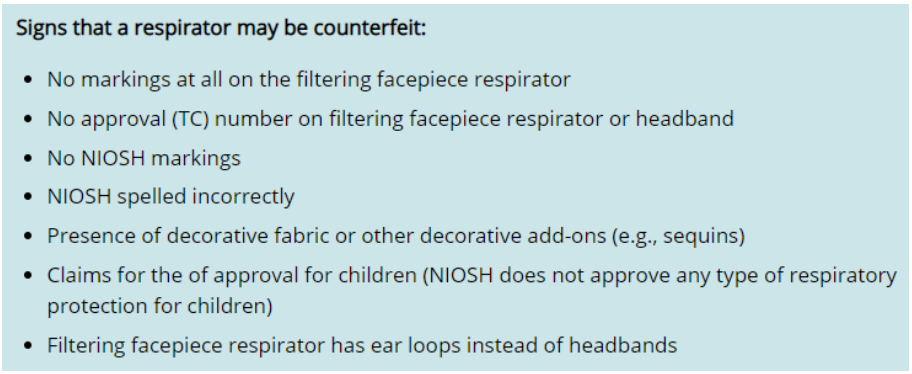

Figure 2: Signs that a respirator may be falsified.
Source: figure copied from Centers for Disease Control and Prevention[21].
With NOISH:,National Institute for Occupational Safety and Health.

People being informed about their respirator being substandard or falsified does not necessarily prevent them from using them. An article reports of a distributor in India who was selling SF N95: the clients were buying these SF respirators because "*some protection is better than nothing*" (report ID: 594003).

[19] 3M. Press release: https://news.3m.com/English/press-releases/press-releases-details/2020/3M-Sues-Seller-on-Amazon-Who-Charged-Grossly-Inflated-Prices-for-Fake-Defective-and-Damaged-N95-Respirators-Falsely-Advertised-Under-3M-Brand/default.aspx

[20] Centers for Disease Control and Prevention. **Additional Tips for Spotting Counterfeit Respirators**: https://www.cdc.gov/niosh/npptl/usernotices/AdditionalTips.html

[21] Centers for Disease Control and Prevention. **Counterfeit Respirators / Misrepresentation of NIOSH-Approval**: https://www.cdc.gov/niosh/npptl/usernotices/counterfeitResp.html

4.6 COVID-19 trial medicines

There is a plethora of clinical trials of repurposed and investigational antiviral and immune-based COVID-19 therapies including, but not limited to hydroxychloroquine/chloroquine, azithromycin, antivirals (such as lopinavir&ritonavir, favipiravir, umifenovir, remdesivir), immunomodulators (such as tocilizumab, sarilumab, baricitinib, rexolitinib, anakinra, interferon), vitamin C and D, corticosteroids (such as dexamethasone and methylprednisolon) and colchicine[22,23,24].

The chloroquine and hydroxychlorquine incidents described in this section illustrate the warning launched by WHO, Interpol[25], Europol[26] (report ID: 533066) and scientists[27] worldwide (report ID: 519747) that as soon as a medicine or vaccine is reported as potentially effective against COVID-19, demand will spike, opening the door for substandard and falsified products in the market. It is a warning for heightened SF risk in the light of the promising results of clinical trials with dexamethasone and remdesivir.

Chloroquine & Hydroxychloroquine

Chloroquine and hyroxychlorquine have been used for malaria and some autoimmune diseases, however they are not recommended for the prevention and treatment of COVID-19 outside clinical trials. Despite experts warnings, people rushed to obtain these products, indirectly encouraging mal-intended people to start manufacturing falsified products. At least 30 of the 43 articles in the MQM Globe report on COVID trial medicines mention chloroquine or hydroxychloroquine. Following Operation Pangea XIII in the beginning of March, Interpol reported an increase (compared to 2018 operation) in seizures of more than 100% for chloroquine (report ID: 491989, 593100).

WHO-Rapid Alerts on chloroquine (see section 3.1). In early April, the Cameroonian army seized a large volume of falsified chloroquine on a boat at the maritime borders (report ID: 511160), which was followed by warnings in neighbouring countries such as Nigeria (report ID: 515261). The tablets were labelled as chloroquine phosphate 250mg tablets, manufactured by Jiangsu Pharmaceuticals Inc, China, and bearing a fake NAFDAC registration number. They did not contain any detected active pharmaceutical ingredient. On the 9th of April WHO launched a Medical Product Alert about several falsified chloroquine products after multiple reports of confirmed falsified chloroquine products in Burkina Faso, Cameroon, Democratic Republic of Congo, France, and Niger. Subsequently newspapers published safety alerts issued by the health authorities in Pakistan (report ID: 530243)

[22] World Health Organisation. **Clinical management of COVID-19**: https://www.who.int/publications/i/item/clinical-management-of-covid-19

[23] World Health Organisation. **International Clinical trials Registry Platform**: https://www.who.int/ictrp/en/

[24] IDDO. **Covid-19 Clinical Trials Interactive Tool**: https://www.iddo.org/tool/covid-19-clinical-trials-interactive-tool

[25] Interpol. **COVID-19: the global threat of fake medicines.** *News release*. 2020 Mai. https://www.interpol.int/en/content/download/15305/file/20COM0356%20-%20IGGH_COVID-19%20threats%20to%20medicines_2020-05_EN.pdf

[26] Europol. **Beyond the pandemic - how COVID-19 will shape the serious and organised crime landscape in the EU.** *Report*. 2020 April 30. https://www.europol.europa.eu/publications-documents/beyond-pandemic-how-covid-19-will-shape-serious-and-organised-crime-landscape-in-eu

[27] Newton PN, Bond KC. **COVID-19 and risks to the supply and quality of tests, drugs, and vaccines.** *Lancet Glob Health*. 2020 June; 8(6): e754–e755. doi: 10.1016/S2214-109X(20)30136-4. Epub 2020 Apr 9. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7158941/

and Ghana (report ID: 532700). The customs and police in Cameroon performed in April (report ID: 537636) and in June (report ID: 617920), additional seizures of falsified anti-malarial medications, together with other falsified medicines. In both cases the medicines were smuggled into the country through neighbouring Nigeria. The Nigerian NAFDAC announced re-enforced post-marketing surveillance of COVID-19 medical products (report ID: 591853). In May a news article was published explaining how in the end of March a faith based drug supply organisation launched the initial alert on falsified chloroquine tablets in Cameroon and Congo (report ID: 566023). A mobile laboratory helped to identify the tablets as falsified, an external laboratory confirmed the analysis (see section 2: Gnegel et al. 2020), after which the WHO was informed.

In the MQM-Globe the first article of hydroxychloroquine seizure in the United States was captured in mid-April (report ID: 530144) and was followed by many others. As of June 1st the US Customs and Boarder Protection had seized more than 11,000 FDA-prohibited chloroquine tablets in 91 incidents (report ID: 593883).

In April, a licensed physician was charged with fraud for selling COVID-19 "Miracle Cure" (report ID: 531585). He smuggled hydroxychloroquine from China and concealed the shipment from customs authorities as "yam extract".

The US FDA warned that products marketed for veterinary use or "for research only" are not evaluated for safety or effectiveness in humans (report ID: 530361). They stated their concern that chloroquine phosphate, an unapproved animal drug, might be mistaken for a US FDA-approved human drug in the prevention of COVID-19. In the US, at least one person died after taking unapproved chloroquine phosphate intended for treating aquarium fish.

Remdesivir

Remdesivir is an investigational molecule, known from studies against multiple viral pathogens. In May 2020 it became authorised as Veklury® in COVID-19 treatment through an exceptional approval pathway in Japan[28] and in the United States[29]. In the end of June also the European Medicines Agency (EMA) recommended it for conditional marketing authorisation[30]. Remdesivir has shown to shorten the time to recovery for COVID-19 patients with pneumonia requiring supplemental oxygen[31]. At this stage there is no public report of substandard or falsified remdesivir but the risk

[28] Gilead. **Gilead Announces Approval of Veklury® (remdesivir) in Japan for Patients With Severe COVID-19**: https://www.gilead.com/news-and-press/press-room/press-releases/2020/5/gilead-announces-approval-of-veklury-remdesivir-in-japan-for-patients-with-severe-covid19

[29] United States, Food and Drug Administration. **Coronavirus (COVID-19) Update: FDA Issues Emergency Use Authorization for Potential COVID-19 Treatment**: https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-issues-emergency-use-authorization-potential-covid-19-treatment

[30] European Medicines Agency. **First COVID-19 treatment recommended for EU authorisation**: https://www.ema.europa.eu/en/news/first-covid-19-treatment-recommended-eu-authorisation

[31] In addition, July 10th 2020, Gilead published a press release on the comparative analysis of the Phase 3 SIMPLE- Severe trial and a real-world retrospective cohort of patients with severe COVID-19. Remdesivir would be associated with a reduction in the risk of mortality compared with standard of care. Results need to be confirmed in a prospective study.
Source: Gilead. **Gilead Presents Additional Data on Investigational Antiviral Remdesivir for the Treatment of COVID-19**: https://www.gilead.com/news-and-press/press-room/press-releases/2020/7/gilead-presents-additional-data-on-investigational-antiviral-remdesivir-for-the-treatment-of-covid-19

must be high. The risk is enhanced due to, at the end of June, the United States bought virtually all the stocks of this first authorised therapeutic for Covid-19[32]. The order covers the production for July, August and September, and leaves almost none for the rest of the world.

Dexamethasone

The RECOVERY trial demonstrated that dexamethasone improved mortality, by reducing death by up to one third in hospitalised patients with severe respiratory complications of COVID-19[33].

In the past there have been occasional reports of falsified and substandard formulations of dexamethasone. In 2019 the US FDA alerted about problems in the production process of Cadila Healthcare, one of India's major manufacturer of intravenous dexamethasone[34,35]. From August 2019 to June 2020 the US FDA alerted on shortages of intravenous dexamethasone[36]. WHO has 21 records of falsified dexamethasone in the WHO Global Surveillance and Monitoring System database. The most recent report was received in February 2020 from the Eastern Mediterranean[37]. After the release of the RECOVERY trial test results, demand has already surged and WHO Director-General Dr Tedros Adhanom Ghebreyesus warned about falsified dexamethasone[38].

The MQM Globe captured one report on dexamethasone of substandard quality. In May 2020 the CDSCO results of quality tests performed mentioned dexamethasone of substandard quality (stated details Brand name: Uni-Dexa Injection, M/s. Unital Formulations, Solan, India) that failed sterility and the API assay (report ID: 600118).
The MQM Globe did not find articles of falsified dexamethasone. The following MQM Globe articles for dexamethasone are not related to its use for COVID-19. but point to the SF risk. The Health Sciences Authority of Singapore alerted about hidden drug ingredients in herbal products: several cases were found of dexamethasone in herbal products for pain relief. In March a man was arrested while smuggling the product from Indonesia into Singapore and a women experienced chest discomfort after taking a herbal product bought by a friend in Malaysia containing dexamethasone (report ID: 480102). Also in May a woman took a product from a friend who bought it into Malaysia (report ID: 582195).

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[32] **US secures world stock of key Covid-19 drug remdesivir**. Sarah Boseley: https://www.theguardian.com/us-news/2020/jun/30/us-buys-up-world-stock-of-key-covid-19-drug

[33] Recovery Trial – Dexamethasone results: https://www.recoverytrial.net/results/dexamethasone-results

[34] **Drug recently shown to reduce coronavirus death risk could run out, experts warn**. Eli Cahan: https://www.sciencemag.org/news/2020/06/corticosteroid-drug-recently-shown-reduce-coronavirus-death-risk-could-run-out-experts

[35] United States Food and Drug Administration. **Cadila Healthcare Limited**: https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/warning-letters/cadila-healthcare-limited-584856-10292019

[36] United States Food and Drug Administration. **Dexamethasone Sodium Phosphate Injection Status**: https://www.accessdata.fda.gov/scripts/drugshortages/dsp_ActiveIngredientDetails.cfm?AI=Dexamethasone%20Sodium%20Phosphate%20Injection&st=c

[37] World Health Organisation. **Q&A dexamethasone and COVID-19**: https://www.who.int/news-room/q-a-detail/q-a-dexamethasone-and-covid-19

[38] World Health Organisation. **WHO Director-General's opening remarks at the media briefing on COVID-19 - 22 June 2020**: https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---22-june-2020

Sildenafil

In several countries and hospitals, clinical trials have been launched to test inhaled nitric oxide for preventing progression of COVID-19. Oral sildenafil enhances nitric oxide mediated vasodilatation and in China, Wuhan, a pilot study was launched to explore the use of sildenafil in mild and severe COVID-19.

The articles captured by the MQM Globe on sildenafil are most probably not related to COVID-19 since sildenafil is widely smuggled and falsified. Nevertheless we report on the articles related to SF-sildenafil cases to highlight the risk. In January two men were arrested in India for smuggling sildenafil and other stimulating drugs to pharmacies into the US (report ID: 435956). In March a man was charged in the USA for selling falsified Viagra (report ID: 488165).
Ten other articles were found on the MQM Globe because sildenafil was mentioned as hidden drug ingredient in sexual enhancement product, in Brunei Darussalam (report ID: 460253), Canada (report ID: 522265), Uganda (558937), Ireland (601213), and the United States (report ID: 447702, 447701, 447703, 469364,469365, 473467, 611477). There are many examples of falsified sildenafil before January 2020.

Other trial medicines

In the USA many other COVID-related products that have been included in COVID-19 clinical trials have been seized, mainly at customs in April, May and June. The seized medicines mentioned in the articles were azithromycin, Lianhua Qingwen Jianonang capsules, Huoxiang Zhengqi dripping pills, oseltamivir and paracetamol (report ID: 530144, 566171, 593883, 593984, 602903). Some Lianhua Qingwen capsules originated from Hong Kong and unapproved for use in the USA, were given to COVID-patients (report ID: 564727).

Other alerts captured on the MQM Globe are not necessarily linked to the treatment of COVID-19 patients. We nevertheless share the information since the medical products contained APIs used in COVID-19 trials. In January GSK recalled two Excedrin products containing salicylic acid, for which the ingredients may have been measured improperly (report ID: 435578). In April International Laboratories launched a recall for clopidogrel out of concern that some bottles might contain the wrong medicines due to mislabelling of the packaging (report ID: 530298).
The Indian CDSCO releases monthly the results of their routine quality tests. Some of the medicines that failed testing have the same active pharmaceutical ingredients as COVID-19 trial medicines. In January samples of amoxicillin-potassium clavulanate; telmisartan; paracetamol; vitamin B-complex; and methylprednisolone (report ID: 456231) failed tests. In April ramipril; calcium with vitamin D3; clopidogrel & aspirin; tranexamic acid; amoxicillin-potassium clavulanate; paracetamol, phenylephrine hydrochloride and chlorpheniramine maleate combination product (report ID: 609090) failed tests. In May iron, folic acid & vitamin B 12 combination product; atorvastatin (report ID: 600118) failed tests. In February, the MQM Globe yielded an alert that at some governmental hospitals where patients were supposed to receive telmisartan tablets, the wrappers contained powder instead (report ID: 449695). In the same month the Bureau of Pharma PSUs of India recalled several batches of 52 drugs including telmisartan and ramipril (report ID: 455388).

We do not include discussion of the many examples of fraudulent claims and quackery, as there are so many, but we alert to this investigative journalist documentary from Ghana published by BBC News Africa: 'Corona Quacks, Exposing fake coronavirus cures in Ghana'[39].

4.7 Ventilators and PEEP

Sufficient ventilation devices, such as ventilators, oxygen concentrators, ensuring optimal positive end-expiratory pressure (PEEP), are vital in treating patients with severe COVID-19. The MQM Globe database holds 2 reports linked to ventilation equipment.

In June the Nigerian NAFDAC warned in general on the increasing volume of SF medical products in the market and mentioned scam websites offering ventilators (report ID: 591853). Prior, in April, Europol reported on a vendor on the dark web (ToRRenz Market) offering oxygen concentrators and ventilators[40]. There were no recorded sales though.
In India there was a problem with falsified ventilators in government hospitals in Gujarat state (reportID: 575647, 627561)[41]. The Gujarat government distributed mechanised bag valve masks bags as Gujarat-made "ventilators". Several problems were highlighted with regards to the governments purchase of the 900 'Dhaman-1' ventilators: (1) the device did not have the mandatory licence from Drug Controller General of India, (2) the equipment was only trialled on one patient, and (3) the ethics committee that authorized the trial was not formed according to standards. The use of these falsified ventilators may have led to the death of 300 patients.

Other issues related to the quality of ventilation devices reached the media. In April Bikash Chatterjee, Pharmatech Associates, launched a call to ensure quality in ventilator production scale-up[42]. He notes that the United States FDA has adapted the cGMP requirements for the Emergency Use Authorization program[43], but after this change substandard quality antibody tests entered in the market. He warns that quick scale up of ventilators should not be at the sacrifice of quality: "*it is still possible to control the sources of variation that can impact product quality and safety by addressing them as part of the manufacturing process design and scale-up exercise*".

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[39] BBC News Africa. **Corona Quacks: Exposing fake coronavirus cures in Ghana - BBC Africa Eye documentary**: https://www.youtube.com/watch?v=qX0jbLxFQ90

[40] Europol. **Viral marketing - counterfeits, substandard goods and intellectual property crime in the COVID-19 pandemic.** *Report*. 2020 April 17. https://www.europol.europa.eu/publications-documents/viral-marketing-counterfeits-substandard-goods-and-intellectual-property-crime-in-covid-19-pandemic

[41] ReportID 627561 only mentions the problem with ventilators but does not go into detail. More information on the case was found in a previous articles from the same news site:

- https://ahmedabadmirror.indiatimes.com/ahmedabad/cover-story/the-fake-ventilator-scam-no-dgci-licence-for-900-fake-ventilators-performance-trial-held-only-on-one-patient/articleshow/75815096.cms.
- https://ahmedabadmirror.indiatimes.com/ahmedabad/cover-story/fake-ventilators-leave-gujarat-model-gasping-for-breath/articleshow/75795508.cms

[42] **Ensuring Quality In Ventilator Production Scale-Up For COVID-19.** Bikash Chatterjee: https://www.outsourcedpharma.com/doc/ensuring-quality-in-ventilator-production-scale-up-for-covid-0001

[43] US Food and Drug Administration. **Emergency Use Authorization**: https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#abouteuas

Doctors in the United Kingdom expressed their concerns on Shangrila 510 ventilators made by Beijing Aeonmed Co. Ltd. in China[44]. In a letter to the United Kingdom National Health Service, they outlined their quality concerns: that the devices had a variable and unreliable oxygen supply, cannot be cleaned properly, and have an unfamiliar design. In addition, the instruction manual is confusing. The doctors were requesting a withdrawal of the machines.

In May Russia suspended the use of some Aventa-M ventilators after the ventilators were linked to fires in two hospitals[45]. In total 6 people died and hundreds of others were evacuated from the hospitals. The same type of ventilators were sent from Russia to the United States at the beginning of April to prevent an anticipated ventilator shortage. Ultimately the ventilators were not needed in the US and were never used. Nevertheless, Reuters reported in May that the ventilators were never authorized by the US FDA[46]. The ventilators should have received the US FDA's Emergency Use Authorization (EUA) prior to distribution. However, different from ventilators of other sources which received FDA EUA, the Russian ventilators were distributed bypassing the FDA EUA.

In late June, Philips Respironics launched a recall of a subset of its V60 ventilator through the UK MHRA[47]. The ventilators may shut down unexpectedly due to a premature component failure. The sudden loss of power may not always be accompanied by an alarm or visual warning.

[44] **British doctors warn some Chinese ventilators could kill if used in hospitals.** Alexander Smith: https://www.nbcnews.com/news/world/british-doctors-warn-chinese-ventilators-could-kill-if-used-hospitals-n1194046

[45] **US says it won't use Russian ventilators sent to it by Moscow after deadly hospital fires.** Holly Ellyatt**:** https://www.cnbc.com/2020/05/13/russian-ventilators-sent-to-us-held-after-st-petersburg-hospital-fire.html

[46] **Russian ventilators reached U.S. states without FDA oversight.** Marisa Taylor and Gleb Stolyarov: https://www.reuters.com/article/us-health-coronavirus-usa-ventilators-ex/exclusive-russian-ventilators-reached-u-s-states-without-fda-oversight-idUSKBN22Y2F4

[47] Medicines & Healthcare products Regulatory Authority - **Medical device alerts, drug alerts, field safety notice, and drug alert: company-led Philips Respironics V60 ventilator**: https://www.gov.uk/drug-device-alerts/philips-respironics-v60-ventilator-potential-unexpected-shutdown-leading-to-complete-loss-of-ventilation-mda-2020-017?utm_source=bb206eed-a38d-40fa-bada-00a0080df05e&utm_medium=email&utm_campaign=govuk-notifications&utm_content=daily

5 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 4 'Lay literature' are detailed in the annexes. To consult the reportIDs, please see the extended version, containing the annexes, and/or consult the online MQM Globe[48], using the report ID in the search box.

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[48] IDDO. **Medicine Quality Monitoring Globe**: https://www.iddo.org/medicine-quality-monitoring-globe