Medical Product Quality Report – COVID-19 Issues

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UNIVERSITY OF OXFORD

IDDO INFECTIOUS DISEASES DATA OBSERVATORY

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1. Summary of findings

This year we first saw a wave of substandard and falsified (SF) COVID diagnostics together with a rising number of problems linked to personal protective equipment. From June to August there was a growing number of articles linked to SF hand sanitizers but that has reduced from September mainly due to a lower number of incidents identified in the United States. In October the MQM Globe yielded the lowest number of new articles linked to SF COVID-19 supplies since February.

There have been several recent alerts on SF hand sanitizers in Canada whose list of recalls is growing. We have also seen a decrease in number of incidents linked to SF personal protective equipment, especially for masks.

Although there are very encouraging reports of three COVID-19 vaccines trials, no vaccine has fully completed all three phases of the clinical trial process. However, falsified versions are allegedly circulating in Brazil, the United States of America (USA) and in Myanmar. For October the MQM Globe did not yield reports on SF corticosteroids and dexamethasone in particular, the only proven effective treatment against severe COVID-19. Remdesivir has no or little effect[1], nevertheless people are making profit out of it on the black market. Although Eli Lilly & Co is developing a Covid-19 antibody therapy, the US Food and Drug Administration found serious quality-control problems at one of their production plants.

Although we captured fewer articles on SF COVID-19 products in October, monitoring and data sharing remain key as patients health remains at risk in low, middle and high income countries. Since the beginning of the pandemic, we identified incidents worldwide (figure 1) and all levels of the supply chain seem to have been affected. Focus should be on optimizing risk-based post-marketing surveillance to prevent, detect and respond to SF COVID-19 medical products. An objective evidence base is needed to plan risk-based post market surveillance for COVID-19 vaccines for when they are approved and distributed.

[1] WHO. Solidarity clinical trial for COVID-19 treatments. Published October 15, 2020. Accessed November 20, 2020. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments

Figure 1. Incidents on poor quality medicines and medical products from January to October 2020 linked to COVID-19. This Image was generated with the Medicine Quality Monitoring Globe using COVID-19 (and synonyms) as search terms . It includes incidents identified by the system in English, French, Vietnamese, Mandarin and Spanish languages.
The data are geographically heterogeneous and an important caveat is that no/few news or reports from a country or area does not imply that medical product quality there is good but that there are no/few accessible data from that country or area, or that articles were not published in the languages included in our system. Similarly, many news and reports of poor quality medical products in a country does not imply that medical product quality there is universally grave in comparison to elsewhere. Countries with many news reports should be lauded for facilitating such reporting. Only English articles are described in the monthly COVID-19 issues.

2. Introduction

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

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

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

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

- **Substandard medical products**
  Also called “out of specification”, these are authorized medical products that fail to meet either their quality standards or their specifications, or both.

- **Unregistered/unlicensed medical products**
  Medical products that have not undergone evaluation and/or approval by the national or regional regulatory authority for the market in which they are marketed/distributed or used, subject to permitted conditions under national or regional regulation and legislation.

- **Falsified medical products**
  Medical products that deliberately/fraudulently misrepresent their identity, composition or source.

We emphasise the difference between the use of the terms ‘falsified’ and ‘counterfeit’ medical products. ‘Falsified’ is a broad term including all the various types of deliberate misrepresentation of a medical product from a public health perspective. The term ‘counterfeit’ is specifically linked to intellectual property rights, ‘trademark counterfeit goods’[3] and ‘pirated copyright goods’[4] as used in the Trade-Related Aspects of Intellectual Property Rights (TRIPS) agreement.

The reports presented were mostly extracted from the Medicines Quality Monitoring Globe (the MQM Globe is accessible on the IDDO website[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. We also include preprint of articles. Please note that preprints should be viewed with additional caution as they have not been peer-reviewed. They should not be relied on to guide clinical practice or health-related behaviour and should not be reported in news media as established information.

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[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. Part III — Enforcement of Intellectual Property Rights. Accessed August 14, 2020. https://www.wto.org/english/docs_e/legal_e/27-trips_05_e.htm#fnt-14

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

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

Please note the caveats for the lay literature (MQM Globe disclaimer and caveats are accessible on the IDDO website[6]); 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 fifth issue of the monthly report 'Medical Product Quality Report – COVID-19 Issues' covers information published during the month of October. The previous issues covered publications from January 1st to September 30th 2020 and are available on the IDDO website[7]. We also include publications and reports published prior to October 2020 that were missed in the previous issues of the report. We are developing a system for scraping regulatory authority and international organisation websites for alerts. Any remarks or additions to content are greatly appreciated (please write to medicinequality@iddo.org).

3. Scientific literature

3.1. General

Badnjević A, Pokvić LG, Džemić Z, Bečić F. **Risks of emergency use authorizations for medical products during outbreak situations: a COVID-19 case study.** *Biomed Eng Online*. 2020;19(1):75. doi:10.1186/s12938-020-00820-0

> Abstract. *« (*)Background. The world is facing an unprecedented outbreak affecting all aspects of human lives which is caused by the COVID-19 pandemic. Due to the virus novelty, healthcare systems are challenged by a high rate of patients and the shortage of medical products. To address an increased need for essential medical products, national authorities, worldwide, made various legislative concessions. This has led to essential medical products being produced by automotive, textile and other companies from various industries and approved under the emergency use authorizations or legal concessions of national regulatory bodies. This paper presents a narrative commentary of the available documentation on emergency use authorizations and legal concessions for medical products during COVID-19 pandemic.*
> *(*)Methodology. The basis for narrative commentary includes scientific articles published in Web of Science, Scopus, PubMed and Embase databases, official publications of international organizations: Food and Drug Agency, World Health Organisation, World Bank and United Nations, and national regulatory agency reports in native languages (English, German, Bosnian, and Croatian) published from November 1, 2019 to May 1, 2020. This paper focuses on three types of essential medical products: mechanical ventilators, personal protective equipment and diagnostic tests. Evidence-informed commentary of available data and potential identified risks of emergency use authorizations and legal concessions is presented.*
> *(*)Discussion. It is recognized that now more than ever, raising global awareness and knowledge about the importance of respecting the essential requirements is needed to guarantee the*

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

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

appropriate quality, performance and safety of medical products, especially during outbreak situation, such as the COVID-19 pandemic. Emergency use authorizations for production, import and approval of medical products should be strictly specified and clearly targeted from case to case and should not be general or universal for all medical products, because all of them are associated with different risk level.
(*)Conclusion. Presented considerations and experiences should be taken as a guide for all possible future outbreak situations to prevent improvised reactions of national regulatory bodies. »

Islam MT, Talukder AK, Siddiqui MN, Islam T. **Tackling the COVID-19 pandemic: the Bangladesh perspective.** *J Public health Res*. 2020;9(4):1794. doi:10.4081/jphr.2020.1794

Extract from the paper. *« Lack of safety equipment. There is inadequate supply of personal protection equipment (PPE), standard masks, and hand gloves to the health service providers, which is one of the major constraints in providing treatment facilities. A significant lack of safety equipment is fueling the concern for frontline health service providers like doctors and nurses. Some corrupt officials of health ministry were involved in importing low quality protective equipments. Some factories were also involved in producing cheap and poor quality antiseptic liquids, face masks, hand gloves and PPE all over Bangladesh. These low quality healthcare products are now posing great risk to public health amid the ongoing pandemic COVID-19. A large number of doctors, nurses, and persons of law enforcing agencies have already diagnosed as COVID-19 patients in the country. Of note, until August 11, 2020, approximately 92 doctors have been died of this disease in Bangladesh. Collectively, the limitation of PPE and inadequate test facilities of real-time RT-PCR are the big challenges for Bangladesh. The government has to make available more test facilities and import high quality of these protective gears immediately. »*

Jairoun AA, Al-Hemyari SS, Shahwan M, El-Dahiyat F, Jamshed S. **Scale validation for the identification of falsified hand sanitizer: public and regulatory authorities perspectives from United Arab Emirates.** *BMC Public Health*. 2020;20(1):1595. doi:10.1186/s12889-020-09707-0

Abstract. *« (*)Background. Since the time of declaration of global pandemic of COVID-19 by World Health Organization (WHO), falsified hand sanitizers surfaced regularly in markets, posing possible harm to public due to unlisted inclusion of methanol. The current research is an attempt to develop and validate a tool to document falsified hand sanitizer in the UAE community.*
(*)Method. A descriptive cross-sectional community-based study was conducted among 1280 randomly selected participants. Respondents were sent a web-based electronic link to the survey via email. Content validity, factor analyses and known group validity were used to develop and validate a new scale to identify falsified hand sanitizer. Test-retest reliability, internal consistency, item internal consistency (IIC), and intraclass correlation coefficients (ICCs) were used to assess the reliability of the scale. SPSS version 24 was used to conduct data analysis.
(*)Results. A total of 1280 participants were enrolled in the study. The content validity index (CVI) was 0.83 with the final scale of 12 items. The Kaiser-Meyer-Olkin (KMO) value was 0.788, with the Bartlett test of sphericity achieving statistical significance ($p < 0.001$). Our factor analysis revealed a 3-component model. The 3-factor solution was confirmed by PCFA analysis and had associations with good fit values. The PCFA for NFI was 0.970, CFI 0.978, and TLI 0.967. All values were in excess of 0.95, with RMSEA values below 0.06 at 0.03; all of these values indicated a good model fit. The Cronbach's alpha was good overall (0.867). All factors had a Cronbach's alpha value in excess of 0.70. The instrument demonstrated that every item met the IIC correlation standard ≥0.40. The scale displayed good overall ICC statistics of 0.867 (95% CI 0.856–0.877) with statistical significance ($p < 0.001$). The scale's test-retest reliability was assessed through correlation of the falsified hand sanitizer identification score of respondents at the two time points. The test-retest correlation coefficient was 0.770 (p value < 0.01). Participants with post-graduate education were more likely to identify the falsified hand sanitizer compared to

those with high school education. (p < 0.001).
(*)Conclusions. This study developed and validated a new scale for the measurement of falsified hand sanitizer. This is expected to improve and promote collaboration between the health regulators and the public and hereby encourage customer satisfaction and participation. »

Mukherjee S, Bonatsos V, Raza A. **The Urologist, Personal Protective Equipment (PPE) and COVID-19.** *J Endoluminal Endourol*. 2020;3(4):e1-e14. doi:10.22374/jeleu.v3i4.104

Extract from the paper. *« Substandard or poor-quality PPE. As well as shortages of PPE there have been reports of poor-quality PPE supplies that do not meet safety standards putting both patients and HCW's lives at risk of contracting COVID-19 infection. The Health and Safety Executive (HSE) has issued a safety alert against the use of KN95 facemasks as there is no independent assurance of their quality and it has been confirmed by testing that they do not meet safety standards. HSE has recalled around 1.5 million KN95 masks and halted around 25 million items of inappropriate FFP3 respirators entering the supply chain. There was also a surge in homemade and non-medical companies providing PPE to the NHS free of charge i.e. homemade visors; however, such equipment should not be used unless it has been approved by HSE or the local NHS Trust for safe use. The British Medical Association Guidance states that if adequate amounts of properly tested PPE are not available this matter should be raised with the local trust and HCWs can refuse to treat patients if staff PPE is deemed to be unsafe or inappropriate. »*

Nigro F, Tavares M, Sato de Souza de Bustamante Monteiro M, et al. **Changes in workflow to a University Pharmacy to facilitate compounding and distribution of antiseptics for use against COVID-19.** *Res Soc Adm Pharm*. Published online 2020. doi:10.1016/j.sapharm.2020.09.016

Abstract. « *This article is a report from an experience about a work developed by Farmácia Universitária at UFRJ (FU-UFRJ) during the nCov-19 pandemic period. The aim of this work was to describe its contribution in the production of antiseptic supplies used to prevent contagion by the new coronavirus. The work routine at the pharmacy has been changed to allow the implementation of local workflow during the pandemic, and to adapt the protection rules to meet the safety measures. FU-UFRJ started to manipulate two antiseptic formulations: 70% ethyl alcohol and gel alcohol, which are included in the National Form, manufacturing around 100 L of these formulations, weekly, to donate to different health units. The experience enabled the adaptation to emergency health standards, planning and meaningful guidance to pharmacists and technicians to attend clinics at university hospitals, vaccination center and UFRJ city hall, in order to facilitate the access to adequate hand hygiene to the population.* »

Ogunleye OO, Basu D, Mueller D, et al. **Response to the Novel Corona Virus (COVID-19) Pandemic Across Africa: Successes, Challenges, and Implications for the Future.** *Front Pharmacol*. 2020;11. doi:10.3389/fphar.2020.01205

Abstract. « *(*)Background. The COVID-19 pandemic has already claimed considerable lives. There are major concerns in Africa due to existing high prevalence rates for both infectious and non-infectious diseases and limited resources in terms of personnel, beds and equipment. Alongside this, concerns that lockdown and other measures will have on prevention and management of other infectious diseases and non-communicable diseases (NCDs). NCDs are an increasing issue with rising morbidity and mortality rates. The World Health Organization (WHO) warns that a lack of nets and treatment could result in up to 18 million additional cases of malaria and up to 30,000 additional deaths in sub-Saharan Africa.*
(*)Objective. Document current prevalence and mortality rates from COVID-19 alongside economic and other measures to reduce its spread and impact across Africa. In addition, suggested ways forward among all key stakeholder groups.
(*)Our Approach. Contextualise the findings from a wide range of publications including internet-based publications coupled with input from senior-level personnel.

(*)Ongoing Activities. Prevalence and mortality rates are currently lower in Africa than among several Western countries and the USA. This could be due to a number of factors including early instigation of lockdown and border closures, the younger age of the population, lack of robust reporting systems and as yet unidentified genetic and other factors. Innovation is accelerating to address concerns with available equipment. There are ongoing steps to address the level of misinformation and its consequences including fines. There are also ongoing initiatives across Africa to start addressing the unintended consequences of COVID-19 activities including lockdown measures and their impact on NCDs including the likely rise in mental health disorders, exacerbated by increasing stigma associated with COVID-19. Strategies include extending prescription lengths, telemedicine and encouraging vaccination. However, these need to be accelerated to prevent increased morbidity and mortality.
(*)Conclusion. There are multiple activities across Africa to reduce the spread of COVID-19 and address misinformation, which can have catastrophic consequences, assisted by the WHO and others, which appear to be working in a number of countries. Research is ongoing to clarify the unintended consequences given ongoing concerns to guide future activities. Countries are learning from each other. »

3.2. Seizures/Surveys/Case Reports/Reviews

Berardi A, Cenci-Goga B, Grispoldi L, Cossignani L, Perinelli DR. **Analysis of Commercial Hand Sanitisers amid CoViD-19: Are We Getting the Products that We Need?** *AAPS PharmSciTech*. 2020;21(7):1-6. doi:10.1208/s12249-020-01818-6

Abstract. *« The CoViD-19 pandemic has caused a sudden spike in demand and production of hand sanitisers. Concerns are rising regarding the quality of such products, as the safeguard of consumers is a priority worldwide. We analyse here the ethanolic content of seven off-the-shelf hand sanitiser gels (two biocides and five cosmetics) from the Italian market, using gas chromatography. The WHO recommends that products containing ethanol should have 60–95% (v/v) alcohol. Four of the tested hand gels have ethanolic contents within the recommended range, while three products (all cosmetics) contain < 60% (v/v), i.e. 52.1% (w/w), ethanol. The product with the lowest alcoholic content has 37.1% w/w ethanol. Toxic methanol is not found in any of the hand sanitisers. We show, in addition, that products with the highest ethanolic content have generally greater antibacterial activity. In conclusion, all tested products are complying with the EU regulations, as the three "substandard" products are classified as cosmetics, whose purpose is cleaning and not disinfecting. Nevertheless, if such hand cleaners were inappropriately used as hand disinfectants, they might be ineffective. Thus, consumer safety relays on awareness and ability to distinguish between biocidal and cosmetics hand gels. The obtained results might sensitise the scientific community, health agencies and ultimately consumers towards the risks of using hand sanitisers of substandard alcoholic concentration. If the wrong product is chosen by consumers, public health can be compromised by the inappropriate use of "low-dosed" cosmetic gels as disinfectants, particularly during the period of the CoViD-19 pandemic. »*

Brochot C, Saidi MN, Bahloul A. **How Effective Is the Filtration of 'KN95' Filtering Facepiece Respirators During the COVID-19 Pandemic?** *Ann Work Expo Heal*. 2020;2020:1-9. doi:10.1093/annweh/wxaa101

Abstract. *« (*)Objectives. The high demand of filtering facepiece respirators (FFRs) worldwide during the period of the COVID-19 pandemic has led to a critical situation for decision-makers regarding their supply. After authorizing the use of FFRs certified by other regions of the world, decision-makers in many countries have published alerts, particularly concerning the 'KN95' type. (*)Methods. This paper investigated the filtration performance of different FFRs using an experimental setup already employed during several studies on FFRs filtration performance. Its high-resolution measuring devices permit to determine filtration performance according to the normative criteria: the pressure drop and the filtration efficiency. Eight different FFRs have been used: four NIOSH-approved FFRs and four not NIOSH-approved with a 'KN95' shape available*

during the beginning of the COVID-19 pandemic.
(*)Results. The data show a high disparity between different FFRs purchased by healthcare establishments, and between those that are NIOSH-approved and those that are not NIOSH-approved. The results confirm that the NIOSH certification offers good protection according to the normative criteria. The 'KN95' types present pressure drops which correspond to the normative value, however their efficiencies are lower than the efficiencies of FFRs certified by NIOSH and lower than 95% at the most penetrate particle size.
(*)Conclusions. FFRs marking is not sufficient to conclude on the FFRs' efficiency. Visual inspection cannot determine which samples are counterfeit or have manufacturing defects. »

Eboibi FE. **Cybercriminals and Coronavirus cybercrimes in Nigeria, the United States of America and the United Kingdom: cyber hygiene and preventive enforcement measures.** *Commonw Law Bull*. Published online 2020. doi:10.1080/03050718.2020.1834424

Abstract. *« There seems to be no lockdown for cybercriminals who are capitalizing on the global lockdown to perpetrate cyber coronavirus crimes. Qualitatively, this paper examines these crimes, their peculiarities, and how they can be curtailed. Although the United States of America (US) and the United Kingdom (UK) have put in place cyber hygiene and preventive enforcement measures to curtail the activities of cybercriminals in cyberspace, the same cannot be said of Nigeria. Arguably, cybercrime institutions in Nigeria lack adequate capacity building, professional competence, and inter-agency cooperation concerning cyber coronavirus crimes. Consequently, it calls for the adaptation of the US and UK measures to protect cybercitizens. »*

4. International organisations

UNODC. **Good Practices Compendium on Combating Corruption in the Response to COVID-19.** 2020. Accessed November 20, 2020. https://www.unodc.org/pdf/corruption/G20_Compendium_COVID-19_FINAL.pdf

Executive summary. *« The rapid spread of the COVID-19 pandemic and its ensuing consequences have affected almost every aspect of society and created opportunities for corruption to thrive and grow, as actions taken to quickly address the needs presented by the crisis may lead to sacrifices in transparency and accountability. Corruption risks have proliferated across a variety of fields threatening life-saving aid and further hurting the most marginalized and vulnerable populations. In response to these growing threats, the G20 Anti-Corruption Working Group (ACWG) sought to identify key anti-corruption practices undertaken by G20 countries to address COVID-19. A survey was disseminated to all G20 countries in July 2020 to better understand the new and existing anti-corruption threats and countermeasures used to respond to the crisis and share experiences to inform global policy and strengthen international cooperation. 22 countries responded, with many using similar strategies and techniques to address common corruption risks arising from or exacerbated by COVID-19, with unique manifestations depending on national contexts and priorities. »*

Extract from the text. *« The number of G20 countries that identified certain corruption risks emanating from the COVID-19 crisis. Nine countries indicated risks pertaining to cyberfraud which include the utilization of new Information and Communication Technologies and cyber-scams. 13 countries reported increased corruption vulnerabilities in the exploitation of stimulus packages including dedicated employment furlough schemes and other economic aid. 15 countries identified heightened health-related fraud which includes risks emanating from counterfeit medicines, overpriced medical equipment, health procurement collusion, among others. It is worth noting that these risks were also identical to the new and emerging risks identified by G20 countries. »*

UNODC. **Research Brief: The Impact of COVID-19 on Organized Crime.** 2020. Accessed November 20, 2020. https://www.unodc.org/documents/data-and-analysis/covid/RB_COVID_organized_crime_july13_web.pdf

Extract from the text. *« The aim of this research brief is to present an abbreviated assessment of the growing impact of the COVID-19 pandemic on OCGs' [organized criminal groups] infiltration of the legal economy and their illegal governance activities. »*

« High demand coupled with low supply in key sectors opens way for OCGs. The pandemic has brought dramatic spikes in demand to some sectors, for example medical devices, pharmaceutical products, e-commerce, food retail, cleaning, and funeral services. The demand for sanitary masks, breathing devices, and medicines has also risen notably. As governments seek to shore up their defences against the pandemic, procurement procedures in some countries have been relaxed. There is already evidence from countries around the world that organized crime has moved into these sectors – especially where traditional means of making illicit profits, such as illicit drugs and firearms trafficking and smuggling of migrants are being tightly constricted by restrictions on movement. For The impact of covid-19 on organized crime 2 example, falsified medical masks have been seized in Spain and Italy, attempts to smuggle vital equipment have been stopped in Ukraine, Iran, and Azerbaijan; one Mexican cartel has been promoting the production of falsified COVID-19 medical products and forcing pharmacies to sell them. »

UNODC. **Research Brief: COVID-19 and the Drug Supply Chain: From Production and Trafficking to Use.** 2020. Accessed November 20, 2020. https://www.unodc.org/documents/data-and-analysis/covid/Covid-19-and-drug-supply-chain-Mai2020.pdf

Extract from the text. *« The aim of this research brief is to present a rapid assessment of the impact of the COVID-19 pandemic on the drug supply chain, from drug production and trafficking to consumption. »*

« Organized criminal groups react adaptively to market changes. Past experience has demonstrated the capacity of such groups to rapidly adapt their modus operandi or switch market in response to shocks or new opportunities. For example, following a poppy blight in Afghanistan in 2010 and concurrent political developments, cannabis was increasingly produced in the country and international drug trafficking groups increased trafficking in cannabis products from Afghanistan to Europe. In the past, in some parts of Peru, coca cultivation was scaled back concurrently with an increase in illicit mining in response to increases in the price of gold. The rapid adaptation of organized criminal groups to new environments has already been reported in some Balkan countries where certain organized criminal groups involved in drug trafficking are moving into forms of crime linked to the COVID-19 virus, such as cybercrime and trafficking in falsified medicines. »

5. Miscellaneous

Publications prior to October 2020

NABP. **Rogue Online Pharmacies in the Time of Pandemic: Capitalizing on Misinformation and Fear.** 2020. Accessed November 13, 2020. https://nabp.pharmacy/wp-content/uploads/2020/05/Rogue-Rx-Activity-Report-May-2020.pdf

> Extract from the text. « *In an effort to protect vulnerable consumers, government agencies are cracking down on COVID-related cybercrime. NABP applauds these efforts. Regulators, members of Congress, and state attorneys general are also asking the private sector for assistance. Many internet intermediaries have stepped up to the plate, shutting down fraudulent face mask, vaccine, and test kit sellers. However, illegal internet "pharmacies" continue, largely unabated, to peddle falsified, substandard, and dangerous drugs, including purported treatments for COVID-19. This behavior is predictable; these bad actors have been around for over 20 years. We can – and must – stop it now.* »

6. Lay literature

6.1 Disclaimer & Notes

The information included below is based on the data used to create the Medicine Quality Monitoring Globe[8] (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[9].

The Google News search tool is used to capture data from online news sources. Articles matching the search terms are loaded into a database and curated by trained analysts. Because the Globe system extracts newspaper articles from journals referenced in Google News only, reports not referenced in Google News would not be captured. Please consult the IDDO website for full methodology[10]. On the 20th of March, the search terms were adapted to capture more papers on substandard and falsified (SF) medical supplies for COVID-19 from Google News.

The news articles discussed in the sections below are available in the Globe-reports, in this report's annexes, or on the online MQM Globe using the report ID (six digits code). The MQM Globe-reports are generated with pre-defined search terms, which enable quick access to reports of (a) COVID vaccines, (b) COVID diagnostics, (c) Personal Protective Equipment (PPE), (d) Sanitisers and disinfectants, (e) COVID medicines, and (f) Ventilators and Positive end-expiratory pressure. For alerts from January to September the Globe-report for PPE included sanitisers and disinfectants. From October onwards sanitisers and disinfectants are grouped in a separate Globe-report. The search terms applied to search the Globe database to compile the Globe-reports were revised in October. Therefore caution is required when interpreting the number of alerts or articles over time.

In this report we share articles captured by the MQM Globe that are linked to medical products potentially used in the context of COVID-19 or to active pharmaceutical ingredients (APIs) that are being trialled for COVID-19 treatment and/or prevention. In theory there is a distinction between (a) SF incidents that are due to or increased by the COVID-19 epidemic; and (b) incidents that would have happened in any case. It can be difficult to make the distinction between the two types of incidents and some

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

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

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

reports cited below are not directly linked to the treatment of COVID-19. Nevertheless we have included them as crossover risks and to assess the evolution of the alerts on these medical products over time. Although oxycodone is trialled[11], we do not include issues related to oxycodone as the system would become swamped by reports on its inappropriate use and cases of pills laced with fentanyl due to its wide occurrence on the black market.

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

6.2 Articles on substandard or falsified medical products for COVID-19: main characteristics

Since the beginning of the pandemic we have identified over 414 relevant articles on quality problems of COVID-19 medical products (see table 1). For October we report on 35 articles linked to SF COVID-19 supplies alerted through the MQM Globe database. Within those articles, 3 alerted on falsified vaccines, 4 on diagnostics, 12 are linked to personal protective equipment (PPE), 7 to hand sanitisers and disinfectants, and 16 report on COVID-19 related treatments (see figure 2 and 3). Since June, the MQM Globe did not identify any report linked to ventilation equipment.

Table 1. Number of articles on the Medicines Quality Monitoring Globe linked to substandard or falsified COVID-19 supplies by month. As some articles describe more than one category of products, the sum of alerts per month as shown in figure 2 and 3 may exceed the sum of articles per month of table 1.

Month	Number of articles
January	2
February	10
March	49
April	50
May	47
June	64
July	42
August	62
September	53
October	**35**

[11]Hashemian SRM. Evaluation the effects of Oxycodone administration on pain control in patients with COVID-19. Iranian Registry of Clinical Trials. Published June 8, 2020. Accessed October 9, 2020. https://en.irct.ir/trial/48534

In the beginning of October an article reported on several seizures performed by the US Customs and Border Protection (US CBP) throughout the Mid-Atlantic region in the United States of America (USA) in the 6 previous weeks including falsified masks, COVID-19 related medication, and COVID-19 test kits (report ID 757518). In the end of October an FDA official released the results of operation called “Quack Hack”, launched in March (report ID 786684). The aim to proactively identify threats to consumers linked to COVID-19 related products led to 120 US FDA warning letters, 270 reports sent to online marketplaces and 225 complaints sent to domain registrars. The US FDA identified more than 1100 fraudulent and unproven COVID-19 related medical products such as medicines, tests and PPE.

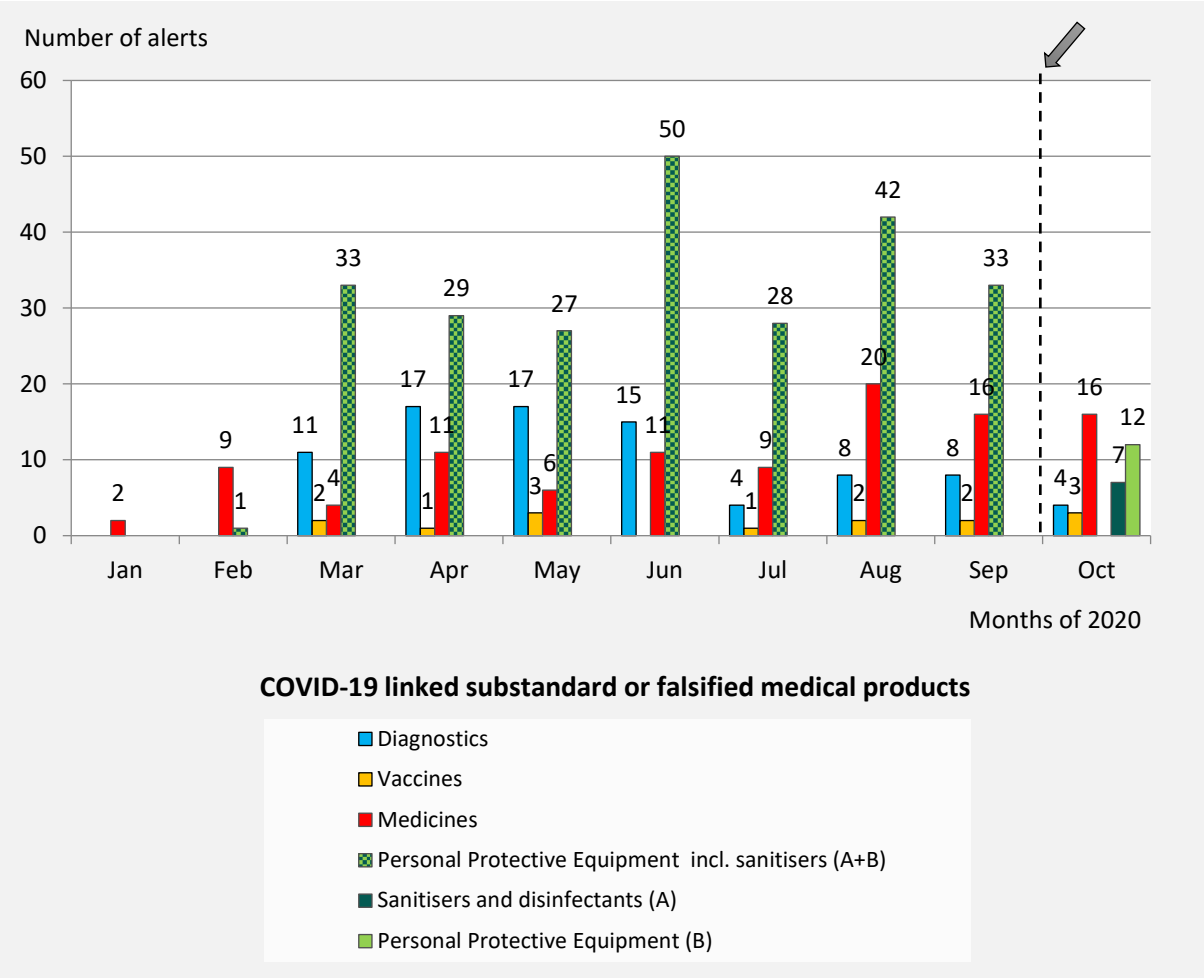

Figure 2. Number of alerts on the Medicines Quality Monitoring Globe by category of products and by month.

ALERTS ARE FOR SUBSTANDARD OR FALSIFIED PRODUCTS LINKED TO COVID-19. AS SOME ARTICLES DESCRIBE MORE THAN ONE CATEGORY OF PRODUCTS, THE SUM OF ALERTS PER MONTH MAY EXCEED THE SUM OF ARTICLES PER MONTH REPORTED IN TABLE 1.

THE ARROW INDICATES THE END OF SEPTEMBER WHEN THE CATEGORY OF “PERSONAL PROTECTIVE EQUIPMENT INCL. SANITISERS” WAS SPLIT IN TWO DISTINCT CATEGORIES: (A) SANITISERS AND DISINFECTANTS, AND (B) PERSONAL PROTECTIVE EQUIPMENT.

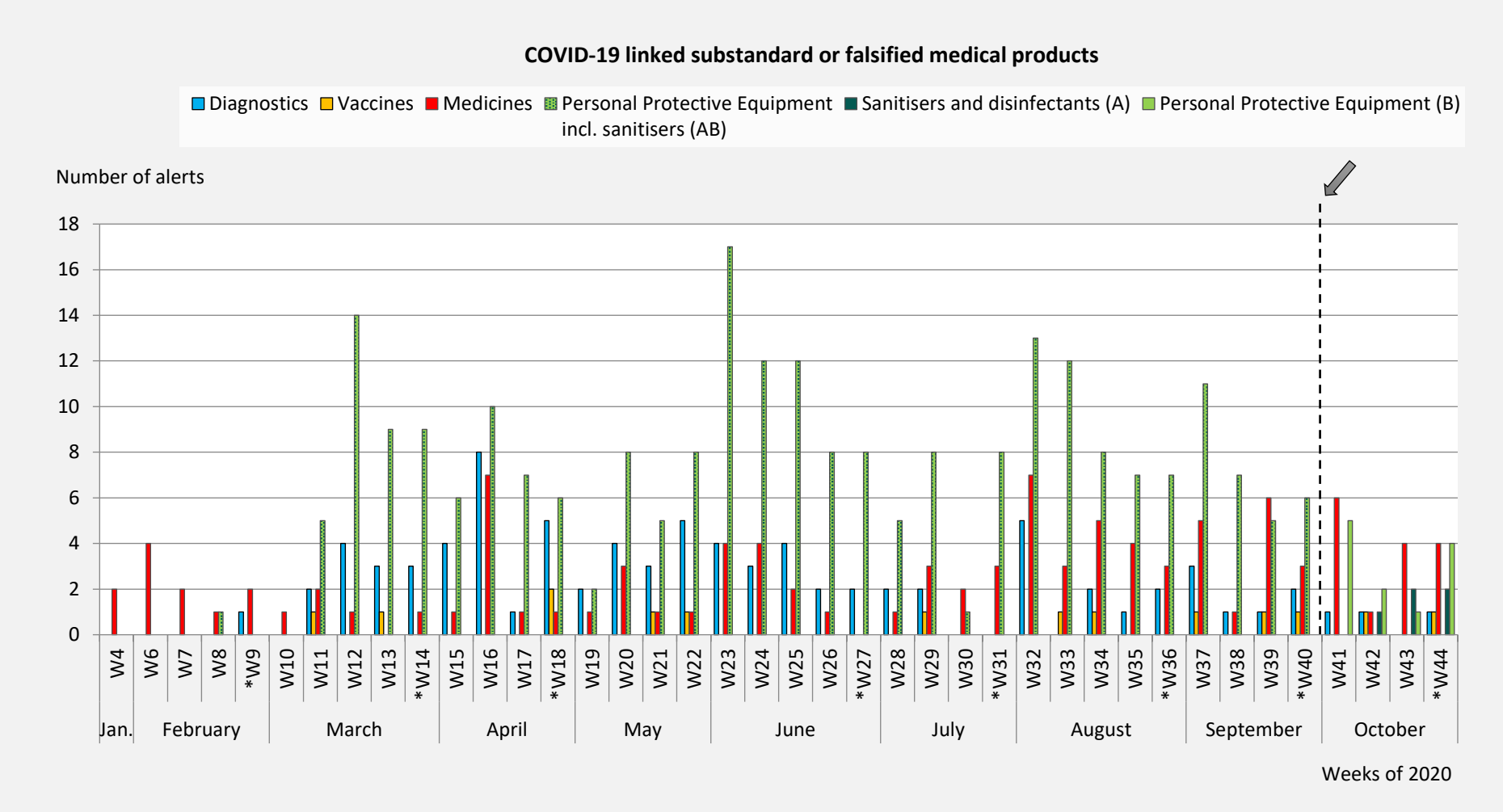

Figure 3. Number of alerts on the Medicines Quality Monitoring Globe by category and by week.

ALERTS ARE FOR SUBSTANDARD OR FALSIFIED PRODUCTS LINKED TO COVID-19. WEEK 4 STARTS ON MONDAY 20TH OF JANUARY 2020 AND WEEK 44 ENDS ON WEDNESDAY 31TH OF OCTOBER 2020. WEEKS WITH AN ASTERISK ARE OVERLAPPING 2 MONTHS, EACH TIME THE WEEK IS ATTRIBUTED TO THE EARLIEST MONTH. AS SOME ARTICLES DESCRIBE MORE THAN ONE CATEGORY OF PRODUCTS, THE SUM OF ALERTS PER MONTH MAY EXCEED THE SUM OF ARTICLES PER MONTH REPORTED IN TABLE 1. THE ARROW INDICATES THE END OF SEPTEMBER WHEN THE CATEGORY OF "PERSONAL PROTECTIVE EQUIPMENT INCL. SANITISERS" WAS SPLIT IN TWO DISTINCT CATEGORIES: (A) SANITISERS AND DISINFECTANTS, AND (B) PERSONAL PROTECTIVE EQUIPMENT.

6.3 Vaccines

No vaccine has fully completed all three phases of the clinical trial process. Both in Myanmar and in the USA, the Food and Drug Administrations warned the public for falsified COVID-19 vaccines (report ID 750450, 787356). In the USA the warning is mainly linked to online sales. In Myanmar "COVID-19 vaccines" are being smuggled into the country and sold online. Brazilian authorities report the sale of falsified COVID-19 vaccines in Rio de Janeiro state (report ID 764662). Those are allegedly sold as the vaccine developed by AstraZeneca and the University of Oxford.

6.4 COVID-19 diagnostics

Substandard antibody test kits were allegedly imported into Nigeria (report ID 765842). The tests did not meet the minimum acceptable criteria. The authorities warned to only use validated rapid and PCR test kits. In Myanmar COVID-19 tests allegedly coming from China are sold on Facebook (report ID 750450). Amongst other products, the US CBP of the Mid-Atlantic region seized several counterfeit or unapproved test kits in the past few weeks (report ID 757518).

6.5 Personal protective equipment

In the light of pandemic-related crimes, Taiwan authorities revealed that they have seized almost 260 million falsified masks so far (report ID 785855). In October an article reported on seizures performed by the US CBP throughout the Mid-Atlantic region in the 6 previous weeks including approximately 59,000 falsified masks during 21 seizures (report ID 757518). Two articles report on the Indian police performing raids at factories and performing seizures of 437 masks and 1,532 trademark symbols at one clandestine manufacturer (report ID 787164) and 5,000 falsified masks and printing equipment from another manufacturer (report ID 760491).

In shops in the United Kingdom "*basic masks*" were seized together with other falsified coronavirus protection products (report ID: 778246). The packaging stated that the masks were of KN95 standards. In the USA an investigation by 'Associated Press' and the PBS series "Frontline" found that falsified masks are available in the market in multiple sectors (report ID 758727). Analysis of 'a handful of different masks' at the University of North Carolina showed that "*All of it was counterfeit, as defined by OSHA's definition of counterfeit or fraudulently labelled"*, some showed less than 50% effectiveness. Falsified Makrite N95 respirators were unwillingly distributed to employees of a hospital group in Rhode Island, USA (report ID 768161). The group was alerted due to a lower performance of the fit-test of the respirators and their fear was confirmed by Makrite. During spring, the Estonian government bought FFP3 respirators from a Chinese company (report ID 758487). One hundred thousand respirators appeared to be of substandard quality.

Since the beginning of the pandemic several lawsuits related to masks have been filed in the USA. From October the MQM Globe yielded an article about a distributor of personal protective equipment suing two mask vendors allegedly importing defective KN95 medical masks from China (report ID 765212). The masks came with falsified FDA certification documents and for one the nose clips were glued-on, instead of sewn-in. The company 3M, works together with law enforcement agencies to act

against falsified 3M products (report ID 755069). In the last few months, 1,200 seizures and raids leading to falsified 3M N95 respirators were conducted worldwide. The article sums up some of the recent seizures of falsified N95 respirators: 150,000 N95 respirators in Vietnam, 600,000 in the United Arab Emirates, 100,000 in South Africa and 10,000 in Latin America. Another article reported on a seizure by Hong Kong authorities of 100,000 falsified 3M respirators that were destined to be sent abroad (report ID 788080).

6.6 Sanitisers and disinfectants

Health Canada launched several recalls of hand sanitizers. One example is the recall of a falsified version of 'Zytec Germ Buster Hand Sanitizer' (report ID 749766). The falsified version wears the same national registration number and the same lot number as the genuine product. However the black and white labelling on 1 litre bottles differed from the genuine product which has coloured labels on 3.78 litre bottles. Another example is the registered 'Daily Shield' hand sanitizer, which was recalled after a falsified version was found (report ID 772302). Both products had the same national registration number but a different lot number. Between June and the end of October Health Canada's list of recalled hand sanitizers grew to more than 100 products (report ID 786925, 779042). Sanitizers on the list do not contain the recommended amount of ethanol or contain denaturants which are not permitted such as methanol.

In the Medicine Quality COVID-19 Product Report for the month of July we included an article reporting on 4 deaths in the USA related to exposure to methanol-tainted hand sanitizers. At the beginning of October this number rose to 17 deaths (report ID 749267). In addition, the FDA received 2,000 reports of non-lethal injuries from exposure to hand sanitizers contaminated by methanol. The article further highlights that the US FDA has a Do-Not-Use-List to guide consumers and health care professionals on which hand sanitizers they should avoid for quality reasons. However the FDA does not have the authority to force recalls of hand sanitizers. FDA does send warning letters, asking manufacturers to issue recalls. Most manufacturers act upon the warning letter by launching manufacturer recalls for sanitizers with quality concerns, some however delay taking action. For imported products FDA can place import alerts on the concerned products (for example report ID 782839).

An article published in October highlights the problem of substandard and falsified hand sanitizers in South Africa and raises the concern that there is no regulatory system in place for these products they only rely on companies voluntary compliance with standards (report ID 774016). In this context, sometimes manufacturers falsely claim that their products are certified by the South African Bureau of Standards. An analysis performed in May on 11 hand sanitisers bought from retailers found that 2 products were contaminated with 1-propanol and 4 had a lower alcohol content than claimed on the packaging. The same article also refers to incidents of hand sanitisers with substandard levels of alcohol in the past months in Australia, Guyana, Kenya, Nigeria, Rwanda, United Arab Emirates and Zambia.

6.7 COVID-19 medicines

For October the MQM Globe does not hold reports on SF corticosteroids. We have found no alerts on falsified remdesivir so far but a recall was issued by the Pakistan Drug Regulatory Authority, for 'Redzi 100mg solution for injection' that did not comply with quality standards (report ID 779461). In India two men were arrested for the alleged black-marketing of 'Remdac 100mg injections' (report ID 755217). The US FDA sent out warning letters to 2 companies selling online chloroquine phosphate for veterinary use: one was selling an unapproved product and the other was selling an adulterated product (report ID 782898, 782899). The websites were not promoting the products for human use but nevertheless vigilance is needed as there are reports of people taking those chloroquine products against COVID-19 (report ID 787356).

Many other repurposed and investigational antiviral and immune-based COVID-19 therapies are being trialled[12]. In addition, patients turn to some medicines that are generally used for a cold, pain, fever or to boost the immunity. For all these medicines vigilance is needed considering the risk of substandard or falsified versions.

Acetyl salicylic acid: The US Drug Enforcement Administration saw a rise in seizures of illegal drugs in the past year. They warn for tablets with illicit drugs that are manufactured without quality control and might be disguised as baby aspirin (report ID 776012).

Antibody therapy: Eli Lilly & Co is developing a Covid-19 antibody therapy. During an inspection in August, the FDA found quality-control problems at the plant in New Jersey, USA. They talk about incidents that "*leave room for significant potential impact on product quality*" (report ID 774525).

Metformin[13]: Articles in the USA reported on substandard metformin containing N-nitrosodimethylamine (NDMA). Sun Pharma is the seventh manufacturer that recently launched a recall for metformin (report ID 757820). An article reports on Amneal Pharmaceuticals Inc being sued in federal court for producing and selling NDMA contaminated metformin (report ID: 757820).

Sildenafil: Falsified 'Viagra' has been seized by customs: 15,000 tablets in the USA coming from Turkey (report ID 756371) and 960 tablets with poor packaging in Puerto Rico (report ID 768254).

Miscellaneous: In the USA, a men sells fraudulent COVID-19 prevention treatments in his practice and on his Facebook page, federal authorities are trying to stop the sale (report ID 760484). Myanmar's FDA warns for illegally smuggled COVID-19 medicines in the market (report ID 750450). In the first nine months of 2020 the Counter-counterfeit committee in Cambodia performed at least 12 seizures involving COVID-19 medicines (report ID 775466).

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

[13] Prior issues of the Medical Product Quality Report do not include articles related to metformin. Now it is included in the search terms for the Globe-report on COVID-19 medicines since it is one of the multiple molecules that is trialed for its use in COVID-19.

7. Annexes

The annexes contain the reports generated by the MQM-Globe using pre-defined search terms. The report IDs (six digits code) discussed in section 6 ‘Lay literature’ are detailed in the annexes. To consult the annexes, please see the extended version of the report and/or consult the online MQM Globe[14], using the report ID in the search box.

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