K4D | Knowledge, evidence and learning for development

Drug expiry standards in developing countries

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Question

- *What is the global evidence/experience on expiry of drugs?*
- *Within international development programmes in low- or low and middle-income countries, have any studies been done on the 'expected' or 'acceptable' levels of drug expiry or common standards (in all LIC or LMIC contexts, but particularly in fragile or challenging contexts)?*

Contents

1. Executive summary

This rapid review confirms that strict global guidelines are available for use of expired primary health care drugs on the essential medicines list. There are World Health Organisation (2011) and Partnership for Quality Medical Donations (2018) guidelines for drug donations; the Pan American Health Organisation's recommendations for humanitarian aid provide additional guidance for drug donors (2009). Many LICs/LMICs have adapted the WHO guidelines to their own situations, and limited data is available on 'expected' or 'acceptable' levels of drug expiry or common standards. Key points include:

- India adhered to these expiry date guidelines during the 2001 Gujarat earthquake, resulting in a small proportion of inappropriate donations, although the amount of drugs donated far exceeded the need.
- In Eritrea during the War of independence, and after the 2004 tsunami in Indonesia and Sri Lanka, lack of adherence caused more problems for the authorities than helping the population, in terms of mismanagement (i.e. 'First-in First-out' or FIFO method, which did not always align with the expiry date of health commodities), storage issues, as well as direct and indirect costs of unusable products.
- While drug *donations* are not governed by any law, *disposal* of unwanted drugs in another country with appropriate facilities is highly regulated and subject to the Basel Convention on the Trans Frontier Shipment of Hazardous Waste.
- Drug donations provide benefits, such as tax deductions, and are a very convenient way for industries to get rid of stagnant stocks without having to pay for their controlled and expensive destruction in their country of origin. Like the WHO 1999 guidelines, the United Nations Population Fund has developed a guidance document on responsible management and safe disposal of unusable by-products of the United Nations Population Fund procured commodities.
- Though expired drugs are generally considered harmful, there are few evidences that support this opinion: there have been no case reports of adverse outcomes from the usage of expired ibuprofen, as well as many of the medications listed in the Shelf Life Extension Programme (SLEP) inventories. Exceptions include nitroglycerin, insulin, and liquid antibiotics, but most remaining medications have been theorised by US Food and Drug Administration and Harvard researchers to maintain potency even 10 years after the expiration date.
- For those involved in the use of expired medicines, a delay in the onset of action is enough reason to use them, since patients do not have enough finances to afford an unexpired medicine.
- Ihekwereme and colleagues (2017) note that "a couple of times", imported expired drugs from developed countries have been used by health professionals during medical missions to rural areas in Nigeria. Due to the February 2018 airstrikes of Eastern Ghouta, Syria, doctors have also been forced to use expired drugs, according to the Syrian American Medical Society.
- Health workers in South East Asia admitted to 'pushing' various 'short-dated' antibiotics onto their patients to use up stock. An updated essential medicines list and national formularies were associated with lower antibiotic use.
- In its first two years, the innovative public-private Informed Push Model bridged key gaps and expanded the distribution of contraceptives by private third-party logistics operators

(3PLs) to all public service delivery points in Senegal. This nearly eliminated stockouts and risks of expiry.

- In conclusion, it should be possible to extend the useful lives of medications in LICs/LMICs that pass tests for efficacy and safety – to help save both money and the environment – via SLEPs. However, the official FDA position remains that "using expired medical products is risky and possibly harmful to your health… if your medicine has expired, do not use it."

Evidence found for this review was 'gender blind.' No gender specific or disability specific data was included in this rapid review. There were major gaps in the literature: a limited number of studies focused on 'expected' or 'acceptable' levels of drug expiry. It was not possible to gain responses from hospital pharmacists volunteering in humanitarian settings, or from procurement and logistics departments of the service delivery organisations operating in LICs/LMICs. Although anecdotal evidence shows that expired medications are used in some cases, no experts contacted for this review could confirm that this regularly took place.

Lack of culpability contributed to the poor performance in relation to drug expiry of many health systems in LICs/LMICs. Evidence suggests that these countries should make user accountability for expired drugs part of the routine accountability regimes for their health sectors. In Uganda, for example, to prevent risk to national security, the National Medical Store plans to launch a forecasting tool from 2018 to find which facilities have excess drugs and which ones have shortages. This will provide optimal effectiveness for drug use before expiration.

2. Definitions

Expiry dates

An expiration date is defined based on a drug that is stored under "ideal manufacturer-suggested conditions of temperature, humidity, light exposure, and packaging integrity" (ICH, 2002). The expiry date specified by the manufacturer of a drug product means that a drug should meet the applicable standard of identity, purity, strength and quality at the time of use, provided it is kept under storage conditions indicated by that manufacturer (Farrugia, 2005). Drug manufacturers are required by the US Food and Drug Administration to label their products with expiration dates based on real time or estimated testing data.[1] Most products are released to pharmacies with expiration dates of 1 to 5 years from their date of manufacture (Lyon et al., 2006). In case of drugs stored in temporary, provisional warehouses as in emergency settings. However, it is very hard to rely on the quoted expiry date. This initial expiration date may later be extended based on further stability testing (Lyon et al., 2006). In low- or low- and middle-income countries (LICs/LMICs) it should be possible to extend the useful lives of medications that pass tests for efficacy and safety – and help save both money and the environment – via Shelf Life Extension

[1] Food and Drug Administration. Stability testing and expiration dating. Code of Federal Regulations, 21, Sec. 211.136 and 211.137. 2011. http://www.accessdata.fda. gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm

Programmes or SLEPs[2] (Kamba et al., 2017). Therefore, the printed expiration date may not necessarily represent the ultimate shelf life[3].

Drug extension times

According to the FDA Code of Federal Regulations Title 21 section 211.166, there must be a written testing programme to assess the stability of drug products that is used in determining expiration dates (Coffey, 2013).

Multiple FDA officials have acknowledged that most drugs are "probably as durable" as those maintained via SLEPs. Most remaining essential medications have been theorised to maintain potency even 10 years after the expiration date (Cantrell et al., 2012:1686). The antibiotic ciprofloxacin, for example, has an average shelf life greater than 9½ years past its initial expiration date (Cohen, 2000). However, this additional stability period is highly variable from lot to lot (Lyon et al., 2006). Table 1 shows a list of essential drugs and their average extension time. Extension greatly depends on the individual drug, its production batch, and its storage conditions (Culbertson et al., 2011). Excluding nitroglycerin, insulin, and liquid antibiotics, most medications are as long-lasting as the ones tested by the military.[4]

Table 1: A comparison of essential drugs and their average extension time

Drug types	Drug generic name	Average extension time in months (range)
Analgesics	Morphine sulphate (injectable)	89 (35-119)
	Fentanyl citrate (injectable)	84 (70-96)
	Ketamine HCl (injectable)	64 (42-87)
	Naproxen (tablets)	52 (46-62)

[2] Shelf Life Extension Programme (SLEP) to perform stability testing on more than 100 medications. It is a partnership between FDA and the US Department of Defence. For several decades, the programme has found that the actual shelf life of many drugs is well beyond the original expiration dates. Each year the federal government saved USD600 million to USD800 million because it did not have to replace expired medication.

[3] The International Conference on Harmonisation (ICH, 2002), often cited when discussing medication stability, defines shelf life as "the time period which a drug product is expected to remain within the approved shelf life specification, provided that it is stored under conditions defined on the container label." This could include non-exposure to various environmental factors including temperature, humidity and light (Diven et al., 2015). A drug's shelf life is defined by the period of time where pharmaceutical potency is greater than 90% (Coffey, 2013). The date of expiration marks when a drug's stability has no longer been tested for safety and efficacy (Culbertson et al., 2011). The subtle difference is in the testing. A drug labelled to expire five years after manufacture is so labelled because it only had stability testing up to that point (Coffey, 2013). **Unless further testing is done, its true shelf life is unknown, and the drug may retain its potency for many more years.** It is also almost impossible to assess what is the actual potency of the active ingredient in the product (Ette, 2004).

[4] https://www.health.harvard.edu/staying-healthy/drug-expiration-dates-do-they-mean-anything

Antibiotics	Amoxicillin sodium (tablets)	23 (22-23)
	Ciprofloxacin (tablets)	55 (12-142)
	Doxycycline hyclate (capsules)	50 (37-66)
	Cephalexin (capsules)	57 (28-135)
	Ceftriaxone (powder)	60 (44-69)
Intravenous fluids	Sodium chloride	50 (12-113)
	Dextrose (5%)	65 (13-128)
	Sodium lactate	53 (20-87)

Source: Lyon et al., 2006; Next Generation Combat Medic, 2018

The official FDA position remains that "using expired medical products is risky and possibly harmful to your health… **if your medicine has expired, do not use it**."[5] However, there is little peer-reviewed published data outside of the SLEP to support this statement for many medications.

There have been no case reports of adverse outcomes from the usage of expired ibuprofen, as well as many of the medications listed in the SLEP inventories. However, results from Nigeria on three expired NSAIDs (ibuprofen, diclofenac and piroxicam) do not agree with the SLEP results as the expired drugs were not equivalent to the unexpired brands (Ihekwereme et al., 2017:4). Climate, culture and environment may be responsible for the observed discrepancies. The SLEP encountered no toxicity with tetracycline antibiotic and typically found batches effective for more than two years beyond their expiration dates. The authors therefore suggest that the report of kidney damage in humans associated with consumption of degraded tetracycline (Frimpter et al., 1963) needs to be revisited and re-evaluated in the light of current pharmaceutical manufacturing technology to re-establish relevance of that report (Ihekwereme et al., 2017:4).

The understanding of drug-excipient interactions is very important during selection of appropriate excipients for proposed dosage form. Both drug-excipients and excipient-excipient interactions are known to occur (Ihekwereme et al., 2017:3). According to 'The Medical Letter on Drugs and Therapeutics,' (2015) drugs in solution that have become cloudy or discoloured or show signs of precipitation, particularly injectables, should not be used. The risk of ingesting degraded medication is lessened by their tendency to change in colour or consistency. Like many foods, medications show a visible sign of their inedibility. In a 1996 study, 75% of degraded drugs were

[5] https://www.fda.gov/drugs/resourcesforyou/specialfeatures/ucm481139.htm

observed to discolour from white to shades of yellow or brown (Culbertson et al., 2011). This suggests that it is more likely that a degraded medication will be discarded and not consumed – even in emergency settings – however, global evidence shows varied results of use (see Section 4):

3. Common standards on expiry of drugs

Guidelines and international conventions for donations

Recycling drugs is also described as donating leftover drugs (Bero et al., 2010). During conflicts and natural disasters, large quantities of pharmaceuticals are often donated as part of humanitarian assistance. According to set of strict guidelines for donating drugs written in 1996 and revised in 2010 by World Health Organisation, Pharmaciens Sans Frontières (Pharmacists Without Borders), the International Red Cross and other aid organisations,[6] drugs must be relevant to local disease patterns, packaged and labelled properly, and, on arrival, have a shelf life of at least one year.

Undoubtedly many of the pharmaceuticals save lives and alleviate suffering, but some donations may cause problems. Therefore, despite the rules, a lot can and does go wrong. Well-meaning but ill-informed religious and neighbourhood groups, or individuals ignorant of the established protocols, will mail boxes full of leftover medicines, which could be inappropriate or expired (Coffey, 2013). Businesses can also make mistakes: local pharmacies ship their overstock (i.e. if they purchased more than needed) just before they expire to disaster areas without knowing the rules (Bero et al, 2010). Drug donations provide benefits, such as tax deductions, and are a very convenient way for industries to get rid of stagnant stocks without having to pay for their controlled and expensive destruction in their country of origin (Pinheiro, 2008). A 2006 report, based on a survey of Partnership for Quality Medical Donations (PQMD)[7] members who responded to Hurricane Katrina and the Indonesian tsunami, quotes a frustrated aid worker as saying: "*I observed several big pharmaceutical companies, some of whom are in PQMD, violating all the principles that they so carefully wrote down and live by, and just packing up containers of product and sending it to the tsunami, for example. Most, if not all, of that product ended up rotting on the docks somewhere in a foreign port where they had no forklifts to take the product off.*"[8]

Some entities find it legitimate to send unusable drugs to nations which are not prepared to dispose of them safely and properly. The recipients receive the drugs as donations and instead are obliged to manage them as waste. **Unfortunately, there is no international convention to regulate transfer of non-requested pharmaceutical products and surpluses across borders.** Therefore, in countries where there are no existing relevant laws and regulations, the national governments must legislate on drug donations. LICs/LMICs in need of drug donations should provide a list of medicines as recommended in the guidelines, along with a list of any

[6] Guidelines for medicine donations – revised 2010. Geneva: World Health Organization; 2011. http://www.who.int/selection_medicines/emergencies/guidelines_medicine_donations/en/

[7] PQMD, an alliance of 14 manufacturers of drugs and medical equipment, and 16 non-profit humanitarian groups working in LICs/LMICs.

[8] http://www.pqmd.org/wp-content/uploads/2015/09/PQMD-Key-Barriers-Report-Feb-2008.pdf

financial or human resources needed to store, transport or dispense the drugs. Recipient countries can also publicly request cash rather than drug donations (Bero et al, 2010). The Pan American Health Organisation's recommendations for humanitarian aid provide additional guidance for drug donors.[9] They include using locally-produced drugs as a priority; advising the media not to issue requests for drugs, and discouraging donations from individuals to avoid receiving expired, unsorted, open or partially used products.

The 2018 PQMD Guidelines for Quality Medical Product Donations[10] for pharmaceuticals (7.2.4), consumables (7.4), and consumer products (7.54) state: "No expired product should ever be shipped. Country specific expiry guidelines should be followed at all times, unless written approval or exemption has been obtained." It also states that "Products with expiration dates less than 12 months dating should not be shipped without prior written acceptance from the Distributing Partner" (8.22 pharmaceuticals and medical devices). All applicable laws and regulations in relation to expiration dating for disposable medical consumables should be followed (consumables 8.4.3). "There should be a system of stock usage based on expiration date to ensure appropriate stock rotation (FEFO – First-Expiry/First-Out). Products beyond their expiry date or shelf life should be separated from usable stock. Expired products cannot be sold or supplied, and arrangements need to be made for their destruction" (storage 9.1.2.4). Appendix1 (Section 8) provides more details on drug disposal.

4. Global evidence/experiences on expiry of drugs

Country case studies in emergency settings

East Asia

China

After the 2008 Sichuan earthquake, at least 97% of all drug donations came from China itself. However, Xiao and colleagues (2010) reported a large proportion of inappropriate donations. They also mentioned financial loss for hospitals and doctors due to donations of excessive amounts of free drugs. This is because the income of hospitals and doctors in China is mostly generated by selling drugs. Xu and colleagues (2008) reported that the government hired a company to organise and monitor the medical supply after the disaster period, concluding that there were more drugs (and medical supplies) donated than needed for the emergency situation. Twenty tons of drugs, 10 tons of medical devices and 724.5 tons of disinfection materials had to be to be destroyed because they were inappropriate (mostly expired) and could not be used (van Dijk et al., 2011).

[9] *Be a better donor: practical recommendations for humanitarian aid* Clayton: Pan American Health Organization; 2009. www.saberdonar.info

[10] http://www.pqmd.org/wp-content/uploads/2018/05/PQMD-Guidelines-2018.pdf

South Asia

India

Donations following the 2001 earthquake in Gujarat state complied with WHO drug donation guidelines in terms of drug selection, quality assurance and shelf-life, presentation, packaging and labelling and information and management. Since the drugs were manufactured and donated in the same country, in general, the drugs were clearly labelled and had expiry dates that were at least one year from the time of arrival in India. However, the amount donated far exceeded the need. Consequently, India had to pay for destroying the excess drugs (Bose et al., 2010). However, van Dijk and colleagues (2011) report that there were very small proportions of inappropriate donations, as most donated drugs were manufactured in India and supplied by the Indian government, while funding mostly came from donors.

Indonesia

In 2004, nearly 10 years after WHO first issued its guidelines, Indonesia was inundated with excess drugs after the tsunami. A report by Pharmaciens Sans Frontières stated that "extremely large quantities" of cough medicine and the antibiotic tetracycline would expire before they could be used up, which caused "more problems to the authorities than they help the population." 60% of the donations received were not on Indonesia's list of essential drugs, and 70% were labelled in a foreign language (Burns, 2010).

Sri Lanka

Although Sri Lanka did express the need for specific drugs and medicines in response to the 2004 tsunami, as indicated by the WHO drug donation guidelines, donors failed to comply with the guidelines on matters of quality assurance and shelf-life. According to the Sri Lankan Medical Supplies Division, more than 3,500 truckloads of drug donations were received in the country during the five months after the tsunami. Unprecedented quantities of medications flowed into Sri Lanka, many of which had not been registered in the country before (Mahmood et al., 2011:854). The expiry date was not shown on the labels of 50% of the drugs; 6.5% of the medicines expired on arrival, and 67% expired in less than a year (Bose et al., 2010; Mahmood et al., 2011:854; Cañigueral–Vila et al., 2015:2). Situational analysis shows that some district hospitals are managing to deal with drugs about to expire before they can be used by sending them to other districts where they can be used before expiry (Holloway, 2010:8). Some pharmacists mentioned that there was evidence of removal of expiry dates on some medicines but that this could be avoided if sealed packets were used (Holloway, 2010:16).

Africa

According to an investigation by the Paris-based International Institute of Research Against Counterfeit Medicines (IRACM), Pakistani, Salvadoran, Togolese, Kenyan and Columbian markets have been overflowing with expired drugs in 2017 and 2018.[11] The following examples show the adherence to standards, as well as effects of donated expired drugs, in African countries:

[11] http://www.iracm.com/en/?s=expir&submit=Search

Benin

The country has been in receipt of humanitarian aid for refugees from Togo since 2005. Approximately 7,400 of the 20,850 refugees (35.5%) live in the settlement of Agame in the Tigray region. In 2010, demand for humanitarian aid rose again when 680,000 people were forced to flee their homes after severe flooding from heavy rains, which increased the cases of malaria.

Although Benin's government and multiple aid agencies launched the Emergency Humanitarian Action Plan, supply chain management of drugs is especially weak at the peripheral level. This results in recurrent stockouts, as well as expiration of drugs and rapid diagnostic tests. With these priorities in mind, the 2015-2020 President's Malaria Initiative (PMI) works in close collaboration with the Government of Benin and other Roll Back Malaria in-country partners to reduce these barriers and reinforce the delivery of malaria interventions (USAID, 2018:53). During the last 12-18 months, the Direction des Pharmacies, des Médicaments et Explorations Diagnostiques (DPMED), which supports PMI and other donors, has had to fight against an abundance of substandard, spurious, falsely labelled, expired falsified and counterfeit products. This includes antimalarials, accessible through the informal health sector, especially in the local markets (USAID, 2018:50). However, it is reported that the head of DPMED is currently under suspicion for allowing this to happen."[12]

Eritrea

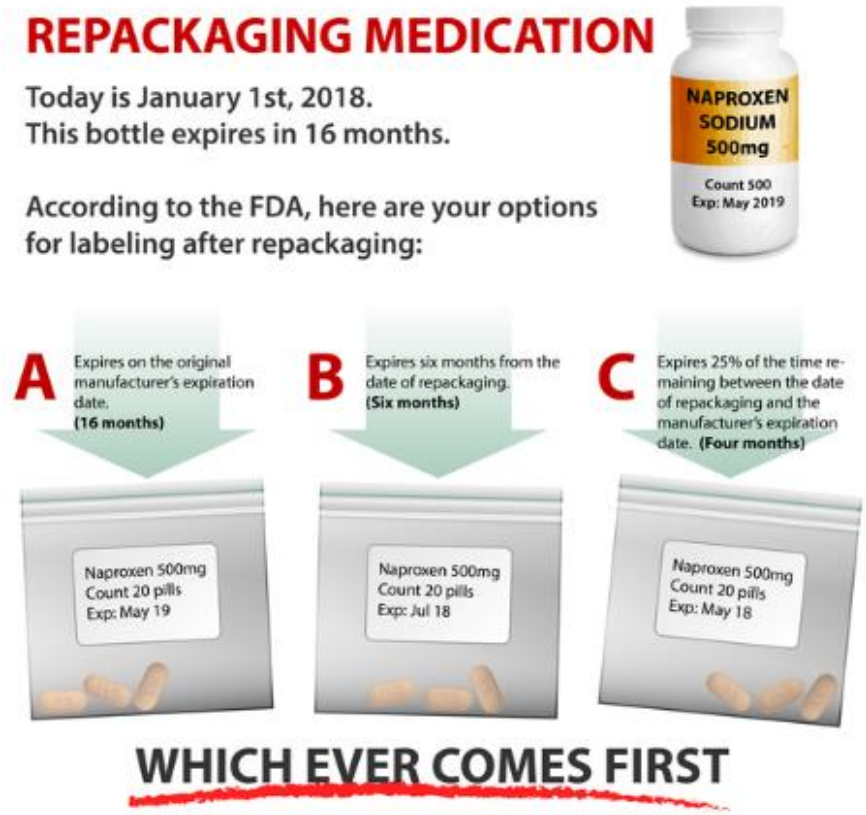
In 1989 during the Eritrean War of Independence, it is reported that donors sent "seven truckloads of expired aspirin tablets that took six months to burn" (Burns, 2010). For several years since then, humanitarian aid has been refused. Recent government acceptance of aid does not include essential drugs or medical attention.

Kenya

Repackaging (when a drug or medication is taken from its original packaging and placed into a smaller, safer and similar type of packaging - see Figure 1) is commonplace in emergency settings. Additional detailed steps include environmental testing, labelling, securing controlled substances, and good record keeping. A drug repackaging scam was stopped by the Kenyan police in April 2018, according to media reports.[13] The Kenya Medical Supplies Authority (KEMSA) lost drugs valued at Sh352 million (USD3.47 million) due to expiry or damage last year alone. The 2016/17 KEMSA report gave no explanation for stocking expired drugs, thereby causing unnecessary loss to the authority when numerous hospitals in the country were complaining of a shortage of drugs.

[12] http://www.dailymail.co.uk/wires/afp/article-5418443/Unprecedented-fake-medicines-trial-opens-Benin.html
[13] http://www.mediamaxnetwork.co.ke/news/425511/cops-bust-expired-drugs-repackaging-sale-racket/

Figure 1: Repackaging drugs for emergency settings



Source: Next Generation Combat Medic, 2018/ FDA

Nigeria

Use of expired drugs has become common in Nigeria. Ihekwereme and colleagues (2017) evaluated how efficacious and safe this practice is by testing expired non-steroidal anti-inflammatory drugs (NSAIDs)[14] for efficacy using the fresh egg albumin-induced mice paw oedema method. Expired drugs are commonly dispensed by Patent and Proprietary Medicines Vendors Licenses holders who usually consider drugs strictly as items of trade, of which they must never make a loss on. The authors note that "a couple of times" imported expired drugs from developed countries are used by health professionals during medical missions to rural areas. Even though the dispensers may be aware, the consumers are unaware of their expiry status. There is no data to show if the expired drugs used were useful, however.

Nigeria represents one of Africa's largest burden of tuberculosis (TB) with 600,000 people estimated to have TB at any one time. This accounts for 7% of the global TB burden. The high HIV prevalence in Nigeria is a major driver of the TB problem. The Global Fund portfolio has two active malaria grants managed by two Principal Recipients: The National Malaria Elimination Programme implements malaria treatment and prevention activities in the public sector, and the

[14] The drugs were diclofenac (hospital pack, never opened, 7 years post-expiration), piroxicam (in original blister pack, never opened, five years post-expiration), and ibuprofen (hospital pack, previously opened, two years post-expiration). These expired medicines were collected from the warehouse of the Nigerian National Agency for Food and Drug Administration and Control.

Society for Family Health implements activities in the private sector. The 2016 Office of the Inspector General audit identified several control weaknesses, covering a broad spectrum of financial, procurement, supply chain and programmatic areas. There have been insufficient controls at the central and state medical stores to ensure that drugs are managed and distributed according to their expiry dates. The Principal Recipients also do not adequately monitor the reception and distribution of drugs at the medical stores to ensure that drugs received by end-users are within the expiry timelines. Both the central and medical stores use the 'First-in First-out' (FIFO) method, which does not always align with the expiry date of health commodities. This was demonstrated by several batches of deliveries made to the central medical store for TB drugs that had earlier expiry dates than batches received before. As a result, TB drugs, for which the Association for Reproductive and Family Health was the responsible implementer, worth USD0.5 million were delivered at the central medical store in 2012 that were not used and were due to expire in March 2016 (The Global Fund, 2016).

Senegal

Data from interviews with facility staff, managers, and other stakeholders revealed that the current "Pull-based" distribution system (where actual customer demand drives the process) was complex and inefficient (Daff et al., 2014). Contraceptives generate relatively low margins in the Pull system, and so they are not a high priority, resulting in either limited or no replenishment of the facility's contraceptive stock (Daff et al., 2014).

To reduce stockout rates to the commercial-sector standard of 2% or less, the Government of Senegal and the Senegal Urban Reproductive Health Initiative developed the Informed Push distribution Model (IPM)[15] and pilot-tested it in the Pikine district of Dakar between February and July 2012. IPM brought the source of supply (a delivery truck loaded with supplies) closer to the source of demand (clients in health facilities) and streamlines the steps in between. With a professional logistician managing stock and deliveries, the health facilities no longer needed to place and pick up orders. Stockouts of contraceptive pills, injectables, implants, and intrauterine devices were completely eradicated at the 14 public health facilities in Pikine over the 6-month pilot phase. The government expanded IPM to all 140 public facilities in the Dakar region, and 6 months later stockout rates throughout the region dropped to less than 2%. IPM has been highly successful in ensuring full availability of contraceptives across regions and health facilities. The model also has facilitated the flow of essential data on consumption and stockouts from facilities up to district, regional, and central-level managers (Hasselback et al., 2017). In its first two years, IPM bridged key gaps and expanded the distribution of contraceptives by private third-party logistics operators (3PLs) to all public service delivery points in Senegal and nearly eliminated risks of expiry (Dicko et al., 2017).

Tanzania

Health facility managers delivering emergency obstetric care in rural Tanzania were interviewed and revealed that supply of expired drugs was a major issue (Mkoka et al., 2014). While supply

[15] Push: a distribution model that adapts commercial distribution principles to improve last-mile contraceptive distribution and stock management (recognised as a best practice in the Access to Medicine Index 2014).

of expired drugs and medical supplies could have endangered users' lives, no clear explanations were given, or disciplinary actions taken against those who were responsible.

Uganda

A cross-sectional survey of six public and 32 private medicine outlets in Kampala and Entebbe municipality was conducted using semi-structured questionnaires (Nakyanzi et al., 2010). Results showed that drugs and medicines prone to expiry include those used for vertical programmes[16], donated drugs, and those with a slow turnover. Even essential medicines expired in the supply chain.

The Ministry of Health of Uganda introduced the 'Pull' system of drug supply in 2003 to overcome the problems of drug availability and expiries. This system requires the health units to determine the types and quantities of medicines and medical supplies they need (Tumwine et al., 2010:557-558).

Records of 27 essential medicines and 11 medical supplies in Kilembe Hospital, western Uganda were reviewed over two periods in a 'Push' (2000 - 2001) and 'Pull' system (2004 - 2005). Results showed that there was higher volume and number of expired drugs and medical supplies in the 2001-2002 period compared to the 2004-2005 period (Tumwine et al., 2010:559). Large quantities of expired drugs and medical supplies were found in most district level facilities (Tumwine et al., 2010:558). Expired drugs were worth USD1,584 (25 items) in 2000/2001 and USD1,307 (13 items) in 2004/2005 (Tumwine et al., 2010:560). The key informants felt that abrupt changes of policies caused expiry of drugs: "There are sometimes abrupt changes in policies, for example, the changes in antimalarial policy whereby the first line drugs were changed from chloroquine and Fansidar to artemether-lumefantrine yet there were already large supplies of the former. These could lead to expiry of the drugs in stock" (Tumwine et al., 2010:560). Now when drugs are received, they are stored according to FIFO and First-Expiry-First-Out (FEFO) principles (Tumwine et al., 2010:562).

However, a more recent media account reports a different story: In February 2018 the Ugandan Ministry of Health announced that expired drugs to the tune of 1,500 tons in stores at 6,619 health facilities across the country would be incinerated. Critics wondered how such a volume of drugs could expire in a country that suffers constant stock outs. The Permanent Secretary of the Ministry of Health stated that it is "naturally expected that about 5% of pharmaceuticals in the distribution chain end up expired." However, results from the Statutory Internal Audit Report for the first quarter 2017/18 commissioned by Kampala City Council Authority, pointed out that most of the drugs that were expiring in health facilities managed by the authority had been delivered to them just a few months from their expiry dates (Nassaka, 2018).

The National Medical Store, a centralised agency mandated to procure and supply drugs to public health facilities across the country, has stated that they were not sure of what exact medicines had expired as they were yet to collect them from facilities. Some of the drugs that were found expired included a HIV drug - Nevirapine syrup that had been supplied to Komamboga Health Facility in October 2016. Of the 810 bottles supplied, 74% (599 bottles) had expired before use by November 2016. Civil Society Organisations that advocate for people

[16] A "vertical programme" is a component of the health. system which: has specific, defined objectives, usually quantitative, and relating to a single condition or small group of. health problems.

living with HIV held a press briefing in January 2018 calling on government to provide people with antiretroviral drugs warning of a bigger danger of drug resistance (Nassaka, 2018). This shows a gap in planning, and that healthcare managers are putting money in wrong priorities. Local NGO Centre for Health Human Rights and Development has refused to accept excuses by officials that some of the drugs expire because they are donated by donors irrespective of what the country needs and can absorb. They recommend that the government needs to work with donors to identify areas most in need, so that they can send medicines that will be used (Nassaka, 2018).

South East Asia

Holloway and colleagues (2017) conducted a rapid assessment of antibiotic use and policies undertaken by South East Asian countries to drive further actions to reduce inappropriate use. Through interviews with health workers, they found that they admitted to 'pushing' various 'short-dated antibiotics (i.e. those with an expiry date of less than six months) onto their patients to use up stock. An updated essential medicines list and national formularies were associated with lower antibiotic use.

Middle East

Lebanon/Syria

According to 2015 estimates, Syrian refugees in Lebanon represent 30% of the country's population. The private sector manages the health system. Refugees residing in informal camps cope with harsh living conditions and very weak infrastructure. Health issues among Syrian refugees in Lebanon include infectious diseases such as hepatitis A, typhoid, leishmaniasis (spread by sandflies) and measles. Hypertension, diabetes, and cardiovascular disease are affecting larger segments of the refugee population. At the time of shipment, products should have at least 75% of their validated shelf life (Sahloul, 2017). Appearance of the medications is also checked. However, due to the February 2018 airstrikes of Eastern Ghouta, Syria, doctors have been forced to use expired drugs, according to the Syrian American Medical Society.[17]

5. Studies on 'expected' or 'acceptable' levels of drug expiry

A limited number of studies have focused on 'expected' or 'acceptable' levels of drug expiry. However, there is data available concerning use of expired drugs for infantile diarrhoea, HIV and malaria within development programmes:

Antibiotics

According to WHO, consumption of low quality antibiotics (including expired and counterfeits) is one of the major problems in development of antimicrobial resistance in LICs/LMICs.[18] A study

[17] https://edition.cnn.com/2018/02/21/middleeast/syria-eastern-ghouta-bombardment-intl/index.html

[18] WHO, Antimicrobial Resistance: http://www.who.int/mediacentre/factsheets/fs194/en/

published in the Pan African Medical Journal in 2014 looked at the in vitro (out-of-body, i.e. in a petri dish) effect of expired paediatric antibiotics on infantile diarrheagenic bacteria samples.[19] This study did demonstrate increased rates of resistance by cultured bacteria to the expired antibiotics, including some strains that were up to 100% resistant to the expired antibiotics compared to antibiotics that were not expired. However, it was significantly limited by the fact that paediatric preparations are liquid, and therefore more susceptible to degrade given the limited lifespan of their preservatives (compared to the protective coating of found on most tablets and pills). Therefore, the applicability of this data to a larger population is difficult.

Antiretrovirals

Leftover drugs prescribed for American patients with HIV have been recycled for use overseas for several years. One such programme is Aid for AIDS in Manhattan - a non-profit group with branches in Italy, Spain and Switzerland - which collects drugs after US patients with HIV switch prescriptions, stop medications, or die (Lemer, 2003). The group passes these very expensive antiretroviral medicines along to people with HIV throughout Africa, the Caribbean, and Latin America. The donated medicines must be unopened or tamper proof, properly transported and stored, and appropriately labelled. Research shows that the drugs can be distributed up to six months after their expiration date (Huff, 2001; Bero et al., 2010).

Antimalarials

Quinoline-containing antimalarial drugs (chloroquine, quinine and mefloquine), are a vital part of the chemotherapeutic armoury against malaria. In 2015, the American Society of Tropical Medicine and Hygiene estimated that 122,000 children under five years of age had died due to taking poor-quality antimalarial drugs in sub-Saharan Africa, which, along with antibiotics as the two most in-demand, are the medicines most likely to be expired or bad copies.[20]

6. Lessons learned

Logistics/staffing issues

Logistic challenges due to the crisis, particularly in the early phase of a humanitarian response, exacerbate existing difficulties in delivering timely supplies at the last-mile. The lack of medical logisticians and pharmacists in the field to procure and manage drugs could exacerbate expiry.[21]

Accountability

Lack of accountability has contributed to the poor performance of many health systems in developing countries (Mkoka et al., 2014). For optimal effectiveness, LICs/LMICs should make

[19] Ogunshe, A., & Adinmonyema, P. (2014). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4427466/

[20] https://dailytimes.com.pk/183422/fake-medicines-flourish-africa-despite-killing-thousands/

[21] Jurman, D. (UNFPA) & Noznesky, E. (Care International). SRH Supplies in Emergency Response. https://www.rhsupplies.org/fileadmin/uploads/rhsc/Uploads/Other/SRH_Supplies_in_Emergency_Response.pdf

user accountability for expired pharmaceuticals part of the routine accountability regimes for their health sectors (Kamba et al., 2017).

Forecasting

The Ugandan Ministry of Health has stated that expired pharmaceuticals are a growing concern in the country, with fears that it can result in a risk to national security. Both critics and officials agree that having expired drugs in circulation poses a risk of public health hazards, pilferage, and re-labelling due to keeping such items in health facilities for too long. Therefore, the National Medical Store has come up with an innovative IT tool that they plan to be in use this financial year to forecast future drug needs. The tool will be used to retrieve data from a particular facility and its drug needs, in as quickly as five minutes (Nassaka, 2018). Although the tool won't solve all the challenges, it will be easy to see which facilities have excess drugs, and which ones have shortages, because the medicines being supplied will be easily traced. This could be of great use for future challenging contexts.

7. References

Bero, L., Carson, B., Moller, H., & Hill, S. (2010). To give is better than to receive: compliance with WHO guidelines for drug donations during 2000–2008. *Bulletin of the World Health Organization*, 88(12), 922-929. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2995193/

Burns, M. (2010). RX FOR HUMANITARIAN RELIEF. 24 April 2010. https://psmag.com/health-and-behavior/rx-for-humanitarian-relief-14634

Cañigueral–Vila, N., Chen, J.C., Frenkel-Rorden, L., & Laing, R. (2015). Improvements for international medicine donations: a review of the World Health Organization Guidelines for Medicine Donations, 3rd edition. *J Pharm Policy Pract*, 8, 28. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4628229/

Cantrell, L., Suchard, J.R., Wu, A., & Gerona, R.R. (2012). Stability of Active Ingredients in Long-Expired Prescription Medications. *Arch Intern Med*, 172(21), 1685-1686. DOI:10.1001/archinternmed.2012.4501

Coffey, K.C. (2013). Is There a Role for Expired Medications in Developing Countries? *Clinical Pediatrics*, 52(1), 7-9. http://journals.sagepub.com/doi/pdf/10.1177/0009922812448956

Cohen, L.P. (2000). Many Medicines Are Potent Years Past Expiration Dates. The Wall Street. 28 March 2000.

Culbertson, N.T. (2011). What can be done with expired pharmaceuticals? A review of literature as it pertains to Special Operations Force's medics. *J Spec Oper Med,* 11(2), 1-6.

Daff, B.M., Seck, C., Belkhayat, H., & Sutton, P. (2014). Informed push distribution of contraceptives in Senegal improves quality of family planning services. Global Health: Science and Practice, 2(2), 245-252. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4168620/

Dicko, M., Souare, B., Sarr, L.C., & Gueye, B. (2017). When technical achievements aren't enough: Lessons learned from efforts to catalyze policy action on supply chain in Senegal. Vaccine, 35(17), 2209-2213. https://www.sciencedirect.com/science/article/pii/S0264410X17300750

Diven, D.G., Bartenstein, D.W., & Carroll, D.R. (2015). Extending shelf life just makes sense. *Mayo Clin Proc*, 90, 1471-1474.

Ette, E.I. (2004). Conscience, the Law, and Donation of Expired Drugs. *The Annals of Pharmacotherapy*, 38(7), 1310-1313.

Farrugia, C.A. (2005). Controlled temperature storage of medicinals: good practice measures in the community pharmacy. *Journal of the Malta College of Pharmacy Practice*, 10, 30-33.

Frimpter, G.W., Timpanelli, A.E., Eisenmenger, W.J., Stein, H.S., & Ehrlich, L.I. (1963). Reversible Fanconi Syndrome Caused by Degraded Tetracycline. *JAMA*, 184(2), 111-113. https://www.researchgate.net/publication/236314709_Reversible_Fanconi_Syndrome_Caused_by_Degraded_Tetracycline

Hasselback, L., Dicko, M., Viadro, C., NDour, S., NDao, O., & Wesson, J. (2017). Understanding and addressing contraceptive stockouts to increase family planning access and uptake in Senegal. *BMC Health Services Research*, 17, 373. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5446687/

Holloway, K.A. (2010). Sri Lanka Pharmaceuticals in Health Care Delivery Mission Report 23-30 July 2010. 31 December 2010. World Health Organization, Regional Office for South East Asia, New Delhi. http://www.searo.who.int/entity/medicines/sri_lanka_situational_analysis.pdf

Holloway, K., Kotwani, A., Batmanabane, G., Puri, M., & Tisocki, K. (2017). Antibiotic use in South East Asia and policies to promote appropriate use: reports from country situational analyses. *BMJ*, 358, j2291. DOI: https://doi.org/10.1136/bmj.j2291

Huff, B. (2001). *Recycling HIV drugs: exporting medicine, experience, and hope.* In: *The body, the complete AIDS resource* [Internet]. New York: Body Health Resources Corporation. http://www.thebody.com/content/art13570.html

ICH (2002). Bracketing and matrixing designs for stability testing of new drug substances and products - Q1D. International Conference on Harmonization. 7 February 2002.

Ihekwereme, C.P., Chidebelu, C.C., & Nwadiliorah, L.C. (2017). Evaluation of the Effectiveness of Expired Anti-Inflammatory Medicines in Tropical Africa using Mice. *Am J Drug Delv Therap*, 4 (1), 3. https://www.imedpub.com/articles/evaluation-of-the-effectiveness-of-expired-antiinflammatory-medicines-in-tropical-africa-using-mice.pdf

Lyon, R.C., Taylor, J.S., Porter, D.A., Prasanna, H.R., Hussain, A.S. (2006). Stability profiles of drug products extended beyond labeled expiration dates. *J Pharm Sci*, 95, 1549-1560. https://www.ghdonline.org/uploads/drugs-Stability_Profiles-vencimiento.pdf

Kamba, P.F., Ireeta, M.E., Balikuna, S., & Kaggwa, B. (2017). Threats posed by stockpiles of expired pharmaceuticals in low- and middle-income countries: a Ugandan perspective. *Bulletin of the World Health Organization*, 95, 594-598. DOI: http://dx.doi.org/10.2471/BLT.16.186650

Mahmood, M., Riley, K., Bennett, D., & Anderson, W. (2011). The Supply of Pharmaceuticals in Humanitarian Assistance Missions: Implications for Military Operations. *Military Medicine*, 176, 8, 852-857. https://pdfs.semanticscholar.org/dd79/ddebd666d42eb41c0e0559c858d07870623b.pdf

Mkoka, D.A., Goicolea, I., Kiwara, A., Mwangu, M., & Hurtig, A.-K. (2014). Availability of drugs and medical supplies for emergency obstetric care: experience of health facility managers in a rural District of Tanzania. *BMC Pregnancy and Childbirth*, **14**, 108. https://doi.org/10.1186/1471-2393-14-108

Nakyanz, J.K., Kitutu, F.E., Oria, H., & Kamba, P.F. (2010). Expiry of medicines in supply outlets in Uganda. *Bulletin of the World Health Organization*, 88, 154-158. http://www.who.int/bulletin/volumes/88/2/08-057471.pdf

Nassaka, F. (2018). Uganda: Expired Drugs – Who is to Blame? 6 March 2018. The Independent (Kampala). https://www.independent.co.ug/expired-drugs-blame/

Pinheiro, C.P. (2008). Drug donations: what lies beneath. *Bulletin of the World Health Organization*, 86(8), 577-656. http://www.who.int/bulletin/volumes/86/8/07-048546/en/

Sahloul, Z. (2017). Challenges Providing Pharmaceutical Products to Syrian Refugees." *Regulatory Focus.* May 2017. Regulatory Affairs Professionals Society. https://www.raps.org/regulatory-focus%E2%84%A2/news-articles/2017/5/challenges-providing-pharmaceutical-products-to-syrian-refugees

SLEP - Shelf Life Extension Program Database. The Department of Defense/Food and Drug Administration Shelf Life Extension Program (2018). https://slep.dmsbfda.army.mil/portal/page/portal/SLEP_PAGE_GRP/SLEP_HOME

Sukkar, E. (2009). The cost of donated drugs. *BMJ*, 339, 832-833. https://www.bmj.com/bmj/section-pdf/186360?path=/bmj/339/7725/Feature.full.pdf

The Global Fund (2016). *Audit Report. Global Fund Grants to the Federal Republic of Nigeria.* 3 May 2016. Geneva, Switzerland. https://www.theglobalfund.org/media/2655/oig_gf-oig-16-014_report_en.pdf

The Medical Letter (2015). Drugs Past Their Expiration Date. 7 December 2015. The Medical Letter on Drugs and Therapeutics, 1483. https://secure.medicalletter.org/w1483b

Tumwine, Y., Kutyabami, P., Odoi, R.A., & Kalyango, J.N. (2010). Availability and Expiry of Essential Medicines and Supplies During the 'Pull' and 'Push' Drug Acquisition Systems in a Rural Ugandan Hospital. *Tropical Journal of Pharmaceutical Research*, 9(6), 557-564. http://www.ajol.info/index.php/tjpr/article/view/63555

UNFPA (2013). *SAFE DISPOSAL AND MANAGEMENT OF UNUSED, UNWANTED CONTRACEPTIVES.* United Nations Population Fund, Denmark. https://www.unfpa.org/sites/default/files/resource-pdf/Safe%20Disposal%20and%20Management%20of%20Unused%20Unwanted%20Contraceptives_2.pdf

USAID (2018). *President's Malaria Initiative Benin. Malaria Operational Plan FY 2018.* The United States Agency for International Development. https://www.pmi.gov/docs/default-source/default-document-library/malaria-operational-plans/fy-2018/fy-2018-benin-malaria-operational-plan.pdf?sfvrsn=5

van Dijk, D.P.J., Dinant, G.-J., Jacobs, J.A. (2011). Inappropriate Drug Donations: What has Happened Since the 1999 WHO Guidelines? *Education for Health*, 24(2), 462.

http://www.educationforhealth.net/article.asp?issn=1357-6283;year=2011;volume=24;issue=2;spage=462;epage=462;aulast=van

Xiao, H.-T., Liao, Z., Chen, L., Tong, R.-S. (2010). The donation drug of Wenchuan earthquake - focus on Chinese national drug policy. *HealthMED Journal*, 4(2), 356-359.

Xu, J.-K., Deng, X.-G., Li, H., Xie, H., Lu, J., Lu, Y., Zhang, L., Li, Y.-P., Shen. J. (2008). Ensuring medical supplies for the medical rescue after the Wenchuan Earthquake. *Chinese Journal of Evidence Based Medicine*, 8(11), 905-912.

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Key websites

- FDA (2018). *Expiration Dating Extension.* Emergency Preparedness and Response. 2 March 2018. US Food and Drug Administration. https://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMLegalRegulatoryandPolicyFramework/ucm411446.htm
- MedSurplus Alliance Program: http://www.medsurplusalliance.org/vi-donations-in-emergency-situations/
- PQMD Guidelines for Quality Medical Product Donations (April 2018 revision): http://www.pqmd.org/wp-content/uploads/2018/05/PQMD-Guidelines-2018.pdf
- WHO Model Lists of Essential Medicines (updated March 2017): http://www.who.int/medicines/publications/essentialmedicines/en/
- WHO (2018): Section and Use of Essential Medicines: https://www.medbox.org/essential-medicines/selection-and-use-of-essential-medicines/preview?

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About this report

This report is based on five days of desk-based research. The K4D research helpdesk provides rapid syntheses of a selection of recent relevant literature and international expert thinking in response to specific questions relating to international development. For any enquiries, contact helpdesk@k4d.info.

K4D services are provided by a consortium of leading organisations working in international development, led by the Institute of Development Studies (IDS), with Education Development Trust, Itad, University of Leeds Nuffield Centre for International Health and Development, Liverpool School of Tropical Medicine (LSTM), University of Birmingham International Development Department (IDD) and the University of Manchester Humanitarian and Conflict Response Institute (HCRI).

8. APPENDICES

A- Disposal of drugs

While drug donations are not governed by any law, disposal of expired or unwanted drugs in another country with appropriate facilities is highly regulated. International guidelines require that drug donations are responsive to the health needs of the recipient country, and that the drugs involved have a shelf-life of at least one year on arrival (Kamba et al., 2017). However, it has been reported that drugs that are already past their expiry dates have often been unloaded in LICs/LMICs. The drugs may also be inappropriate for the needs of the country. Donated pharmaceuticals with a long shelf-life may be mismanaged. Staff and storage space may be lacking, and the pharmaceutical management system in disarray. The 'WHO Guidelines for Disposal of Unwanted Pharmaceuticals in and After an Emergency'[22] are based on a report on the safe disposal of unwanted and unusable drugs in Mostar, which had accumulated during the war in Bosnia and Herzegovina. Once received into a country, donations cannot be returned to donors, as recommended by the guidelines, because they are considered hazardous cargo and their shipment must respect the Basel Convention on the Control of Transboundary Movements of Hazardous Wastes and their Disposal[23] (Sukkar, 2009). This legal demand involves the existence of consented protocols between exporters and importers, and time-consuming procedures that severely compromise its feasibility. Signatories to the convention are required to take the waste back or arrange for disposal of the waste. This involves obtaining permission, which can take several months, to cross international borders before transportation can take place (UNFPA, 2013:14).

Proper and safe disposal of reproductive health commodities is critical, as consequences of improper and unsafe disposal pose both public health and environmental implications. Many LICs/LMICs have adapted these WHO guidelines to their own situations (Kamba et al., 2017). Although ultra-high-temperature incineration may be the most effective technique for the safe disposal of unwanted pharmaceuticals, it is not a cheap option. In many LICs/LMICs there are no high temperature-chambered incinerators designed to handle more than 1% halogenated compounds, i.e. containing fluorine, chlorine, bromine or iodine (UNFPA, 2013:13). Cement kilns are particularly suited for the disposal of expired pharmaceutical products, chemical waste, and used oil, among others. Cheaper methods of drug disposal include engineered landfill, waste immobilisation by encapsulation, or inertisation (ground and mixed with water, cement and lime) (Kamba et al., 2017).

The United Nations Population Fund (UNFPA) has also developed a guidance document on responsible management and safe disposal of unusable by-products of UNFPA procured commodities. 'The Safe Disposal and Management of Unused, Unwanted Contraceptives' provides recommendations on policies and procedures. However, often there are no established procedures for dealing with a quantity of condoms which are unacceptable for distribution (UNFPA, 2013:20).

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[22] Guidelines for safe disposal of unwanted pharmaceuticals in and after emergencies. Geneva: World Health Organisation; 1999.

[23] *Basel Convention on the Control of Transboundary Movements of Hazardous Wastes and their Disposal*. Secretariat of the Basel Convention No.97/012.; 1998. http://www.basel.int/

B- Essential Medicines List

Availability of drugs and medicines is important as far as the reduction of mortality and morbidity associated with disease burden are concerned. However, lack of essential medicines is still one of the most serious public health problems. About 30% of the world's population lacks the medicines they need (Tumwine et al., 2010). The situation is worse in the poorest parts of Africa and Asia where the figure rises to over 50%.[24]

In most LICs/LIMCs, the supply of pharmaceuticals is centralised, and one state agency is entrusted with the procurement, storage and distribution of pharmaceuticals to all public health facilities (Kamba et al., 2017). However, in some LICs/LMICs, civic observers and government oversight agencies have raised concern over the high incidence of expiry of stocked pharmaceuticals in the public supply system.

Some essential pharmaceuticals are held in reserve for use in emergency situations, such as an outbreak of an infectious disease, and many of these expire before any relevant emergency occurs. This can result in large stockpiles of expired pharmaceuticals, inventory losses and financial losses associated with stock disposal and replacement (Kamba et al., 2017).

The essential medicines concept introduced in 1977 went a long way in improving availability of drugs. Availability was further enhanced with the emergency kit system which was designed to guarantee that certain subsets of medicines essential for primary health care delivery were available at service delivery points. Although these kits were originally meant to be supplemented by other drugs as needed, in many areas they became the main, and at times, the sole drug supplies. This long-term projection of customer demand constitutes the 'Push' system of drug supply (Tumwine et al., 2010:558).

The WHO Model Lists of Essential Medicines (EML) has been updated every two years since 1977. The current versions are the 20th WHO Essential Medicines List (EML) and the 6th WHO Essential Medicines List for Children (EMLc) updated in March 2017 and amended August 2017.

EML classifies medicines in two functional categories (Sahloul, 2017):

- emergency kits, including the Interagency Emergency Health Kit (IEHK) basic, IEHK supplementary, interagency reproductive health kits, diarrheal disease kit, immunisation kit
- medications, such as oral medicines, injectable medicines, external use medicines and infusions

Use of expired essential medicines among the poor in LICs/LMICs is conducted hoping that health benefits will arise from such practice. For those involved in the use of expired medicines, a delay in the onset of action is enough reason to use them, since patients do not have enough finances to afford an unexpired medicine (Ihekwereme et al., 2017).

[24] WHO "Equitable access to essential medicines: a framework for collective action", in WHO Policy Perspectives on Medicines. 2004.