Access to medical products

Fair Pricing Forum
Amsterdam – The first Fair Pricing Forum was held in Amsterdam, the Netherlands, on 11 May 2017. The main objective of this Forum was to discuss options for a fairer pricing system that is sustainable for both health systems and innovation. The event was an initiative of WHO and was organized in collaboration with the Dutch Ministry of Health, Welfare and Sport. About 200 stakeholders from countries around the world came together to explore options to remedy essential medicines shortages that may be due to low profit margins, expand networks for exchange of experience, and identify research gaps specific to the current innovation and pricing system.

Background information about the challenges of the current system of setting prices for medicines is found in the report of the WHO Advisory Group meeting held in November 2016 in preparation for the event.

WHO Essential medicines and health products. Fair pricing of medicines [webpage].

Information guide on biosimilars
Brussels – The EMA and the European Commission (EC) have published a new information guide for healthcare professionals, providing reference information on the science and regulation underpinning the use of biosimilars. It complements earlier EC publications on biosimilars, including a guide for patients and a consensus information paper.

The guide was launched at the stakeholder conference on biosimilar medicines held in Brussels on 5 May 2017. The event was attended by representatives of patients, healthcare professionals, regulatory authorities, payers and the pharmaceutical industry. An updated report on the impact of biosimilar competition in Europe was also released at the conference.

WHO to pilot prequalification of biosimilars
Geneva – WHO has announced that it will launch a pilot project for prequalification of two biosimilar cancer medicines, rituximab and trastuzumab, in 2017. An invitation for expression of interest and submission of applications by manufacturers will be published in September. The WHO prequalification list is used by a wide range of national and international entities and thus promotes competitive pricing.

The decision to launch the pilot follows a two-day meeting between WHO, national regulators, pharmaceutical industry groups, patient and civil society groups, payers and policymakers. WHO also plans to explore options for prequalifying insulin.

To support the biosimilars prequalification pilot, WHO will review its 2009 Guidelines on the evaluation of similar biotherapeutic products. Furthermore the Organization will advocate for greater awareness of the benefits
and risks of biosimilars and will support the development of sustainable price-setting strategies for all biotherapeutics.

Updated Essential Medicines List
Geneva – WHO has published the 2017 update of its Essential Medicines Lists (EML) for adults and children. The list includes new advice on the use of antibiotics and 55 additional medicines, bringing the total to 433 medicines deemed essential for addressing the most important public health needs. The updates were recommended by the WHO Expert Committee on the Selection and Use of Essential Medicines at its 21st meeting, held on 27–31 March 2017.

For the first time, antibiotics used to treat 21 of the most common general infections have been grouped into three categories: “Access” (available at all times for a wide range of infections), “Watch” (first- or second-line treatments for a small number of infections) and “Reserve” (last-resort options for use in the most severe circumstances). The advice supports WHO’s Global action plan on antimicrobial resistance.

Furthermore, the following medicines were added to the EML:
• 10 antibiotics for adults and 12 for children
• dasatinib and nilotinib for oral treatment of chronic myeloid leukaemia that has become resistant to standard treatment;
• sofosbuvir + velpatasvir as the first combination therapy to treat all six types of hepatitis C;
• dolutegravir for HIV infection;
• HIV pre-exposure prophylaxis (PrEP) with tenofovir alone, or in combination with emtricitabine or lamivudine;
• delamanid for children and adolescents, and clofazimine for children and adults with multidrug-resistant tuberculosis;
• child-friendly fixed-dose combination formulations of first-line anti-tuberculosis medicines,
• two artemisinin-based combination therapies (pyronaridine+artesunate and dihydroartemisinin+piperquine) and a rectal artemesunate formulation for young children, for the treatment of malaria; and
• fentanyl skin patches and methadone for pain relief in cancer patients.(1)

The Expert Committee further recommended to develop an Essential Diagnostics List (2).

► (1) WHO News release, 6 June 2017.
WHO Model List of Essential Medicines. 20th List (March 2017).
WHO Model List of Essential Medicines for Children. 6th List (March 2017).
(2) WHO-EMP News, 15 June 2017.

MPP licence for investigational hepatitis C medicine
Amsterdam – The Medicines Patent Pool (MPP) and the Egyptian company Pharco Pharmaceuticals have signed a licence for the investigational medicine ravidasvir, a direct-acting antiviral (DAA) with the potential of working across all six major hepatitis C genotypes.

The new MPP licence expands the geographic scope of an earlier licence signed by the Drugs for Neglected Diseases initiative (DNDi) and Presidio, the original developer of ravidasvir. Combined, the MPP and DNDi agreements would benefit an area which is home to 85% of people living with hepatitis C in low- and middle-income countries.

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Regulatory reforms in Mexico
A recent publication describes the implementation and impact of a multi-faceted series of regulatory and legal reforms instituted by the Government of Mexico and the national medicines regulatory agency, COFEPRIS. The reforms aimed to facilitate the implementation of a new national access to medicines policy and to align the regulatory system with international standards. They encompassed administrative processes, clinical trials oversight, reliance on market authorization information and reports of other trusted regulators, and validation of activities by the Pan American Health Organization (PAHO) and WHO.

The paper shows that the reforms have increased the availability and affordability of safe, effective, quality medicines in the private and public sectors, and have facilitated expansion of the Mexican pharmaceutical industry. The regulatory optimization approach undertaken by Mexico could be a useful model for other countries that wish to facilitate access to needed quality medicines while encouraging local economic development.


Access to Vaccines Index 2017
Amsterdam – The Access to Medicines Foundation has published its first Access to Vaccines Index, the first publically available tool that maps how vaccine companies are responding to global calls to increase access to vaccines. The Index assesses eight key vaccine suppliers, and looks at their efforts to develop, manufacture and supply preventive vaccines for 69 high priority diseases across 107 high-need countries. The Index finds that the companies evaluated do this in a variety of ways depending on their diverse pipelines, portfolios and revenues.

The Access to Medicine Foundation published its first benchmark of industry activity in the 2008 Access to Medicine Index, which is now in its fifth iteration. The Foundation is also developing the first Antimicrobial Resistance Benchmark.


Reporting of clinical trial results
Geneva - Some of the world’s largest funders of medical research and international non-governmental organizations have agreed on new standards that will require all clinical trials they fund or support to be registered, and the results to be disclosed publicly. New policies will be developed and implemented within the next 12 months. Most of these trials and their results will be accessible via WHO’s International Clinical Trials Registry Platform.

Today, about half of all clinical trials go unreported, often because the results are negative. This leaves an incomplete and potentially misleading picture of the risks and benefits of vaccines, medicines and medical devices and can lead to use of suboptimal or even harmful products. The agreement means that the ethical principles laid down in the 2015 WHO position on public disclosure of results from clinical trials, which builds on the World Medical Association’s 2013 Declaration of Helsinki, will now be enforced in thousands of trials every year.


WHO. International Clinical Trials Registry Platform (ICTRP) [website].
http://www.who.int/ictrp/en/
Safety evaluation and monitoring

Confirmatory clinical studies lacking
The outcomes of a systematic review show that post-market studies are not always conducted to confirm the expected benefits of medicines that gained regulatory approval based on limited evidence. The review characterized the prospective controlled clinical studies for novel drugs that were first approved by the U.S. FDA between 2005 and 2015 on the basis of limited evidence. It included 117 products approved on the basis of a single pivotal trial, pivotal trials that used surrogate markers of disease as primary endpoints, or both. The review found that the quantity and quality of post-approval clinical evidence varied substantially for these products, with few controlled studies published after approval that confirmed efficacy using clinical outcomes for the original FDA-approved indication. (1)

► Pease AM, Krumholz HM, Downing NS. Postapproval studies of drugs initially approved by the FDA on the basis of limited evidence: systematic review. BMJ 2017;357:j1680.

Importance of monitoring new drugs
A third of FDA-approved medicines have significant post-market safety events. In a recent study 71 of 222 novel therapeutics approved by the FDA in the period from 2001-2010 were affected by one or more significant event (withdrawal, “boxed warning” and/or safety communication). Products that gained accelerated approval were twice as likely to have postmarket safety events than other products. Safety events were also found to be more likely for biologicals, medicines to treat psychiatric conditions, and products approved near the regulatory deadline for approval.

These findings highlight the importance of continuous safety monitoring of medicinal products throughout their life cycle.


Medicines supply and use

New industry alliance to curb antimicrobial resistance
Berlin – The International Federation of Pharmaceutical Manufacturers & Associations (IFPMA) has announced the launch of the AMR Industry Alliance, which brings together research-based companies to drive and measure industry progress to curb antimicrobial resistance (AMR). The announcement was made at the B20 Health Conference in Berlin. The Alliance will ensure that signatories collectively deliver on the commitments made in the the Industry Declaration on AMR signed at the World Economic Forum in Davos in January 2016 and the AMR Roadmap. A reporting mechanism will be developed to track progress, identify gaps and set targets for the future.


Antibiotics consumption in eastern Europe and central Asia
A new report released by the WHO Regional Office for Europe sheds light on antibiotic consumption in eastern European and central Asian countries. The data were gathered through the WHO Antimicrobial Medicines Consumption (AMC) Network and include information from a number of non-EU countries.
The WHO AMC Network was established by the WHO Regional Office for Europe in 2011 to assist countries in setting up or strengthening national AMC surveillance and to contribute to region-wide AMC surveillance.


Off-label use of medicines in Europe
A new study describes the complex field of off-label use of medicinal products in the EU, i.e. the use of the products outside the terms approved as part of the marketing authorization under which a product can be used safely and effectively.

The study was conducted by the Netherlands institute for health services research (NIVEL), the Dutch National Institute for Public Health and the Environment (RIVM) and the European Public Health Alliance (epha) for the European Commission. Applying a wide range of methods, it provides information on the prevalence and incidence of off-label use and its drivers. It investigates the balance between the benefits and risks for patients and describes the national frameworks that govern the off-label use of medicinal products in EU Member States. The study shows how authorities have addressed the issue and how patients, healthcare professionals and industry react to this.


Combating medication errors
Geneva – WHO has launched a global initiative to reduce severe, avoidable medication-associated harm by 50% over the next five years. The Global Patient Safety Challenge on Medication Safety aims to improve the ways in which medicines are prescribed and distributed in health systems, and to increase awareness among patients about the risks associated with the improper use of medication.

Medication errors cause at least one death every day and injure approximately 1.3 million people annually in the United States of America alone. While low- and middle-income countries are estimated to have similar rates of medication-related adverse events to high-income countries, the impact is about twice as much in terms of the number of healthy life years lost. Globally, the cost associated with medication errors has been estimated at US$ 42 billion annually or almost 1% of total global health expenditure. Many countries lack good data, which will be gathered as part of the initiative.


Toolkit to protect supply chains
The Asia Pacific Economic Cooperation (APEC) has published an interactive PDF document to protect the medical product supply chains. (1). The document contains interactive links to recommended best practices and tools that can help to prevent and detect substandard and falsified medical products before they reach the consumer, and to efficiently respond to incidents. The document is the outcome of collaboration of ten work streams under the APEC Global Supply Chain Security and Integrity Roadmap project. It includes links to relevant tools and guidance provided by the WHO Member State mechanism on substandard/spurious/false-labelled/falsified/counterfeit medical products.
and the WHO Global Surveillance and Monitoring System.

  APEC. Supply chain security toolkit for medical products (PDF, 6.6 MB).

## Disease updates

### Poliomyelitis:

#### Towards eradication

**Geneva, Brazzaville, New York, Dakar** — The largest-ever synchronized vaccination campaign of its kind was conducted in 13 countries across west and central Africa to tackle the threat of polio. All children under five years of age in Benin, Cameroon, Central African Republic, Chad, Côte d’Ivoire, Democratic Republic of Congo, Guinea, Liberia, Mali, Mauritania, Niger, Nigeria and Sierra Leone – were immunized with bivalent oral polio vaccine (bOPV).

The security-compromised areas in Borno state, north-eastern Nigeria, is widely considered to be the last remaining polio reservoir. Due to its epidemic-prone nature the virus could easily spread to under-protected areas of neighbouring countries. With the strong commitment of Africa’s leaders polio could now be eradicated.\(^1\)

In May 2017 the WHO Emergency Committee under the International Health Regulations concluded that polio remains a public health emergency of international concern, but that the world is now closer to polio eradication than ever before. The Committee’s temporary recommendations will be maintained for another 3 months, with some changes to the categories of countries subject to the recommendations.\(^2\)

\(^1\) Joint UNICEF/WHO news release, 23 March 2017.
\(^2\) WHO Statement, 2 May 2017.

### Depression:

#### Leading cause of disability

**Geneva** – WHO has released its new estimates of the prevalence of depression and other mental disorders at the global and regional level, together with data concerning the consequences of these disorders in terms of lost health. More than 300 million people were living with depression in 2015, an increase of more than 18% since 2005.

On average, only 3% of government health budgets are invested in mental health. Fewer than half of people affected globally (and fewer than 10% in many countries) receive appropriate treatment. This is mainly because of a lack of resources and trained health care providers, and because of social stigma associated with mental disorders.

Depression increases the risk of substance use disorders and diseases such as diabetes and heart disease. Conversely, people with these conditions have a higher risk of depression. According to a WHO-led study, low levels of recognition and access to care for depression and anxiety cause economic losses of a trillion US dollars every year in total to households, employers and governments.

\(^1\) WHO News release, 30 March 2017.


### Neglected tropical diseases:

#### Remarkable achievements

**Geneva** – The fourth WHO report on neglected tropical diseases shows that there is tremendous progress in some areas, but also much remaining to do. The report was released at the Global Partners’ Meeting on Neglected Tropical Diseases (NTDs) on 19 April 2017. The event marked ten years of multi-stakeholder collaboration and the
5th anniversary of the WHO NTD Roadmap and the London Declaration.

Remarkable achievements have been made in tackling lymphatic filariasis, onchocerciasis, Guinea-worm disease, African human trypanosomiasis, trachoma, visceral leishmaniasis and rabies. The report outlines four main areas that remain to be addressed. Firstly there is a need for investments to develop innovative disease prevention and management interventions. Secondly, vector control needs to be strengthened globally as it can prevent the transmission of many NTDs. A response plan for 2017–2030 was welcomed by the delegates at the Seventieth World Health Assembly. The WHO Prequalification team will play a crucial role in assessing the quality of long-lasting insecticide-treated bed nets, indoor residual spraying, space sprays and larvicides. Thirdly, public health measures must be intensified to combat zoonotic diseases, for example to ensure the availability of rabies vaccine meeting internationally accepted quality standards. Finally, safe water, sanitation and hygiene are critical in fighting NTDs, and measures to this effect will be part of the global plan.


Malaria: Push for prevention
Geneva, Nairobi – On World Malaria Day 2017 WHO has called for a faster scale-up of efforts to prevent malaria. Proven prevention approaches include insecticide-treated nets – which account for more than two thirds of cases prevented since 2001 – as well as indoor residual spraying with insecticides and preventive medicines for pregnant women, under-fives and infants. Across the Sahel, WHO also recommends malaria chemoprevention during the rainy season. The uptake of some of these measures needs to be accelerated, especially in Africa, which bears 90% of the global malaria burden.\(^{(1)}\)

Brazzaville – The World Health Organization Regional Office for Africa (WHO/AFRO) has announced that Ghana, Kenya and Malawi will participate in a WHO-coordinated malaria vaccine pilot programme in selected areas, beginning in 2018. The vaccine under study, the RTS,S\(^*\) vaccine, could be added to the current malaria control tools as a complementary preventive measure. The pilot will show whether the vaccine’s protective effect in children aged 5–17 months shown in Phase III testing can be replicated in real life. Specifically, the pilot programme will assess the feasibility of delivering the required four doses of RTS,S\(^*\), the vaccine’s potential role in reducing childhood deaths, and its safety in the context of routine use.\(^{(2)}\)


Hepatitis: Need for urgent global response
Geneva – A new WHO report describes, for the first time, the global and regional estimates on viral hepatitis in 2015. The data set the baseline for tracking progress in implementing the new global strategy endorsed by the World Health Assembly in 2016. The report highlights the urgency of closing the gaps in access to life-saving testing and treatment.

The report focuses on hepatitis B and C, which cause 96% of overall hepatitis mortality. An estimated 325 million people worldwide are living with chronic hepatitis B
or C virus infection. Mortality is increasing, with 1.34 million deaths in 2015.

For hepatitis B virus (HBV) new infections are falling thanks to increased vaccination coverage among children. HBV infection requires lifelong treatment, WHO currently recommends tenofovir for this purpose.

For hepatitis C virus (HCV) there is currently no vaccine available. Unsafe injections are considered to be the most common route of transmission. Approximately 1.75 million people were newly infected in 2015, bringing the global total of people living with HCV to 71 million. HCV infection can now be cured with the new direct-acting antiviral medicines (DAAs). Prices are falling but remain unaffordable in many countries.


Ebola: Response to new outbreak

A new outbreak of Ebola virus disease has been reported from the Democratic Republic of the Congo (DRC). The outbreak appears to be geographically relatively limited. WHO and partners are supporting the Ministry of Health in all aspects of the response, including epidemiological investigation, surveillance, logistics and supplies, communications and community engagement.

Following the official confirmation of the outbreak, Gavi, the Vaccine Alliance has stated that it stands ready to support the Government of the DRC in bringing the epidemic under control. A 2016 agreement between Gavi and Merck, the developer of the Ebola vaccine rVSV-ZEBOV, ensures that 300 000 vaccine doses are available for emergencies. The WHO and others will determine if and when deployment of vaccine in this outbreak is warranted.

Gavi, the Vaccine Alliance. Statement, 12 May 2017.

Upcoming events

Ireland to host 18th ICDRA
Dublin – Ireland has been confirmed as the location for the next International Conference of Drug Regulatory Authorities (ICDRA). The Conference will take place in Dublin on 3–7 September 2018. This biennial WHO-organized event provides regulatory authorities with a unique forum to meet and discuss ways to strengthen global collaboration in the area of medicines’ regulation in order to improve the quality, safety and efficacy of medicines globally.

► HPRA News, 19 April 2018.
WHO. International Conference of Drug Regulatory Authorities (ICDRA) [webpage]. www.who.int/medicines/icdra/en/

Joint manufacturers meeting

The 2017 joint UNICEF–UNFPA–WHO manufacturers meeting will take place in Copenhagen, Denmark, on 18–21 September 2017. The joint manufacturers meeting provides information for suppliers of medical products for use by UN agencies and other international organizations.

WHO Prequalification website. Events. https://extranet.who.int/prequal/
Seventieth World Health Assembly

Geneva – The Seventieth World Health Assembly was held in Geneva on 22–31 May 2017. Delegates made decisions on a wide range of health-related issues, including WHO’s response to health emergencies, the International Health Regulations and Pandemic Influenza Preparedness. Important decisions were also taken relating to polio, antimicrobial resistance, access to medicines and vaccines, the health of refugees and migrants, improving vector control, adolescent health and chemicals management, as well as on noncommunicable diseases (NCD), including dementia, cancer – including access to affordable treatment – and preparations for the 2018 UN General Assembly High-Level Meeting on NCDs.

The Assembly approved the programme budget for the biennial period 2018–19, which includes a 3% increase in assessed member contributions. In past years, voluntary contributions – which are often tied to specific activities – have overtaken assessed contributions, providing the majority of WHO’s income.

New WHO Director-General elected

Geneva – The Member States of WHO have elected Dr Tedros Adhanom Ghebreyesus as the Organization’s new Director-General. Prior to his election he served as Minister of Foreign Affairs of Ethiopia from 2012–2016 and as Minister of Health from 2005–2012. Dr Tedros has also served as chair of the Board of the Global Fund to Fight AIDS, Tuberculosis and Malaria; as chair of the Roll Back Malaria (RBM) Partnership Board; and as co-chair of the Board of the Partnership for Maternal, Newborn and Child Health.

Dr Tedros Adhanom Ghebreyesus will succeed Dr Margaret Chan, who has been WHO’s Director-General since 1 January 2007. He will begin his five-year term on 1 July 2017.

Medicines prequalification updates

1. The WHO Prequalification Team: medicines (PQTm) has prequalified the following “firsts”:
   - First sofosbuvir active pharmaceutical ingredient (API) – providing a quality source for generic manufacturers who wish to produce hepatitis C medicines.
   - First ethionamid dispersible tablet, a child-friendly formulation to treat tuberculosis. (1)

2. The following revised invitations for evaluation of products (“EOIs”) have been published:
   - 14th EOI for APIs;
   - 4th EOI for anti-hepatitis products;
   - 15th EOI for antimalarials; and
   - 15th EOI for HIV-related products. (2)

3. PQT-m has clarified its expectations regarding bioequivalence (BE) studies. On a trial basis, PQTm will consider prior scientific justification from applicants for the use of the reference-scaled approach for AUC acceptance criteria in BE studies for highly variable APIs. (3)

(2) WHO Prequalification of medicines. FPPs & APIs Eligible for Prequalification (“EOIs”).