Publications and events

Research and ethics

Revised CIOMS ethical guidelines
Geneva – The Council for International Organizations of Medical Sciences (CIOMS) has released its revised *International Ethical Guidelines for Health-Related Research Involving Humans* (1). The Guidelines were written in close collaboration with WHO. They aim to indicate how the ethical principles for research involving humans – as set forth in the Declaration of Helsinki – can be effectively implemented, particularly in low- and middle-income countries.

The scope of the Guidelines has been broadened to include research on health-related data. The revised Guidelines place more emphasis on the scientific and social value of research to ensure that important unsolved questions are addressed, and on the context in which research is conducted. They recognize that low resource settings may exist in high- and middle-income countries. They further call for governance systems to protect the interests of individuals in a world where informed consent is proving inappropriate for the growing number of health-related studies.

A commentary on the revised Guidelines has been published in *JAMA* (2).


Access to medicines

UN High Level Panel report on access to health technologies
New York – The United Nations High Level Panel on access to medicines has published a groundbreaking new report, stating that the world must take bold new approaches to health technology innovation and ensuring access so that all people can benefit from the medical advances that have dramatically improved the lives of millions around the world in the last century.

The Panel suggested that initially governments should begin negotiating a code of principles for biomedical research and development (R&D) and report annually on their progress, in preparation for negotiating a binding convention that de-links the costs of R&D from end prices. The Panel noted with grave concern reports of governments being subjected to undue political and economic pressure to forgo the use of the flexibilities provided in the World Trade Organization (WTO) Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), and felt strongly that this was undermining their efforts to meet their human rights and public health obligations. The Panel views transparency as a core component of accountability frameworks to hold all stakeholders responsible for the impact of their actions on innovation and access.

The High Level Panel was established by the United Nations Secretary-General to propose solutions for addressing the incoherences between international human rights, trade, intellectual property
rights and public health objectives. Humanitarian organizations have welcomed the report, urging governments and the international community to implement its recommendations.


Report of the Lancet Commission on Essential Medicines

London – The Lancet Commission on Essential Medicines has presented its report. The Commission was established in late 2014 to take stock of progress and challenges in providing access to affordable and quality-assured essential medicines for all. Thirty years after the first international conference on essential medicines policies, held in 1985 in Nairobi, the report provides recommendations to implement effective essential medicines policies in five crucial areas.

• Paying for a basket of essential medicines: An estimated US$ 13–25 per person per year is required to finance a basic package of 201 essential medicines. Yet in 2010, the majority of low-income countries and 13 of 47 middle-income countries spent less than US$ 13 per capita on pharmaceuticals.

• Making essential medicines affordable. National and global policies – such as promoting the use of generic medicines, price transparency and pooled procurement – can support sustainable access to essential medicines if they are implemented effectively. Related to this, the Commission warns that flexibilities included in the World Trade Organisation’s Agreement on Trade-related Aspects of Intellectual Property Rights (TRIPS), which provide governments with options that allow for the protection of public health, are under continual threat from the TRIPS-plus obligations included in bilateral and regional trade agreements.

• Assuring the quality and safety of medicines. The Commission’s recommendations build on existing procurement strategies for certain donor-funded medicines and on emerging trends towards regulatory collaboration and electronic communications. They call for the use of an international standard regulatory dossier with a harmonized content and format, and for a moving focus of WHO Prequalification on new essential medicines. Recommendations are also made on good practices in procurement and regulation, with concrete targets and a public accountability mechanism for the performance of regulatory authorities.

• Promoting the appropriate use of essential medicines. The Commission’s recommendations focus on strategies that enable collaboration among patients, health-care providers, insurers, supply chain managers, and others – including the pharmaceutical industry – to incentivize and support quality medicines use. The authors say that a key driver of inappropriate medicines use is pharmaceutical promotion, which should be controlled and monitored by robust regulatory authorities.

• Global research and development (R&D) framework. The Commission recommends that the costs of R&D should be delinked from the price of medicines and funded up-front from a Global Research Fund. Following the success of patent
Publications and events

pools for antiretrovirals and other medicines categories the report calls for the creation of a general essential medicines patent pool, to licence patents to other companies in order to create a competitive generics market. The Commission calls for strong government and international leadership to effectively implement essential medicines policies and create accountability, and proposes a set of 24 indicators to measure progress.

The work of the Commission was funded by the Bill & Melinda Gates Foundation, WHO, the University Medical Centre Groningen, Boston University, and by academic institutions and other organizations that allowed their staff to devote time to the work of the Commission.

Press release, 7 November 2016.

Access to Medicine Index 2016

The Index ranks 20 of the world’s largest pharmaceutical companies on their efforts to improve access to medicine in low- and middle-income countries, identifies best practices and highlights progress and remaining gaps. The findings show that the pharmaceutical industry is extremely diverse. GSK leads the ranking for the fifth time, followed by Johnson & Johnson, Novartis and Merck KGaA.

Pharmaceutical companies have 850 products on the market for the 51 most burdensome diseases in low- and middle-income countries, and are developing another 420. Seven companies have published new or expanded pledges since 2014 to waive or abandon patent rights for certain products in certain regions, and new commitments are pointing the way to broader use of voluntary licensing in the future. However, middle-income countries outside of sub-Saharan Africa are more likely to be left out of licensing agreements. Also, companies apply for marketing authorization in only 25% of the countries that the Index identifies as highest priority.

The Index is published every two years by the Access to Medicine Foundation, an independent non-profit organisation funded by the UK Government (UK AID), the Dutch Ministry of Foreign Affairs and the Bill & Melinda Gates Foundation.


High price of hepatitis C treatment
Geneva – A new WHO report shows that over one million people in low- and middle-income countries have been treated with the new direct-acting antiviral medicines for hepatitis C since their introduction two years ago, despite the very high cost of these products. The report includes information on access, prices, patents and registration of hepatitis C medicines, supporting country efforts to increase access to these medicines.

Among middle-income countries, the prices of hepatitis C medicines vary greatly. For example, a three-month treatment with sofosbuvir and daclatasvir costs from US$ 9 400 in Brazil to US$ 79 900 in Romania. The report shows how political will, civil society advocacy and pricing negotiations are helping to
make treatment accessible for people who need it. Nevertheless, the high prices of hepatitis C treatments remain a major barrier to their access. WHO is working on new pricing models for these and other expensive medicines in order to increase access to all essential medicines in all countries.


Medicines patent and licences database upgraded
Geneva – The Medicines Patent Pool (MPP) has upgraded its patent database to include patent and licensing data for HIV, hepatitis C and tuberculosis medicines. The Medicines Patents & Licences Database (MedsPaL) includes data covering 4 000 national patent applications in more than 100 low- and middle-income countries (LMICs).

MedsPaL offers searchable information on 35 patented medicines and more than 100 pharmaceutical formulations for the treatment of HIV, hepatitis C and tuberculosis included in WHO guidelines or in its Essential Medicines List. The information is regularly updated through automatic data feeds from the European Patent Office’s public database Espacenet, online searches, expert analysis and collaboration with national patent offices.

► MPP Press release, 5 October 2016.

The Medicines Patents & Licences Database is available at: www.medspal.org

Updated paediatric ARV formulary and list
The Inter-Agency Task Team (IATT) on the Prevention and Treatment of HIV Infection in Pregnant Women, Mothers and Children has published the 2016 update to the IATT Paediatric ARV Formulary and Limited-Use List. This edition reflects the 2016 WHO Consolidated Guidelines and takes account of changes in the markets. The formulary serves as guidance for treatment programmes, procurement agencies, funders and manufacturers to select optimal dosage forms for children.

► WHO/IATT/UNICEF. Policy brief. IATT paediatric ARV formulary and limited-use list: 2016 update.

Quality of medicines

Sample testing survey on medicines for women and children
Geneva – WHO has published a report of a quality testing survey of selected medicines from the list of 13 life-saving commodities as identified by the UN Commission on Life-Saving Commodities for Women and Children (UNCoLSC) (1). The survey was organized by the WHO Prequalification Team in cooperation with the national medicines regulatory authorities and Ministries of Health of Burkina Faso, Kenya, Madagascar, Nepal, Nigeria, Tajikistan, Tanzania, Uganda, Viet Nam and Zimbabwe. A total of 204 samples were collected and tested, of which 157 (77%) complied with the specifications set for the survey. Eleven samples of WHO-prequalified medicines were included in the survey, and all complied with specifications. A summary of the findings was published in an earlier issue of this journal (2).
The survey provides a snapshot of the quality of the sampled products and their availability in selected countries. The results enable WHO to confirm to which extent compliant testing results are supported by compliance with good manufacturing practice and proper regulatory documentation.


(2) Quality and availability of selected life-saving reproductive health medicines in developing countries. WHO Drug Information 2015;29(3):324-333.

Fighting poor-quality medicines in low- and middle-income countries

An article in the Journal of Pharmaceutical Policy and Practice highlights the divide in pharmaceutical quality between the North and the South. The authors warn that despite an increasing awareness of the problem and the launch of some positive initiatives the issue continues to expose patients in low- and middle-income countries to the risk of receiving poor-quality medicines. They call for more advocacy to achieve universal access to quality-assured medicines and emphasize that this advocacy should be based on evidence from research and monitoring programmes, should target all stakeholders – regulators, international organizations, journalists, purchasers, prescribers, programme managers, policy makers, public health actors and patients – and should be grounded in a common understanding of the technical concepts.


Antimicrobial resistance

Landmark UN declaration on antimicrobial resistance

New York – For the first time, Heads of State have committed to taking a broad, coordinated approach to address the root causes of antimicrobial resistance across multiple sectors, especially human health, animal health and agriculture. The pledge was made at a high-level meeting on antimicrobial resistance convened by the President of the 71st session of the UN General Assembly. Countries reaffirmed their commitment to develop national action plans based on the “Global Action Plan on Antimicrobial Resistance” developed in 2015 by WHO in coordination with the Food and Agriculture Organization of the United Nations (FAO) and the World Organisation for Animal Health (OIE). They pledged to strengthen the regulation of antimicrobials, improve knowledge and awareness, promote best practices, and foster innovative approaches using alternatives to antimicrobials and new technologies for diagnosis and vaccines. (1)

This is only the fourth time a health issue has been taken up by the UN General Assembly. The other issues were HIV, non-communicable diseases and Ebola. In her opening speech, the WHO Director-General stressed that actions are urgently needed, and that a global crisis of this magnitude demands attention at the highest political level. The declaration was spearheaded by a campaign led by health officials from the United Kingdom (2)

(1) Office of the President of the UN General Assembly (OPGA)/WHO/FAO/OIE Joint news release. 21 September 2016.

The economic threat of drug-resistant infections

New York – The World Bank has released a new research report showing that by 2050, drug-resistant infections could cause global economic damage similar to that of the 2008 financial crisis. The impact of antimicrobial resistance would reduce annual global gross domestic product (GDP), pushing up to 28 million people into poverty by 2050. At the global level the volume of real exports would shrink, healthcare costs could increase by more than US$ 1 trillion per year, and economic losses could amount to an estimated US$ 100 trillion by 2050.

The report recommends a number of solutions to address the crisis. It highlights the need to strengthen investments in public and veterinary health systems and overall preparedness to tackle infectious diseases, with surveillance for antimicrobial resistance as an integral component. It strongly supports implementation and adequate financing of the WHO Action plan on Antimicrobial Resistance, which was endorsed in 2015.


Clinical use of medicines

Mentoring programme

Basle – The Clinical Division of International Union of Basic and Clinical Pharmacology (IUPHAR) has initiated a pilot programme to establish a list of “mentor departments” who are willing to provide advice in the area of clinical pharmacology, ranging from simple communication through to collaborative research and researcher exchange. Five centres – located in Scotland, Spain, South Korea, Australia and Canada – were listed at the time of writing. (1)

There is a pressing need to improve the use of medicines to maximize their effectiveness and minimize their harms. This can be best achieved by expanding knowledge and expertise of clinical pharmacology and therapeutics around the world. The mentoring centres will support, mentor or train future generations with skills to undertake research and teaching in this area and to serve on governmental organizations involved in medicines regulation and health technology assessment. The pilot programme is consistent with WHO initiatives such as the Essential Medicines List, and is in line with the joint IUPHAR/WHO publication Clinical Pharmacology in Health Care, Teaching and Research (2).

► (1) IUPHAR Clinical Divisions. Mentoring Centres [website].


Disease updates

Tuberculosis: WHO global report

Geneva, Washington – WHO has published its 2016 Global tuberculosis report. The report highlights the inequalities among countries with respect to access to medical products to fight tuberculosis, and signals the need for bold political commitment and increased funding.

In low- and middle-income countries, most of which continue to rely heavily on international donations, investments to curb the tuberculosis epidemic are almost US$ 2 billion short of the US$ 8.3 billion needed in 2016. In addition, WHO
estimates that at least US$ 1 billion per year is needed to accelerate the development of new vaccines, diagnostics, and medicines. In 2015, there were an estimated 10.4 million new tuberculosis cases worldwide. Six countries accounted for 60% of the total burden. India has the most cases, followed by Indonesia, China, Nigeria, Pakistan and South Africa. An estimated 1.8 million people died from tuberculosis in 2015, of whom 0.4 million were co-infected with HIV. Although global deaths from tuberculosis fell by 22% between 2000 and 2015 the disease was among the top 10 causes of death worldwide in 2015, responsible for more deaths than HIV and malaria. Gaps in diagnosis and reporting remain major challenges. An estimated 480 000 people contracted multidrug-resistant tuberculosis in 2015, with India, China, and the Russian Federation together accounting for nearly half of all cases.


Measles: immunization gap persists

New York/Atlanta/Geneva – New data show that despite a 79% worldwide decrease in measles deaths between 2000 and 2015, the disease remains one of the leading causes of death among young children globally with an estimated 134 000 children having died from it in 2015. Mass measles vaccination campaigns and a global increase in routine measles vaccination coverage saved an estimated 20.3 million young lives between 2000 and 2015, according to UNICEF, WHO, Gavi, the Vaccine Alliance, and the Centers for Disease Control and Prevention (CDC).

But progress has been uneven, and the target of the Global Vaccine Action Plan implementation to eliminate measles in four of six WHO regions by 2015 has been missed. The Democratic Republic of the Congo, Ethiopia, India, Indonesia, Nigeria and Pakistan accounted for half of the unvaccinated infants and 75% of the measles deaths in 2015. Large outbreaks were reported in Egypt, Ethiopia, Germany, Kyrgyzstan and Mongolia, and outbreaks were also reported in Nigeria, Somalia and South Sudan. In Germany and Mongolia older persons were affected, highlighting the need to vaccinate adolescents and young adults who have no protection against measles.


Malaria: funding secured for vaccine pilots

Geneva – Funding has been secured for the initial phase of pilot projects to roll out the world's first malaria vaccine in sub-Saharan Africa. Vaccinations are due to begin in 2018. The Global Fund to Fight AIDS, Tuberculosis and Malaria has approved US$ 15 million covering the first phase of the pilot. Earlier in 2016, Gavi, the Vaccine Alliance had committed up to US$ 27.5 million and UNITAID had pledged US$ 9.6 million.

The vaccine, known as RTS,S, provides partial protection against *P. falciparum* malaria in young children. It was developed through a partnership between GlaxoSmithKline and the PATH
Malaria Vaccine Initiative (MVI), with support from the Bill & Melinda Gates Foundation and from a network of African research centres. In July 2015 the EMA issued a positive scientific opinion of the RTS,S vaccine, and in October 2015, two independent WHO advisory groups recommended its pilot implementation in 3–5 settings in sub-Saharan Africa.

The RTS,S vaccine is proposed as a tool to complement the current WHO-recommended malaria interventions.


Zika: end of public health emergency
The fifth meeting of the Emergency Committee (EC) on Zika and microcephaly was convened by the Director-General under the International Health Regulations (IHR 2005) on 18 November 2016. Research has now demonstrated the link between Zika virus infection and microcephaly, making it necessary to develop a robust longer-term mechanism to manage the global response.

The EC felt that, while Zika virus and associated consequences remain a significant public health challenge, they no longer represent a Public Health Emergency of International Concern (PHEIC). The EC recommended that a sustained programme of work should be established with dedicated resources to address the long-term nature of the disease and its associated consequences, and agreed to the proposed WHO Zika transition plan. Based on this advice, the Director-General declared the end of the PHEIC and reissued the Temporary Recommendations, which will be incorporated into the longer-term response mechanism.

► WHO Statement, 18 November 2016.

WHO matters

Model prequalification dossier
Geneva – The WHO Prequalification Team – medicines (PQTM) has published a model dossier on its website, illustrating how data should be submitted to WHO for prequalification. The model dossier is intended to serve as a training tool for regulators, as guidance for applicants, and as an example case for organizations involved in harmonizing regulatory requirements.

WHO requires that dossiers for generic medicines are submitted in the Common Technical Document (CTD) format of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). The model dossier includes the completed quality templates and the corresponding data expected in CTD Module 3, with proprietary information redacted.

► PQ update, 14 September 2016.

Feedback is encouraged and should be sent to: Dr. M. Stahl, Group Leader Medicines Assessments, WHO Prequalification Team – Medicines; stahlm@who.int.

New medicines invited for prequalification
Geneva – WHO has published new invitations for Expression of Interest for prequalification (EOI). The 14th EOI for anti-TB medicines newly includes isoniazid/rifapentine 150mg/150mg dispersible tablets and 300mg/300mg coated tablets or capsules, as well as gatifloxacin 200mg tablets and 400 mg scored tablets. The 11th EOI for active pharmaceutical ingredients newly includes gatifloxacin.

► PQ Updates, 6 October and 7 October 2016.
Seminar for laboratories held in China
Shenzhen – The 5th WHO Interregional Seminar for Quality Control Laboratories involved in WHO Prequalification was held in Shenzhen, Guangdong Province, China in October 2016. It is the first time that this seminar was held in China. More than 60 laboratory directors from 42 countries and representatives from 26 provincial drug testing institutions of China participated in the technical discussions.
► China Food and Drug Administration (CFDA) News, 26 October 2016.

“Green” procurement of health commodities
Geneva - WHO has joined other international agencies in signing a Statement of Intent to align and “green” the procurement of health commodities, in an effort to protect the environment and contribute to sustainable development.

WHO and the other signatories — including GAVI, UNDP, UNICEF, the Global Fund, UNITAID, UNFPA and UNOPS — procure an estimated US$ 3 billion in health commodities each year. They have agreed to reflect their common commitment in their standard engagement with suppliers and manufacturers. They will also include it in their institutional strategies and policies.
► WHO News release, 7 December 2016.

New prequalification fee structure
Geneva – WHO, industry groups and key partners have agreed on a new fee structure that aims to support financial predictability, sustainability and expansion of prequalification services including the setting and public disclosure of quantitative performance targets.

The new arrangement is modelled on the practice of national regulatory authorities around the world, which charge application fees for evaluation and registration services. It will be launched in January 2017 for vaccines and medicines and in early 2018 for diagnostics.

WHO began to charge prequalification fees in 1999 for vaccines, in 2008 for diagnostics, and in 2013 for medicines. Before fees were introduced, the sole donor for vaccines prequalification was UNICEF, and medicines prequalification was funded by two donors, the Bill & Melinda Gates Foundation and UNITAID. The new fee model is expected to generate revenues of about US$ 20 million annually, which will cover about half of the programme’s operating costs.
► PQ update, 30 September 2016.

Upcoming events
2017 joint UNICEF-UNFPA-WHO manufacturers meeting
The 2017 joint UNICEF-UNFPA-WHO manufacturers meeting will take place in the week of 3 April 2017 in Copenhagen, Denmark. The manufacturers meeting provides information for suppliers of medical products for use by UN agencies and other international organizations.
► WHO Prequalification update, 30 September 2016.