Publications and events

Research and development

“Disease X” added to WHO research priority list
Geneva – In its annual review of its R&D Blueprint, WHO has added “Disease X” to the research priorities for pathogens that could cause serious epidemics and for which there are no or insufficient countermeasures. Disease X represents a known or unknown pathogen that is yet to be found to have potential to cause a serious international epidemic.

The list was first published in December 2015 and is reviewed annually. It now includes (in no particular order) Crimean-Congo haemorrhagic fever (CCHF), Ebola virus disease and Marburg virus disease, Lassa fever, Middle East respiratory syndrome coronavirus (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS), Nipah and henipaviral diseases, Rift Valley fever (RVF), Zika, and Disease X. The R&D Blueprint explicitly seeks to enable cross-cutting preparedness that is also relevant for a future Disease X.

► WHO. List of Blueprint priority diseases [webpage].

Vaccines for emerging pathogens
In a recent article in JAMA, Dr Anthony Fauci and co-authors provide their views on the development of vaccines for emerging infectious diseases with pandemic potential. The authors conclude that the traditional approach of isolating and growing the pathogen does not support an effective response to these continually emerging threats. They emphasize that it will be critical to exploit modern-day technological advances, pre-emptively establish detailed information on each family of viral pathogens, and invest in more infrastructure for surveillance in developing countries to expedite pathogen identification and jump-start the process of vaccine development.


Access to medicines

European Parliament resolution
Brussels – The European Parliament has adopted a resolution calling for national and EU-wide measures to guarantee the right of patients to universal, affordable, effective, safe and timely access to essential and innovative therapies. (1) In its Report on European Union (EU) Options for Improving Access to Medicines the Committee on the Environment, Public Health and Food Safety points to the need for innovation with a clear clinical, social and economic added value, greater transparency of research data and costs; greater public investment in research; improved regulation and mechanisms to monitor conflicts of interest; and patient-oriented research priorities.

Health Action International (HAI) has commended the European Parliament for its report and has urged the European Commission and member states to follow
up on the recommendations in order to improve access to medicines in the EU.\(^{(2)}\)

\(^{(1)}\) European Parliament resolution of 2 March 2017 on EU options for improving access to medicines.

\(^{(2)}\) HAI Media statement, 3 March 2018.

The role of the pharmacist

The Hague – The International Pharmaceutical Federation (FIP) has published a report that highlights the important role of the pharmacist in ensuring access to safe and effective medicines in a variety of contexts.

Pharmacists are involved at all stages of the life cycle of medicines, from the production of raw materials through to their use by patients. In a landscape of challenges such as substandard and falsified medicines, globalization, and a shortage of human resources in health systems, the pharmacist’s expertise is critical as part of a team approach to the management of medicines. Recognizing that regulation and supply systems have different levels of maturity in countries, the report emphasizes the importance of investments in further training and education to strengthen the competencies of health professionals in ensuring supply chain integrity and rational use of medicines.

\(^{1}\) FIP News, 8 May 2018.


Pharmaceutical waste management

Pharmaceutical pollution and AMR

Brussels – The European Public Health Alliance has published the report of a recent event held to discuss the links between pharmaceutical pollution and antimicrobial resistance (AMR).\(^{(1)}\) In Europe, pollution is mainly due to pharmaceutical consumption, while the contribution of manufacturing facilities is considered as negligible.\(^{(2)}\)

On the other hand, industrial pollution is a major problem in India, where pharmaceutical manufacturing is being stepped up to supply most of the world’s generic medicines.\(^{(3)}\) This has significant global impacts as the residues in the environment are becoming a reservoir for the development of resistant pathogens. A 2017 study of samples of effluent discharges in the Hyderabad area were found to have unexpectedly high levels of antibiotic residues and—correlated with this—high levels of resistant pathogens.\(^{(4)}\)

The event participants recognized that manufacturing of pharmaceuticals in China and India is a problematic and growing issue that is fuelling AMR. It was proposed that this global issue should be addressed as part of the European strategy on Pharmaceuticals in the Environment (PiE), which is currently under public consultation \(^{(5)}\) and is due to be released by May 2018. The participants concluded that, given the high costs of inaction on the closely connected challenges of PiE and AMR, a coherent policy with the right tools and instruments are urgently needed for action to be taken before the European Parliament elections in 2019.


Medical waste in India increases

India – According to a recent study, India’s medical waste is growing by 7% every year and will reach 775.5 tons by the year 2022. The study outlines the key challenges in biomedical waste management in India: slow data availability at state and central pollution control boards, underreporting of waste generated, limited handling capacity, unauthorized healthcare facility operations, and delays in developing biomedical waste treatment facilities in some states and territories.

The study report was released at a conference on biomedical waste management organized in New Delhi on 22 March 2018 by the Associated Chambers of Commerce & Industry of India (ASSOCHAM) in collaboration with the Directorate of Health Services within the Department of Health and Family Welfare of India. Releasing the report, Dr Kirti Bhushan, Director General of Health Services of the Delhi government stressed that safe and effective management of waste is not only a legal necessity but also a social responsibility.

▸ India’s medical waste growing at 7% annually: ASSOCHAM. The Times of India. 22 March 2018.

Diagnostics

First WHO essential diagnostics list

Geneva – WHO has published its first Essential Diagnostics List (EDL). The list focuses on in vitro diagnostics (IVDs) and comprises 113 tests: 58 general IVDs for primary health care, and 55 tests for the detection, diagnosis and monitoring of global priority diseases including HIV, tuberculosis, malaria, hepatitis B and C, human papillomavirus and syphilis. The EDL describes IVDs according to their biological targets, indicating the test purpose, assay format, specimen type, and whether it is appropriate for primary health care or for health facilities with clinical laboratories. The list also provides links to WHO Guidelines or publications and, when available, to prequalified products.

The proposal for the first EDL was agreed by WHO’s new Strategic Advisory Group of Experts on In Vitro Diagnostics (SAGE IVD) in response to a recommendation made by the WHO Expert Committee on the Selection of Essential Medicines at its 2017 meeting. It is intended as a reference for countries to update or develop their own list of essential diagnostics, alongside measures to ensure appropriate and quality-assured supplies, training of health care workers and safe use. WHO will expand the list over the next few years to include tests related to antimicrobial resistance, emerging pathogens, neglected tropical diseases and additional non-communicable diseases.


**Disease updates**

**Ebola:**

**Outbreak in DRC**

Geneva, Brazzaville, Kinshasa – A new Ebola outbreak has been reported from Bikoro in the Democratic Republic of the Congo (DRC). WHO is working with the Government of the DRC and a broad range of partners to rapidly scale up its operations and mobilize health partners, using the model of a successful response to a similar outbreak in 2017.(1)

As at 13 May there were 39 reported Ebola cases, including 2 confirmed, 20 probable (of which 18 were fatal), and 17 suspected cases. WHO has released US$ 2.6 million from its Contingency Fund for Emergencies to support response activities. The estimated budget for an international response is US$ 18 million for a three-month operation.(2)

► WHO News release, 8 May 2018.
(2) WHO News release, 13 May 2018.

**Dengue:**

**Outbreak in La Réunion**

Geneva – WHO has been notified about a sharp increase of dengue fever in the French overseas territory of La Réunion in the Indian Ocean. As of 23 April, 1816 cases have been confirmed for the year 2018, including 428 probable and confirmed cases reported in the week of 16–23 April 2018 alone. In comparison, less than 100 cases were reported in all of 2017. The western and southern parts of the island are the most affected. The national authorities have stepped up their response and are implementing an emergency plan corresponding to a low level epidemic.

WHO has recommended a range of measures to reduce populations of mosquito vectors and minimize individual exposure. The Organization advises against any travel or trade restrictions at this stage.

► WHO Disease outbreak news, 1 May 2018.

**Yellow fever:**

**Strategy to end epidemics**

Abuja – WHO and the Ministry of Health of Nigeria have launched the “Eliminate Yellow fever Epidemics (EYE) in Africa” strategy, which aims to end yellow fever epidemics in Africa through vaccination campaigns and routine immunization, prevention of international spread, and rapid containment of outbreaks. By 2026, nearly one billion people are to be vaccinated against yellow fever in 27 high-risk African countries. The campaign will be supported by WHO, Gavi – the Vaccine Alliance, UNICEF and more than 50 health partners.

In recent years yellow fever has re-emerged as a serious global public health threat. The ease and speed of population movements, rapid urbanization and a resurgence of mosquitoes due to global warming have significantly increased the risk of urban outbreaks with international spread.

► WHO News release, 10 April 2018.

**Cholera:**

**Largest-ever vaccine drive**

Geneva, Brazzaville – A spate of cholera outbreaks across Africa has prompted the largest cholera vaccination drive in history, with more than two million people to receive oral cholera vaccine. Major campaigns are under way in Zambia, Uganda, Malawi, South Sudan and Nigeria. The vaccines are sourced from the global stockpile, which is managed by the Global Task Force on Cholera Control (GTFCC) and funded by Gavi, the Vaccine Alliance.(1)
A resolution on cholera was endorsed at the 71st World Health Assembly, urging cholera-affected countries to implement a roadmap that aims to reduce deaths from the disease by 90% by 2030. (2)

► (1) WHO News release, 7 May 2018.
(2) WHO News release, 24 May 2018.

**Hepatitis C:**
Treatment access increasing

**Geneva** – WHO has published an update to its 2016 report on access to treatment of hepatitis C virus (HCV) infection. Access to life-saving direct-acting antivirals (DAA) is still low, but is increasing in champion countries such as Egypt, Pakistan, Brazil, China and Georgia. Drawing on surveys in 23 low- and middle-income countries and among innovator and generic companies, as well as interviews and other new data, the report looks at the key factors that determine access to DAA medicines and highlights areas for action by ministries of health and other government decision-makers, pharmaceutical manufacturers and technical partners. (1)

With the advent of DAAs, HCV infection has become curable. As the cost of the medicines is coming down, treatment becomes cost-saving because it substantially reduces the burden of liver cirrhosis and cancer as well as diseases such as depression and diabetes. New evidence suggests that all people aged 12 or above diagnosed with chronic HCV (with the exception of pregnant women) should be offered treatment. WHO expects to release new HCV treatment guidelines soon. (2)

(2) WHO. Hepatitis C: simplified curative treatments can drive global scale-up. 13 April 2018.

**Tuberculosis:**
World’s biggest infectious killer

**Brussels** – On the eve of World Tuberculosis Day, four European Commissioners have underlined the EU’s commitment to ending the tuberculosis epidemic by 2030 and have called on governments all over the world to redouble their efforts and make this happen. The EU is also working to address antimicrobial resistance, which is inextricably linked to tuberculosis, as well as the social conditions that encourage the disease to spread. (1)

**Geneva** – WHO and the Stop TB Partnership have launched the first-ever joint advocacy and communications campaign to support thousands of partners, activists and persons affected by tuberculosis. The disease remains among the top 10 causes of death worldwide, and is the major cause of deaths related to antimicrobial resistance and the leading killer of people with HIV. To commemorate World Tuberculosis Day, the partners have provided a joint advocacy and communications toolkit containing practical guidance and information. (2)

**Geneva** – Based on an expedited review of preliminary results from the STREAM Stage 1 randomized controlled trial, WHO has advised national tuberculosis programmes and other stakeholders to continue using the shorter regimens lasting 9–12 months to treat multi-drug-resistant tuberculosis. (3)

WHO has also provided recommendations for the management of isoniazid-resistant tuberculosis. (4) Consolidated guidelines and an update of the Companion Handbook to the WHO guidelines for the management of drug-resistant tuberculosis are planned to be released later in 2018.
At the 71st World Health Assembly, held in May 2018 in Geneva, delegates agreed on a resolution committing Member States to accelerate their actions to end tuberculosis. The resolution also requests the Secretariat to develop a new global strategy for tuberculosis research and innovation.(5)

(2) WHO TB News, 2 March 2018.
(3) WHO. Position statement on the continued use of the shorter MDR-TB regimen following an expedited review of the STREAM Stage 1 preliminary results. April 2018.

Non-communicable diseases: Major health gains from investments

Geneva – A new WHO report shows that even modest investments into actions to address non-communicable diseases (NCDs) generate significant benefits. In low- and lower middle-income countries (LLMICs), where almost half of all premature deaths from NCDs occur, every dollar invested will yield a return to society of at least US$ 7 in increased employment, productivity and longer life. Among the most cost-effective interventions are increasing taxes on tobacco and alcohol, reducing salt content in food products, providing medicinal therapy and counselling to people who have had a heart attack or stroke, vaccinating girls aged 9–13 years against human papillomavirus, and screening women aged 30–49 years for cervical cancer. However, global financing to combat NCDs is severely limited. The report calls on donors to provide kick-start funding to governments of LLMICs for ambitious scaling-up of “best buy” policies.

WHO. Saving lives, spending less: a strategic response to NCDs. 2018.

HTLV-1: A scourge yet to be addressed

Sixty representatives from 26 countries have signed an open letter calling for WHO’s support to help prevent the transmission of human T-cell lymphotropic virus type 1 (HTLV-1), a virus similar to HIV and transmitted by the same routes. HTLV-1 is the most potent carcinogenic oncovirus, and potentially the most oncogenic risk factor including chemical carcinogens. Although it was discovered almost 40 years ago, effective intervention strategies have not been actively publicized. The authors warn that HTLV-1 remains a strong threat to individual and community health, and even more so to global health because of the accelerated rate of human migration in recent times.

The letter proposes a WHO vision for the prevention of HTLV-1 transmission, with five intervention strategies to reduce the incidence of HTLV-1 infection. These are based on evidence that transmission can be averted by condom use, by avoiding the transfusion and transplantation of infected blood and organs, by avoiding breastfeeding (if deemed safe) or reducing its duration to 3–6 months, by using sterile needles, and by educating healthcare professionals and the population about prevention strategies.

71st World Health Assembly
Geneva – The 71st World Health Assembly was held on 21–26 May 2018 in Geneva, Switzerland. Delegates adopted an ambitious strategic “triple billion” five-year plan which aims to ensure that by 2023 one billion more people benefit from universal health coverage; one billion more people are better protected from health emergencies; and one billion more people enjoy better health and wellbeing. (1) Several of the decisions and resolutions agreed upon at the Assembly were related to improving access to quality-assured medical products.

Access to medicines
The delegates asked WHO to elaborate a five-year roadmap to increase access to safe and effective essential medicines, vaccines and other health products – something that is becoming increasingly challenging across economic settings as medicines prices are rising. Member States also urged stakeholders to implement the recommendations for priority actions under WHO’s Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property, as identified in the review panel’s report. (2)

Specific medical products
The Member States adopted a landmark resolution on containment of poliovirus materials under strict biosafety and biosecurity handling and storage conditions in a limited number of facilities that serve critical functions in vaccine production or research. (3) They further agreed on a resolution for a coordinated global response to rheumatic heart disease, including by ensuring a consistent supply of quality-assured antibiotics. (4) Resolutions were also adopted regarding snakebite, underlining the urgent need to improve access to safe, effective and affordable antivenoms. (4) Resolutions were furthermore adopted to improve access to assistive technology such as wheelchairs or hearing aids, and digital technologies for example to track disease outbreaks or send mobile phone text messages for positive behaviour change. (4)

Public health preparedness
Delegates welcomed a proposed five-year global strategic plan to improve public health preparedness and response through the implementation of the International Health Regulations (IHR), a legal instrument introduced in 2007 that is binding on 196 countries and WHO in their work to uphold global public health security. (4) An update was provided on the new Ebola outbreak (see page 222) and on the systems put in place for a faster and more predictable response than during the previous outbreak. (2) Delegates also approved the recommendations of the Review of the Pandemic Influenza Preparedness Framework. (4) On the margins of the Assembly, WHO and the World Bank Group launched the Global Preparedness Monitoring Board as a new mechanism to ensure stringent independent monitoring and regular reporting to tackle outbreaks, pandemics, and other emergencies with health consequences. (5)

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► (1) WHO News release, 23 May 2018.
(2) WHO News release, 23 May 2018 (2).
(3) WHO News release, 26 May 2018.

The meeting documents are available at: http://apps.who.int/gb/e/e_wha71.html
WHO prequalification updates

**ICH Q3D introduced for APIs**

**What is ICH Q3D?**
The ICH Q3D guideline presents a process to assess and control elemental impurities in drug products using the principles of risk assessment.

**How will it be used in prequalification?**
The ICH Q3D risk assessment includes consideration of the impurity profile of the active pharmaceutical ingredient (API). Therefore, the WHO Prequalification Team (PQT) has decided to adopt the ICH Q3D guideline for the assessment of the elemental impurities information in new applications for both procedures: the API master file (APIMF) procedure and the procedure for prequalification of APIs. The implementation of ICH Q3D for finished pharmaceutical products (FPPs) is still under consideration within PQT.

**Must a risk assessment be provided?**
Since the ICH Q3D guideline applies to the finished product, providing a risk assessment as part of the APIMF procedure is not a mandatory requirement. However, many API manufacturers may wish to undertake a risk assessment in order that this may then be used in an assessment of the finished pharmaceutical product with respect to ICH Q3D.

Therefore when submitting an APIMF, either through the APIMF procedure or as part of the API Prequalification procedure, the applicant has two possibilities:
- **Option 1:** Do not provide a risk management summary (RMS); or
- **Option 2:** Provide a risk management summary (RMS) for elemental impurities that may be present in the final API.

Applicants should indicate the selected option on the application form.

**What will happen during assessment?**
- If no RMS is provided, only the elemental impurities that have been intentionally added will be investigated as part of the assessment, and the need for inclusion of controls for elemental impurities in the API specifications will be determined on this basis.
- If an RMS is provided then this will be considered as part of an assessment in line with ICH Q3D:
  - For an APIMF participating only in the APIMF procedure, the outcome of the RMS assessment will be recorded in the internal assessment report and remain available if needed for reference as part of an FPP assessment.
  - For APIs seeking prequalification, a statement indicating whether a risk assessment for elemental impurities has been provided will be mentioned on the Confirmation of API Prequalification document (CPQ). In case an RMS is submitted it will be annexed to the CPQ.

**What about APIMFs that are already under assessment?**
For those APIMFs that have already been accepted for assessment, the applicant can submit an RMS for elemental impurities at any time through the amendment procedure. There is no specific change category in the APIMF amendments guideline for such a revision, but applicants should submit such a change as 11 (AIN). However for ongoing applications it should not be provided as part of responses, since these invariably delay the completion of the application.

New WHO stability guideline published

The updated WHO stability guideline has now been published in the WHO Technical Report Series (TRS) No. 1010, Annex 10. This guideline replaces the previous stability guideline in TRS 953 Annex 2 (2009) and should be taken into account in preparing the quality part of product dossiers for prequalification.
► WHO Prequalification News, 7 June 2018.

“Firsts”

- First flucytosine product prequalified (HA693). Flucytosine is used to treat cryptococcal disease and other HIV/AIDS-related fungal infections.
- First dispersible ethambutol tablets for children prequalified (TB334). Ethambutol is used in the treatment of tuberculosis.
- First amikacin injection prequalified (TB319). Amikacin is used for second-line treatment of tuberculosis.
► WHO. List of prequalified Medicines/Finished Pharmaceutical Products

- First Quality Control Laboratory (QCL) in sub-Saharan West Africa prequalified: United States Pharmacopoeia (USP) Ghana. This is also a first under the USP banner.
► WHO. List of prequalified Quality Control Laboratories.

- First Medicines Quality Workshop for Manufacturers, held on 4–6 July 2018 in Copenhagen, Denmark. This new type of workshop is aimed at manufacturers that are participating, or intend to participate, in medicines prequalification. The speakers are senior WHO prequalification assessors.
► WHO Prequalification of medicines website Events. First PQT Medicines Quality Workshop for Manufacturers.

Additional medicines invited

Anti-tuberculosis medicines
- Bedaquiline (fumarate), tablet 100mg*
- Delamanid, tablet 50mg*
- Delamanid, tablet 50mg (dispersible)*
- Rifapentine, tablet 300 mg**
- Isoniazid 150 mg/rifapentine 150 mg and Isoniazid 300 mg/rifapentine 300 mg (preferably dispersible or crushable tablets in fixed-dose combination format)**
- Rifapentine, tablet 150 mg (dispersible)**
- Rifapentine, tablet 300 mg (scored and dispersible)**
► * 16th Invitation to Manufacturers of Antituberculosis Medicines, 6 March 2018.
** 17th Invitation to Manufacturers of Antituberculosis Medicines, 26 March 2018.

Anti-malarial medicines

Additional product:
- Artesunate/pyronaridine tablet 20mg/60mg (preferably dispersible)

Additional product strengths:
- Dihydroartemisinin/piperaquine phosphate tablet 60mg/480mg
- Dihydroartemisinin/piperaquine phosphate tablet 30mg/240mg (preferably dispersible)
► 16th Invitation to Manufacturers of Antimalarial Medicines, 16 March 2018.

Coming soon: Biosimilars

Pakistan joins collaborative registration

The regulatory authority of Pakistan is the 34th authority to join the WHO’s collaborative registration procedure. The purpose of this procedure is to shorten the time to registration of WHO-prequalified medicines to a target period of 90 days, based on confidential sharing of WHO assessment and inspection reports with permission of the manufacturer.
WHO Prequalification website. Accelerated Registration of Prequalified FPPs.
Upcoming events

August

WHO-UMC-HSA Inter-Regional Pharmacovigilance Training workshop
Singapore, 15–17 August 2018
Expert pharmacovigilance trainers from WHO, the Uppsala Monitoring Centre (UMC), and the Health Sciences Authority (HSA) of Singapore will share with participants their expertise and experience over a three-day workshop, jointly organized with the WHO, UMC, HSA, and the Duke-NUS Medical School’s Centre of Regulatory Excellence (CoRE) in Singapore. The workshop is part of a continuation of efforts to enhance pharmacovigilance capabilities in the ASEAN region.

Given this year’s underlying theme of Partnerships to Protect Public Health, the organizers welcome participation from non-regulators, such as people from the industry and non-government organizations (NGOs).


September

78th FIP World Congress of Pharmacy and Pharmaceutical Sciences
Glasgow, United Kingdom, 2–6 September 2018
The 2018 FIP congress in Glasgow, Scotland, invites pharmacy practitioners and pharmaceutical scientists from around the world to come together to consider ways of extending the role of pharmacists so that they play a full part in ensuring that patients and health systems achieve full benefit from the medicines people take. The one-size-fits-all approach is clearly failing many patients around the globe for the pharmacological treatment of disease. Pharmacists and pharmaceutical scientists are uniquely trained and qualified health care professionals capable of personalising therapy for improving patient outcomes.

► www.fip.org/glasgow2018/

18th International Conference of Drug Regulatory Authorities (ICDRA)
Dublin, Ireland, 3–7 September 2018
The 18th ICDRA will be organized around the theme Smart Safety surveillance: A life-cycle approach to promoting safety of medical products. The pre-ICDRA event on 3–4 September is open to all interested stakeholders. The ICDRA conference will be held on 5–7 September and is open to representatives of governments and national regulatory authorities.

► www.icdra2018.ie/

HPRA. Invitation to Exhibit at the HPRA PRE-ICDRA conference 3-4 September 2018.

Joint UNFPA-UNICEF-WHO meeting
Copenhagen, Denmark, week of 24 September 2018
The Joint UNICEF-UNFPA-WHO Meeting with manufacturers and suppliers of in vitro diagnostic, vaccines, finished pharmaceutical products, active pharmaceutical ingredients, contraceptive devices and vector control products will provide updates on UN-funded procurement, prequalification and cross-cutting issues. There will be opportunities for one-to-one discussions.

► extranet.who.int/prequal/events/2018-unicef%20%3A%20WHO%20meeting-pre-announcement