World Health Organization

Executive Summary

The Selection and Use of Essential Medicines

2017

Report of the 21st WHO Expert Committee on the

Selection and Use of Essential Medicines

WHO headquarters, Geneva

27-31 March 2017

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Annexes

Executive summary

The 21st meeting of the WHO Expert Committee on the Selection and Use of Essential Medicines took place in Geneva, Switzerland, from 27 to 31 March 2017. The goal of the meeting was to review and update the 19th WHO Model List of Essential Medicines (EML) and the 5th WHO Model List of Essential Medicines for Children (EMLc).

The Expert Committee considered 92 applications, including proposals to add 41 new medicines, extend the indications for 6 existing listed medicines, 5 applications to delete medicines from the lists, and a comprehensive review of the antibacterials listed in sections 6.2.1 and 6.2.2 and their use in the treatment of 21 common, priority infectious syndromes, five paediatric infectious diseases and three sexually transmitted infections. In accordance with approved procedures[1], the Expert Committee evaluated the scientific evidence for the comparative effectiveness, safety and cost-effectiveness of the medicines.

All changes to the lists are shown in Table 1. In summary, the Expert Committee:

- recommended the addition of 30 new medicines to the EML (17 to the core list and 13 to the complementary list);
- recommended the addition of 25 new medicines to the EMLc (13 to the core list and 12 to the complementary list);
- recommended adding additional indications for 9 currently listed medicines; and
- rejected 20 applications for inclusion and/or deletion of medicines.

As part of the review of antibacterials, 10 additions were made to the EML and 12 to the EMLc, and a new categorization of antibacterials into three groups was proposed:

- ACCESS – first and second choice antibiotics for the empiric treatment of most common infectious syndromes;
- WATCH – antibiotics with higher resistance potential whose use as first and second choice treatment should be limited to a small number of syndromes or patient groups; and
- RESERVE – antibiotics to be used mainly as 'last resort' treatment options.

Main recommendations are briefly described below in order of their appearance on the Model Lists:

Section 2.2: Opioid analgesics

The Expert Committee considered a review of methadone, fentanyl and tramadol for treatment of cancer pain. Accepting that there is a need for additional opioid treatment options for treatment of cancer pain, and noting that access to morphine is limited and patients suffering from cancer often do not receive pain relief treatments, particularly in low- and middle-income countries, the Committee recommended the addition of transdermal fentanyl to the core list of the EML and addition of a new indication for methadone for management of cancer pain to the complementary list of the EML and EMLc. The Expert Committee did not recommend the addition of tramadol, as the evidence reviewed showed that this product is a sub-optimal treatment for cancer pain compared to morphine and other strong opioids.

[1] See: http://www.who.int/selection_medicines/committees/subcommittee/2/eeb1098%5b1%5d.pdf

Section 6.2: Antibacterials

Section 6 of the Essential Medicines List covers anti-infective medicines. Disease-specific sub-sections within Section 6 of the EML such as those covering medicines for tuberculosis, HIV, hepatitis and malaria, have been regularly reviewed and updated, taking into consideration relevant WHO treatment guidelines. However, antibacterial medicines in sections 6.2.1 (beta-lactam medicines) and 6.2.2 (other antibacterials) have not been similarly reviewed and updated and so were the focus of a comprehensive review in 2017. This revision addresses Objective 4 of the WHO's Global Action Plan on Antimicrobial Resistance to "optimize the use of antimicrobial medicines in human and animal health".

Some antibacterials listed in Sections 6.2.1 and 6.2.2 are also listed for the treatment of multi-drug resistant tuberculosis (MDR-TB). The impact of this review on antibacterials for treatment of tuberculosis was carefully considered, given the increasing problem represented by MDR-TB and the need to preserve effective treatments, but the Committee did not change antibiotic listings in Section 6.4.2 Antituberculosis medicines as a result of this review.

Having considered the proposals put forward for its consideration, the Expert Committee decided to only consider treatments for common infectious syndromes, excluding rare or hospital-acquired infections. The Committee then identified empiric treatment choices for common, community-acquired infections that are broadly applicable in the majority of countries, using parsimony as a guiding principle. Alternative options for patients with allergy to specific products were not considered. The Committee recommended first and second choice antibiotics for each syndrome. First and second choice antibiotics are included on the Model Lists with the specific indication(s).

Taking account of the global recognition of the need for effective antimicrobial stewardship, as well as the need to ensure access to necessary antibiotics and appropriate prescribing, the Expert Committee also proposed that these antibiotics could be categorized in three groups: ACCESS, WATCH and RESERVE groups.

The Committee specifically noted that the evidence base for recommending specific antibiotics and classes into the different categories was weak and the List will need further revision over time as new evidence is identified. It was also clearly recognized that the general principles of Access/Watch/Reserve apply to many other antimicrobials, including antituberculosis, antimalarial, antivirals, antifungals and others.

The groups are described and defined in detail below.

ACCESS GROUP

This group includes antibiotics recommended as empiric, first or second choice treatment options for common infectious syndromes and are listed in the EML/EMLc with the syndromes for which they are recommended. They should be widely available, at an affordable cost, in appropriate formulations and of assured quality. First choices are usually narrow spectrum agents with positive benefit-to-risk ratios, and low resistance potential, whereas second choices are generally broader spectrum antibiotics with higher resistance potential, or less favorable benefit-to-risk ratios.

Where antibiotics in the ACCESS group are recommended only for a limited number of indications and there are also concerns about existing or potential resistance, they may be listed in the WATCH group as well. Their use should be limited and monitored.

Access group antibiotics			
6.2.1 Beta-lactam medicines		**6.2.2 Other antibacterials**	
amoxicillin	cefotaxime*	amikacin	gentamicin
amoxicillin + clavulanic acid	ceftriaxone*	azithromycin*	metronidazole
ampicillin	cloxacillin	chloramphenicol	nitrofurantoin
benzathine benzylpenicillin	phenoxymethylpenicillin	ciprofloxacin*	spectinomycin (EML only)
benzylpenicillin	piperacillin + tazobactam*	clarithromycin*	sulfamethoxazole + trimethoprim
cefalexin	procaine benzyl penicillin	clindamycin	vancomycin (oral)*
cefazolin	*meropenem**	doxycycline	*vancomycin (parenteral)**
cefixime*			

Italics = complementary list;
*Watch group antibiotics included in the EML/EMLc only for specific, limited indications

WATCH GROUP

This group includes antibiotic *classes* that are considered generally to have higher resistance potential and that are still recommended as first or second choice treatments but for a limited number of indications. These medicines should be prioritized as key targets of local and national stewardship programs and monitoring. This group includes the highest priority agents on the list of Critically Important Antimicrobials (CIA) for Human Medicine[2]. The CIA list ranks antimicrobials according to their relative importance in human medicine and can be used in the development of risk management strategies for the use of antimicrobials in food production animals.

Seven pharmacological classes were identified for this group. As noted above, monitoring systems should be in place to ensure that their use is in line with recommended indications.

Watch group antibiotics
Quinolones and fluoroquinolones e.g. ciprofloxacin, levofloxacin, moxifloxacin, norfloxacin
3rd-generation cephalosporins (with or without beta-lactamase inhibitor) e.g. cefixime, ceftriaxone, cefotaxime, ceftazidime
Macrolides e.g. azithromycin, clarithromycin, erythromycin
Glycopeptides e.g. teicoplanin, vancomycin
Anti-pseudomonal penicillins with beta-lactamase inhibitor e.g. piperacillin + tazobactam
Carbapenems e.g. meropenem, imipenem + cilastatin
Penems e.g. faropenem

[2] http://apps.who.int/iris/bitstream/10665/251715/1/9789241511469-eng.pdf?ua=1

RESERVE GROUP

This group includes antibiotics that should be treated as 'last-resort' options, or tailored to highly specific patients and settings, and when other alternatives would be inadequate or have already failed (e.g., serious life-threatening infections due to multi-drug resistant bacteria). These medicines could be protected and prioritized as key targets of high-intensity national and international stewardship programs involving monitoring and utilization reporting, to preserve their effectiveness. Eight antibiotics or antibiotic classes were identified for this group.

Reserve group ('last-resort') antibiotics	
Aztreonam	Fosfomycin (IV)
4th generation cephalosporins e.g. cefepime	Oxazolidinones e.g. linezolid
5th generation cephalosporins e.g. ceftaroline	Tigecycline
Polymyxins e.g. polymyxin B, colistin	Daptomycin

The Expert Committee recommended the appointment of a standing EML Working Group to:

- consider reviewing additional clinical syndromes not included in the current update, e.g., medical and surgical prophylaxis, dental infections and acute undifferentiated fever;
- adapt or work on the current clinical synopsis reviews into shorter structured documents;
- coordinate the development of a guidance document on optimal dose and duration of antibiotic treatments to maximize clinical efficacy while minimizing the selection of resistance for EML/c;
- review the differential effect of antibiotic classes on the selection of resistance;
- relate the work of the EML/c to the future essential in-vitro diagnostics list which should include work on diagnostics related to antimicrobial resistance as soon as feasible;
- propose improved methods for defining and communicating the key stewardship messages associated with the new categorization and develop more detailed guidance to assist with the implementation of recommendations in national programs.

Section 6.2.4: Antituberculosis medicines

The Expert Committee recommended the listing of clofazimine for the new indication of multi-drug resistant tuberculosis (MDR-TB) on the complementary list of the EML and EMLc. The Expert Committee also recommended the addition of delamanid to the complementary list of the EMLc for the treatment of MDR-TB in children aged 6 to 17 years. Two paediatric fixed-dose combination formulations of isoniazid, pyrazinamide and rifampicin, and isoniazid and rifampicin were recommended for addition to the EMLc for treatment of tuberculosis. The Expert Committee did not recommend listing of gatifloxacin because it was not demonstrated to have a better benefit to harm ratio compared with currently listed alternatives. Ofloxacin (as an alternative to levofloxacin) was deleted in line with updated MDR-TB guidelines and moxifloxacin, the other alternative to levofloxacin, was made into an independent listing. Streptomycin was deleted from the core list of the EML, but is retained on the complementary list of the EML and EMLc.

Section 6.4.2: Antiretrovirals

Noting the updated (2016) WHO Guidelines on the use of antiretroviral drugs for treating and preventing HIV infection, the Expert Committee recommended the addition of dolutegravir to the EML and the addition of raltegravir to the EML and EMLc. The additional indication of pre-exposure prophylaxis (PrEP) for tenofovir disoproxil fumarate, alone, or in combination with emtricitabine or lamivudine was also recommended. The Expert Committee did not recommend the proposed antiretroviral formulations containing tenofovir alafenamide. The Committee recommended the deletion of 26 antiretroviral formulations/strengths, noting they were no longer recommended by WHO guidelines.

Section 6.4.3: Other antivirals

The Expert Committee did not recommend the deletion of oseltamivir from the EML and EMLc, recognizing that it is the only medicine included on the Model Lists for critically ill patients with influenza and for influenza pandemic preparedness. However, the Committee noted that compared to when oseltamivir was first included on the Model List in 2009, there now exists additional evidence of oseltamivir in seasonal and pandemic flu which has reduced the previously estimated magnitude of effect of oseltamivir on relevant clinical outcomes. The Committee recommended the listing of oseltamivir be amended and the medicine be moved from the core to the complementary list, and its use be restricted to severe illness due to confirmed or suspected influenza virus infection in critically ill hospitalized patients. The Expert EML Committee noted that WHO guidelines for pharmacological management of pandemic and seasonal influenza are going to be updated in 2017: unless new information supporting the use in seasonal and pandemic outbreaks is provided, the next Expert Committee might consider oseltamivir for deletion.

Section 8.2: Cytotoxic and adjuvant medicines

The Expert Committee recommended the addition of dasatinib and nilotinib to the complementary list of the EML for the treatment of chronic myeloid leukaemia that is resistant to imatinib (i.e. second-line therapy). The Expert Committee did not recommend listing for other proposed cancer medicines: enzalutamide for metastatic breast cancer; tyrosine kinase inhibitors (erlotinib, gefitinib and afatinib) and anaplastic lymphoma kinase (ALK-) inhibitor (crizotinib) for non-small cell lung cancer; trastuzumab emtansine for metastatic breast cancer. The Committee considered that listing of these medicines was premature and recommended the establishment of an EML cancer medicines working group to coordinate comprehensive evaluation of cancer medicines for the EML.

Section 10.1: Antianaemia medicines

The Expert Committee recommended the addition of erythropoiesis-stimulating agents as a pharmacological class with a square box including biosimilars, to the complementary list of the EML and the EMLc for the treatment of anaemia in patients with chronic renal disease requiring dialysis.

Section 12: Cardiovascular medicines

The Expert Committee did not recommend the addition of two specific fixed-dose combinations (FDCs) of cardiovascular medicines for secondary prevention of cardiovascular events (aspirin + atorvastatin + ramipril), or hypertension (lisinopril + hydrochlorothiazide). However, the Committee considered that FDCs for non-communicable diseases may have advantages over the single medicines given concomitantly, including increased adherence and reduced pill burden. The Committee considered that many different

combinations of cardiovascular medicines exist, with multiple permutations of components from different therapeutic classes, varying strengths and dosages. The Committee recognized that listing a single FDC of cardiovascular medicines would limit choice from the variety of combinations, components and dosages available. The Committee recommended the addition of explanatory text to this effect to section 12 of the EML, enabling discretion at country level to make choices for national EML selection.

Section 18: Hormones, Other Endocrine Medicines & Contraceptives

The Expert Committee did not recommend the inclusion of insulin analogues as a pharmacological class on the EML and EMLc noting the small magnitude of benefit and current high price compared to human insulin.

The Expert Committee did not recommend inclusion of second-line medicines for type 2 diabetes on the EML. Of the second-line therapies considered, the Committee noted that SGLT-2 inhibitors have shown a relevant clinical benefit as second-line therapy in patients at high risk of cardiovascular events, with a reduction in overall mortality but that more data are needed to confirm this finding.

Two new contraceptive products were added to the EML: ulipristal acetate for emergency contraception; and a new formulation of medroxyprogesterone acetate depot injection.

Other applications not recommended

In addition to those indicated above, the Expert Committee did not recommend the addition of ready to use therapeutic food (RUTF) or hypochlorous acid solution. The Committee did not recommend deletion of bevacizumab for ocular indications, nor deletion of the indication of prevention of post-partum haemorrhage from the listing for misoprostol.

General issues

The Expert Committee recommended the formation of expert working groups to support future work for EML reviews and applications. Specifically, working groups were recommended for cancer medicines: to define criteria and thresholds for prioritization of medicines; antibiotics: to work on the implementation at country level of the proposed antibiotic categorization and to evaluate its adoption and potential hurdles; and for issues related to selective outcome reporting, publication bias, and open access to trial data as this can have relevant implications for the decision-making process.

The Committee expressed concerns about the high price of some medicines and supported the objectives of the upcoming Fair Pricing Forum as one initiative to increase awareness and participation of all relevant stakeholders. The issue of access to affordable essential medicines was discussed, notably for those for cancer and diabetes.

The Expert Committee supported the proposal for a WHO list of essential in vitro diagnostics.

All applications and documents reviewed by the Expert Committee are available on the WHO website at: http://www.who.int/selection_medicines/committees/expert/21/en/

Table 1: Summary of recommended changes to the EML and EMLc

EML – New medicines added		**EMLc – New medicines added**	
Medicine	**Indication**	**Medicine**	**Indication**
Artesunate + pyronaridine	Malaria	Artesunate + pyronaridine	Malaria
Atazanavir + ritonavir	HIV	*Aztreonam*	Reserve antibiotic
Aztreonam	Reserve antibiotic	*Cephalosporins – 4th generation*	Reserve antibiotics
Budesonide + formoterol	Asthma	*Cephalosporins – 5th generation*	Reserve antibiotics
Cephalosporins – 4th generation	Reserve antibiotics	Cefixime	Antibiotic
Cephalosporins – 5th generation	Reserve antibiotics	Clarithromycin	Antibiotic
Daptomycin	Reserve antibiotic	*Daptomycin*	Reserve antibiotic
Dasatinib	Chronic myeloid leukaemia	*Delamanid*	Tuberculosis
Dihydroartemisinin + piperaquine	Malaria	Dihydroartemisinin + piperaquine	Malaria
Dolutegravir	HIV	*Erythropoiesis-stimulating agents*	Anaemia of chronic renal disease
Efavirenz + lamivudine + tenofovir DF	HIV	*Fosfomycin (IV)*	Reserve antibiotic
Erythropoiesis-stimulating agents	Anaemia of chronic renal disease	Isoniazid + pyrazinamide + rifampicin	Tuberculosis
Fentanyl	Cancer pain	Isoniazid + rifampicin	Tuberculosis
Fosfomycin (IV)	Reserve antibiotic	Isoniazid + pyridoxine + sulfamethoxazole + trimethoprim	HIV
Isoniazid + pyridoxine + sulfamethoxazole + trimethoprim	HIV	Itraconazole	Fungal infection
Itraconazole	Fungal infection	Lamotrigine	Epilepsy
Lamotrigine	Epilepsy	*Methadone*	Cancer pain
Losartan	Hypertension	*Meropenem*	Antibiotic
Meropenem	Antibiotic	Natamycin	Fungal infection
Natamycin	Fungal infection	*Oxazolindinones*	Reserve antibiotics
Nilotinib	Chronic myeloid leukaemia	Piperacillin + tazobactam	Antibiotic
Oxazolindinones	Reserve antibiotics	*Polymyxins*	Reserve antibiotics
Piperacillin + tazobactam	Antibiotic	Raltegravir	HIV
Polymyxins	Reserve antibiotics	*Tigecycline*	Reserve antibiotic
Raltegravir	HIV	Voriconazole	Fungal infection
Sofosbuvir + velpatasvir	Hepatitis C		
Tigecycline	Reserve antibiotic		
Ulipristal	Emergency contraception		
Voriconazole	Fungal infection		
Zoledronic acid	Bone metastases		

EML - New / changed indications	
Amikacin	Antibiotic
Azithromycin	Yaws
Clofazimine	Tuberculosis
Emtricitabine + tenofovir DF	HIV PrEP
Ivermectin	Anthelminthic
Methadone	Cancer pain
Oseltamivir	Influenza
Oxygen	Hypoxaemia
Tenofovir DF	HIV PrEP

EMLc - New /changed indications	
Amikacin	Antibiotic
Azithromycin	Yaws
Clofazimine	Tuberculosis
Ivermectin	Anthelminthic
Methadone	Cancer pain
Oseltamivir	Influenza
Oxygen	Hypoxaemia

EML - New formulations	
Medicine	**Formulation**
Abacavir + lamivudine	Tablet (dispersible, scored) 120 mg + 60 mg
Amoxicillin	Powder for injection: 250 mg; 500 mg; 1 g
Amoxicillin + clavulanic acid	Powder for injection: 500 mg + 100 mg; 1000 mg + 200 mg
Doxycycline	Powder for injection: 100 mg
Medroxyprogesterone acetate	Injection (SC) 104 mg/0.65mL
Paracetamol	Oral liquid 120 mg/5 mL
Vancomycin	Capsule: 125 mg; 250 mg

EMLc - New formulations	
Medicine	**Formulation**
Abacavir	Tablet (dispersible, scored) 60 mg
Abacavir + lamivudine	Tablet (dispersible, scored) 120 mg + 60 mg
Amoxicillin	Powder for injection: 250 mg; 500 mg; 1 g
Amoxicillin + clavulanic acid	Powder for injection: 500 mg + 100 mg; 1000 mg + 200 mg
Artesunate	Rectal dosage form 100 mg
Doxycycline	Powder for injection: 100 mg
Erythromycin	Eye ointment 0.5%
Lopinavir + ritonavir	Capsule with oral pellets 40 mg + 10 mg
Paracetamol	Oral liquid 120 mg/5 mL
Vancomycin	Capsule: 125 mg; 250 mg
Zidovudine	Tablet (dispersible, scored) 60 mg

EML - Medicines / formulations deleted	
Abacavir	Oral liquid 100 mg / 5 mL
Atazanavir	Solid oral dose form 150 mg
Efavirenz	Capsule 50 mg; 100 mg; 200 mg
Lamivudine	Oral liquid 50 mg / mL
Lamivudine + nevirapine + stavudine	Tablet: 150 mg + 200 mg + 30 mg
	Tablet (dispersible): 30 mg + 50 mg + 6 mg
Ofloxacin	For MDR-TB as an alternative to levofloxacin
Saquinavir	All dose forms/strengths
Stavudine	All dose forms/strengths
Streptomycin (core list)	Powder for injection 1 g
Zidovudine	Capsule 100 mg

EMLc - Medicines / formulations deleted	
Abacavir	Oral liquid 100 mg / 5 mL
Atazanavir	Solid oral dose form 150 mg
Efavirenz	Capsule 50 mg; 100 mg; 200 mg
Lamivudine + nevirapine + stavudine	Tablet (dispersible): 30 mg + 50 mg + 6 mg
Nevirapine	Tablet 200 mg
Ofloxacin	For MDR-TB as an alternative to levofloxacin
Stavudine	All dose forms/strengths
Zidovudine	Capsule 100 mg

List of participants

Expert Committee Members

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Gilles Forte, Coordinator, Office of the Director, Essential Medicines and Health Products Department.

Nicola Magrini, Secretary of the Expert Committee on Selection and Use of Essential Medicines; Innovation, Access and Use, Department of Essential Medicines and Health Products.

Lorenzo Moja, Technical Officer, EML Secretariat; Innovation, Access and Use, Department of Essential Medicines and Health Products.

Bernadette Cappello, Technical Officer, EML Secretariat; Innovation, Access and Use Department of Essential Medicines and Health Products.

Carmem Pessoa da Silva, Medical Officer; Antimicrobial Resistance, Office of the Director-General.

Elizabeth Tayler, Technical Officer; Antimicrobial Resistance, Office of the Director-General.

Filiberto Beltran Velazquez, Technical Officer; Evidence and Programme Guidance, Department of Nutrition for Health and Development.

Declaration of Interests

Declarations of interests of Expert Committee Members and Temporary Advisers

Management of conflicts of interest was a key priority throughout the process of development of recommendations. In reviewing and assessing the declarations of interest of the Members of the 21st Expert Committee on the Selection and Use of Essential Medicines, the WHO Essential Medicines and Health Products Department sought the advice of the Office of Compliance, Risk Management and Ethics.

Over 90 applications for addition, deletion or changes to medicines on the Model Lists were considered by the 21st Expert Committee on the Selection and Use of Essential Medicines. The full list of applications is available on the WHO website[3].

Prior to the Expert Committee meeting, all Members and Temporary Advisers of the 21st Expert Committee on the Selection and Use of Essential Medicines submitted written disclosures of competing interests that were relevant for consideration prior to confirmation as members of the said meeting. These included employment by a commercial entity, consultancy, board or advisory board membership, lecture fees, expert witness income, industry sponsored grants including contracted research, patents received or pending, royalties, stock ownership or options, other personal financial interests; whether the institution or employer has a financial relationship with a commercial entity that has an interest in medicines evaluated by the Expert Committee.

Committee Members and Temporary Advisers were also asked to disclose academic or scientific activities: this included leadership of research or grant applications, in either primary clinical studies or reviews, directly bearing on a decision about a medicine. In addition, at the start of the Expert Committee, all members were asked to update their declaration if any new conflicts may have originated in the meantime.

Members and Temporary Advisers who did declare to not have financial conflicts of interests were: Lisa BERO, Zeba AZIZ, Facundo GARCIA-BOURNISSEN, Sumanth GANDRA, Mohammed HASSAR, Robert MVUNGI, Francis OFEI, Gabriela PRUTSKY-LOPEZ, Shalini SRI RANAGANATHAN, Fatima SULEMAN, Worasuda YOONGTHONG and Mei ZENG.

Dr Lisa BERO is Co-Chair of the Cochrane Collaboration Governing Board. Cochrane is a global non-profit organization consisting of an independent network of researchers producing high quality systematic reviews of evidence for health care interventions. Dr Bero authored studies about reporting biases and promotion of gabapentin, and an editorial on bevacizumab, medicines under evaluation at this meeting.

Dr Franco CAVALLI declared that his institution (Ente Ospedaliero Cantonale, Switzerland) has received funding from Mundipharma for testing a medicine in testicular lymphoma, a disease not under evaluation at this meeting. He also declared that he is the organizer of the International Conference on Malignant Lymphoma, and coordinator of the World Oncology Forum, activities for which he is unpaid.

Dr Graham COOKE declared that his institution (Imperial College London, UK) is involved in multicentre trials as one site of patient recruitment to test the efficacy and safety of medicines on hepatitis C. Oral agents are produced by the pharmaceutical companies Janssen, Bristol-Myers Squibb and Gilead. Dr Cooke declared that he is chairing the Lancet Commission on Hepatitis C, for which he is unpaid.

Dr Stephan HARBARTH is leading the WHO Collaborating Centre on Patient Safety Infection Control Program. Dr HARBARTH declared that his institution (University of Geneva Hospitals, Switzerland) has received funding

[3] http://www.who.int/selection_medicines/committees/expert/21/eml21applications/en/

from Pfizer for designing and conducting a study on antimicrobial resistance burden in several countries. Dr HARBARTH also declared that his institution has received funding from the Innovative Medicines Initiative, a joint undertaking between the European Union and the European Pharmaceutical Industry Association, to lead a work package of the DRIVE-AB (Driving reinvestment in research and development and responsible antibiotic use) Project. These projects are not related to antibiotics under evaluation at this meeting.

Dr Gregory Kearns declared having received honoraria from Janssen Pharmaceuticals and from Roche to provide expert advice on design and conduct of pharmacokinetics studies.

Dr Gabriela PRUTSKY-LOPEZ declared being an unpaid member of the Expert Committee for the Selection and Inclusion of Medicines in the Strategic Fund of the Pan American Health Organization (PAHO).

Dr Celine PULCINI declared that her institution (University of Lorraine, France) has received funding from the Innovative Medicines Initiative, a joint undertaking between the European Union and the European Pharmaceutical Industry Association (EFPIA), to participate in the DRIVE-AB (Driving reinvestment in research and development and responsible antibiotic use) Project (Workpackage 1a). This project is not related to antibiotics under evaluation at this meeting.

Dr Mike SHARLAND chairs the Department of Health's Expert Advisory Committee on Antimicrobial Prescribing, Resistance and Healthcare Associated Infection (APRHAI). His institution (St George's University London), is involved in multicentred trials as one site to test the efficacy of vaccines and antibiotics in children receiving institutional funding from GSK, Pfizer, Medimmune, Janssen, Novartis, Novovax, Regeneron, Ablynx, Alios, Cubist and Cempra.

After analysing each DOI, the Secretariat of the EML, assisted by the Office of Compliance, Risk Management and Ethics, concluded that there were no significant conflicts of interest that would exclude any member from participating fully in the Expert Committee process. Conflicts of interests declared by Dr Gregory Kearns were considered minor. No other member had personal financial or commercial interests related to medicines under evaluation. Institutional grants and funding were considered not creating the potential for inappropriate influence over the Expert Committee members and Temporary Advisers. Therefore, options for conditional participation, partial or total exclusion of any expert were not discussed.

Declarations of interest for the WHO Secretariat

Declarations of interest of the WHO Secretariat were also reviewed (although this was not mandatory) and guidance was sought from the Office of Compliance, Risk Management and Ethics with respect to potential conflicts.

Bernadette Cappello, Suzanne Hill, Nicola Magrini, and Lorenzo Moja had no financial conflicts of interests.

Dr Lorenzo Moja authored one systematic review on safety of a medicine under evaluation (bevacizumab).

In 2014 Dr Nicola Magrini was called to testify by the Italian Antitrust Authority in a case against Roche and Novartis for anticompetitive activities in respect of one medicine (bevacizumab) under evaluation. While it was determined that Dr Magrini did not have any direct conflict of interest with respect to the evaluation of bevacizumab, he was advised he might consider, of his own volition, recusing himself from this part of the evaluation in order to avoid a perceived conflict of interest. Nicola Magrini did decide to recuse himself from participating in the discussions and formulation of the recommendation on bevacizumab.