

STATEMENT

IFPMA key considerations on the scope, utility and processes around updating the WHO Essential Medicines List

07 APRIL 2023, GENEVA – The WHO Essential Medicines List (EML) is an important tool in global health and supports the achievement of the UN Sustainable Development Goals. This document summarizes perspectives from the R&D-based industry on the utility and scope of the EML. This represents IFPMA's perspective as of April 2023, ahead of the publication of the revised version of the EML.

Key points:

1. The R&D-based biopharmaceutical industry, which is at the forefront of developing innovative treatments, recognizes the value of the EML as a foundational list of medicines¹ that meet many of the priority healthcare needs of national health systems and their populations. As a reference list, the EML should not limit governments, healthcare professionals or patients from adopting other treatment options which may not be listed in the EML but are deemed appropriate at a national level.
2. The inclusion of innovative medicines on the EML can enable improved population health only if there is wide access to those medicines. To maximize access, broader healthcare system investments are needed to support efficient and effective access, delivery and uptake (i.e. devising innovative financing and payment methods, improving health workforce balance and quality, improving service delivery infrastructure and accessibility, etc). This is especially the case for products on the complementary list that frequently require additional infrastructure and specialized healthcare workers (e.g., cancer, rare diseases).
3. EML expansion should lead to patient-centric collaborative efforts among governments, payers, civil society, international agencies and the pharmaceutical industry to identify appropriate sustainable approaches with long-term durable impact with regard to safe and effective uptake of essential medicines to the benefit of patients and populations.
4. The decision on whether to include medicines on the EML should be based on the evidence on medical need, clinical efficacy, available real-world evidence and infrastructural requirements. The development of EML should not be based on implicit rationing that does not take societal perspective into account nor should it be guided purely by cost containment objectives.

¹ Throughout this document the term “medicine” is used to refer to all types of medicinal products featured on the WHO's EML, including biologics and vaccines.

5. The WHO should prioritize providing an accurate summary of the data available on clinical effectiveness and safety, whether it is representative of the situation in lower resource settings as well as a summary of the minimal infrastructure requirements to implement a new technology. The WHO should acknowledge where there are data gaps and be cautious about making recommendations on inconsistent data. A generalized cost-effectiveness assessment that does not take into consideration each country's national context will have limited value in informing decision-making and EML recommendations.
6. Given the influence of the EML in structuring basic national benefit packages in low- and middle-income countries, it is important that the processes around the EML are open, inclusive and impartial. Informal advisory groups that establish criteria for EML inclusion (i.e. cancer medicines working group) should include experts with relevant expertise, including from industry, academia and national regulatory agencies who can provide expert advice and knowledge.
7. Principles underpinning inclusion of medicines on the EML should be in line with the primary scope and purpose of EML. WHO should not promote policies or utilise approaches that disregard value and undermine innovation such as compulsory licensing.

Background

For more than 40 years the World Health Organization's (WHO) Essential Medicines List (EML) has served as a helpful model list of the essential medicines that satisfy the priority healthcare needs of patients in various countries. Historically, the EML was largely focused on off-patent medicines, however the percentage of patented medicines has steadily increased over time². Updates of the EML in recent years have added a number of innovative medicines. In fact, the EML has gradually expanded in scope in response to medical innovation, unmet medical needs, and increasing societal expectations. The growing impact of noncommunicable diseases (NCDs) to the global disease burden means NCDs have been prioritized by the WHO and essential medicines for NCDs including cardiovascular disease, neurological disease, diabetes and cancer have been recently added to the list. Such expansion reflected the increased value provided by innovation brought about by investments of the biopharmaceutical industry, academia as well as public and private research agencies. As such, the number of medicines included in the EML has significantly increased from 186 medicines in 1977 to 479 in 2021.

² Schultz M. 2022. Essential medicines and patents on the World Health Organisation Essential Medicines List 22nd Edition. Geneva Network. <https://geneva-network.com/wp-content/uploads/2022/01/2022-WHO-essential-medicines-and-patents-analysis.pdf>

The Purpose of the EML

The EML should serve as a global model of reference³ for countries and procurement agencies making decisions about procurement of medicines. Such decisions, while guided by EML, should also continue to reflect each nation's unique health priorities and landscape, taking into account national disease burden, health system capacities, and socio-cultural characteristics of the population. For these reasons, the actual medicines list of individual countries often differs significantly from the EML both in the number of molecules and in the focus given to different therapy areas⁴.

Historically, the EML has been regarded as a basic minimum standard list designed to help countries in limited resource settings, with limited capacity for medicine selection, or with fragile health systems. However, in recent years with the addition of innovative medicines on the list, the role of the EML is evolving into new areas, including policy, normative guidance, and market-shaping. As a result⁵, the fundamental question of the purpose and utility of the EML is becoming more important as WHO now asserts that the EML is also relevant for high- and middle-income countries, particularly given the more recent additions of newer medicines⁶. Some have raised concerns that these efforts to broaden the EML beyond its original remit of providing a short, specific list of essential medicines for developing countries “may make the tool less relevant to those it was primarily intended to help – decision makers in the developing countries”⁷.

The research-based biopharmaceutical industry shares these concerns. While there is value in establishing a prioritized list of essential medicines, a short, prioritized list of medicines will most likely leave out many valuable medicines and therefore must not be used as an absolute ceiling of what populations should have access to. We believe that as a reference list, the EML should not limit governments, healthcare professionals or patients from adopting other treatment options which may not be listed in the EML but are deemed appropriate in national context.

³ World Health Organization, 'Essential Medicines', webpage, http://www.who.int/medicines/services/essmedicines_def/en/ (accessed 28/4/2016)

⁴ IMS Institute for Health Informatics. 2016. *Ensuring Essential Medicines Satisfy Priority Healthcare Needs of Populations: Evolution, Current State and Future Needs*, <https://www.ifpma.org/resource-centre/ensuring-essential-medicines-satisfy-priority-healthcare-needs-of-populations/>.

⁵ McCarthy, M. 2017 “What makes an essential medicine? WHO's new list focuses on antibiotic resistance, adds expensive drugs, and downgrades Tamiflu”, *BMJ*, 358:j3044 doi: 10.1136/bmj.j3044; Kishore, S. et al. 2018. “Modernizing the World Health Organization List of Essential Medicines for Preventing and Controlling Cardiovascular Diseases”, *Journal of the American College of Cardiology*, <https://doi.org/10.1016/j.jacc.2017.11.056>; Marks, V. et al. 2017. “On Essentiality and the World Health Organization's Model List of Essential Medicines”, *Annals of Global Health*, vol. 83, no. 3-4, <http://dx.doi.org/10.1016/j.aogh.2017.05.005>.

⁶ World Health Organization, 'Essential Medicines', webpage, http://www.who.int/medicines/services/essmedicines_def/en/ (accessed 31/10/2018).

⁷ Manikandan, S. 2015. “Are we moving towards a new definition of essential medicines?”, *Journal of Pharmacology and Pharmacotherapeutics*, July- September, 6(3), p. 125.

The inclusion of medicines on the EML should be based on sound medical evidence reviewed by regulatory authorities and health systems infrastructural requirements

Industry appreciates the WHO's efforts to assist patients to benefit from broader access to medicines through the EML which has an important role in achieving better global health outcomes.

The existing drug approval processes form the foundation by which patient benefit and safety are ensured. Within this framework, physicians and patients should have the ability to make a choice about the right medicine to use fully informed by available scientific evidence on efficacy and safety. Off-label use can be acceptable in some cases, and offering options to physicians and patients where no licensed therapies are available. However, the decision to do so should be based on the availability of adequate scientific evidence on the efficacy and safety, and not for economic reasons. Furthermore, this should be based on a case-by-case benefit/risk assessment by the treating physician, and in consultation with patients in situations where specific patients cannot be satisfactorily treated with an authorized medicine and always under the physician's direct supervision. Listing medicines for off-label use on the WHO EML when alternative licensed therapies are available raises serious concerns as it encourages the use of medicines in indications for which the competent authorities have not performed a benefit/risk assessment.

The strategy of listing medicines on the EML for priority health needs, based on the magnitude of their population level effect on mortality and morbidity should not undermine and diminish the value of other medicines currently approved and deemed safe and effective by National Regulatory Authorities (NRA), but not yet listed on the EML. This approach would effectively exclude recently approved medicines, whose entire therapeutic value is yet to be fully understood or realised through broader clinical use. As such, the EML should not be used to inadvertently disregard or discredit their value and/or prevent further collection of real-world evidence relating to their safety and effectiveness. This would ultimately lead to significant value loss for the society in the long-term.

Use of generalized above-country cost-effectiveness assessment to determine decision-making does not reflect unique country circumstances

The WHO selects medicines for inclusion in the EML by considering evidence of disease prevalence, public health relevance, efficacy, safety and comparative cost-effectiveness. For cost-effectiveness data, it is challenging to pool and compare existing decisions across countries and assess cost-effectiveness in different contexts. This is particularly challenging for newer innovative medicines where cost-effectiveness data may initially only be available for high-income countries and where cost-effectiveness evaluations depend strongly on national thresholds⁸. Given the EML is more impactful in low- and middle-income countries (LMICs), the type of data used to support the WHO's decision-making should come from this setting. An analysis that is based on infrastructure, patient populations

⁸ [Schwarzer R et al.](#), Systematic overview of cost-effectiveness thresholds in ten countries across four continents. (2015) *Journal of Comparative Effectiveness Research*. DOI: 10.2217/ce.15.38

and price data from high-income countries is not an appropriate benchmark in the assessment and the WHO's recommendations should not be based on this. This is particularly relevant as the industry is working directly with individual countries to address health systems, access and affordability challenges, tailoring solutions to local needs.

Over the years there is evidence of a wide variance in both the amount and quality of cost-effectiveness data included in EML applications.⁹ In the absence of meaningful cost-effectiveness data, the WHO should prioritize providing an accurate summary of the data available on clinical effectiveness and safety, and whether it is representative of the situation in lower resource settings. The WHO should acknowledge where there are data gaps and not make recommendations on inconsistencies and parameters that supported by limited evidence.

Medicines added to EML should be accompanied by guidance on how to strengthen health systems to support appropriate uptake

The EML can be an important vehicle for enabling access to needed medicines. In order to ensure that medicines actually reach patients who need them, however, the global and national dialogue on access should be broadened to include other critical aspects of access, including universal health coverage (UHC), health systems strengthening (health workforce, service delivery and data infrastructure, etc.), innovative financing and payment models, good governance, patient awareness and need-led demand, etc.

A key challenge impacting patient uptake of essential medicines are the numerous systemic barriers preventing medicines on the EML from reaching patients. These include a lack of sufficient, sustained healthcare funding, insufficiently capacitated regulatory systems, supply chain problems, lack of frontline health workers or technical expertise, lack of sufficient health system infrastructure that can reach every patient, health illiteracy and counterfeit medicines¹⁰. Some recent EML submissions include treatments which require a biomarker testing infrastructure, pathologists, infusion centres and sophisticated side-effect management in order to be administered properly and safely to patients. Listing a medicine on the EML without addressing the minimal health system requirements and concomitant health investments to overcome these barriers will not lead to greater access and appropriate uptake of these medicines by patients.

When medicines are added to the EML, governments should ensure that their health systems are able to provide such medicines to the people who need them equitably, safely, efficiently and effectively in

⁹ Moucheraud, C., Wirtz, V. J., & Reich, M. R. 2015. Evaluating the quality and use of economic data in decisions about essential medicines. *Bulletin of the World Health Organization*, 93, 693-699.

¹⁰ Matthe, S. et al. 2011. Improving Access to Medicines for Non-Communicable Diseases in the Developing World, RAND Health, http://www.rand.org/content/dam/rand/pubs/occasional_papers/2011/RAND_OP349.pdf (accessed 3/5/2016); R. Laing, *The Patent Status of Medicines on the WHO Model List of Essential Medicines* (Geneva: World Health Organization, World Trade Organization & World Intellectual Property Organization, 2011; Amir Attaran, "How Do Patents And Economic Policies Affect Access To Essential Medicines In Developing Countries?," *Health Affairs* 23, no. 3 (May 1, 2004): 155–66, <https://www.healthaffairs.org/doi/pdf/10.1377/hlthaff.23.3.155>

order to derive the most benefit from their health investment. Many innovative medicines now and in the future will likely require detection, diagnosis and delivery in more complex care settings and thus the need to develop centres of excellence to ensure their safe and effective delivery. Other medicines – indeed the largest proportion of those on the EML – can be delivered within primary care and are commonly administered by patients at home, outside the formal care setting. Recognizing these important differences in access and uptake is critical in ensuring that nations and their citizens gain the best benefit from included medicines.

The inclusion of any medicine on the EML, including innovative and specialty medicines, will result in expanded patient access to new treatment options only if combined with broader activities to support delivery and uptake¹¹. It is important for countries to strengthen their health systems and work with stakeholders, including public and private funders of health systems to ensure that sustained funding will be available and that the health system infrastructure is robust and resilient to safeguard the effective delivery of essential medicines to the community. Moreover, it is critical that the inclusion of these medicines is accompanied by clear guidance on how these medicines should be properly utilized (i.e., treatment guidelines and training) and any necessary supporting systems, including disease surveillance systems, disease registries, pharmacovigilance systems, diagnosis, patient monitoring, adherence, and management of comorbidities. A country's essential medicines list should reflect the capacity of its health system to properly and appropriately deliver these medicines.

For example, it is estimated that less than 50% of the cancer medicines on the EML are currently available in LMICs. In 2020, more than 3.5 million new cancer cases were diagnosed in LMICs and an estimated 2.3 million premature deaths were caused by cancer. If left unchecked, deaths from cancer in LLMICs are expected to rise to 4 million by 2040¹².

The WHO has recognized the importance of specialized infrastructure for speciality medicines by developing the complementary section of the EML. As opposed to the Core List, which presents a list of “minimum medicine needs for a basic health-care system”, the Complementary List presents “medicines for priority diseases, for which specialized diagnostic or monitoring facilities, and/or specialist medical care, and/or specialist training are needed”. The industry welcomes this differentiation, as it is clear that for many disease areas, access to medicine alone does not confer access to effective treatment. In many cases, effective treatment is impeded by barriers such as lack of healthcare funding in countries, low health awareness and literacy, ineffective programs of screening and diagnosis, supply chain problems, lack of frontline health workers, lack of sufficient health system infrastructure, and the underlying social determinants of health. It is critical that their inclusion is accompanied by clear guidance on how these medicines should be properly used and guidance on how health systems can be strengthened to ensure these medicines effectively treat their target

¹¹ Roadmap for access to medicines, vaccines and health product 2019-2023. Comprehensive support for access to medicines, vaccines and other health products. Geneva: World Health Organization; 2019.
<https://apps.who.int/iris/bitstream/handle/10665/330145/9789241517034-eng.pdf>

¹² Globocan 2020: For Low-Income Countries: <https://gco.iarc.fr/today/data/factsheets/populations/989-low-income-factsheets.pdf>(link is external); for Low Middle Income Countries:

populations. Proposals for inclusion should therefore also contain an assessment of minimal requirements for implementation (Minimal Requirements Assessment – MRA). This will help governments to do a proper needs assessment and provide guidance for investment.

The WHO also asserts that medicines can be added to the complementary list on the basis of “consistent higher costs” or less attractive cost-effectiveness. This approach however should acknowledge that a generalized cost-effectiveness assessment that does not take into consideration each country’s national context will have limited value, as it will leave out a number of important data points like disease burden, health system capacities, and socio-cultural characteristics of the population. As the EML continues to expand, the approach taken to assessing medicines takes on greater importance. Methodologies, inputs, assumptions and analysis will all require specialised attention in order for the EML to be of value to countries and national decision-makers.

Intellectual property (IP) is not the major barrier to access to medicines on the EML

Most medicines on the EML are off-patent, and yet access to and uptake of them remains a challenge. Only a small proportion of all medicines on the EML are patented and the patented medicines that are on the EML often have generic equivalents due to arrangements made by originator companies to expand access and share technologies¹³. Although generic competition may broaden access to some extent, the persistent lack of access to the generic medicines that comprise the bulk of the EML demonstrates that broader health system issues, not IP, remain the key barriers to access to medicines by patients. EML listing decisions should consider the capacity of health systems globally to deliver these treatments appropriately.

Inclusion on the EML does not justify activities that undermine a sound innovation system. In recent years there have been proposals, such as automatic compulsory licensing, for all medicines on the EML. Proposals like these weaken the incentive to invest in the development of products that address global health priorities. They do nothing to address the wide range of more fundamental barriers to access in countries’ health systems and are unlikely to lead to improved patient access to medicines.

The EML should encourage multi-stakeholder collaboration to develop solutions to increase access to healthcare and innovative medicines

Listing innovative medicines on the EML should lead to collaborative efforts between governments, payers, international agencies and the pharmaceutical industry to identify sustainable, long-term approaches to strengthen health systems and make progress on universal health coverage to enable broader access to and appropriate uptake of needed medicines. These efforts should focus on how to work together to increase investment to strengthen health systems, increase access to healthcare and recognising the value of innovation. According to the WHO, the EML,

¹³ Beall, R. & Attaran, A. 2016. Global Challenges Report: Patent-based analysis of the World Health Organization’s 2013 Model List of Essential Medicines, WIPO, Geneva.

http://www.wipo.int/edocs/mdocs/mdocs/en/wipo_gc_ip_ge_16/wipo_gc_ip_ge_16_www_334437.pdf

“incorporates the need to regularly update medicines selections to reflect new therapeutic options and changing therapeutic needs; the need to ensure drug quality; and the need for continued development of better medicines, medicines for emerging diseases, and medicines to meet changing resistance patterns”¹⁴.

The innovative pharmaceutical industry shares this view, and encourages the WHO, its Member States and other stakeholders to ensure that decisions on what medicines to include on the EML recognize the importance of investing in innovation now, and into the future, and are not detrimental to the development of new and better medicines.

Process for developing the EML should be open, inclusive and impartial

Given the importance of the EML, it is critical that the processes around updating the EML are sufficiently open, inclusive and impartial. The innovative pharmaceutical industry’s expertise, data and insights about the medicines and vaccines we have developed can support the bi-annual process of reviewing the EML. Within the independent governance structure of the EML review processes, WHO should:

- Recognize the importance of fostering the development of new medicines
- Adopt regulatory standards that are consistent with scientific evidence, national regulatory approvals and globally recognized safety, efficacy and quality standards
- Be predictable, consistent and use transparent processes that respect and appropriately safeguard commercial and business confidentiality
- Allow for collective industry input into developing administrative processes for updating the EML and appointing experts for informal advisory and joint working groups
- Have in place transparency mechanisms about the decision-making process to safeguard stakeholders’ confidence in the EML processes.

Deliberations of the advisory working groups established to advise the Expert Committee would be improved with a broader membership, including NRAs, industry and non-state actors in official relations with WHO. These working groups have membership from individuals nominated by patient groups and a few selected NGOs, but would also benefit from expertise from regulatory agencies. For innovative medicines in particular, data submitted to NRAs for granting marketing authorization and resulting from post-marketing surveillance are often the most detailed source of information regarding these products’ safety and efficacy. Expertise in research, drug development and pharmaceutical manufacturing from the industry that has developed, tested and brought to market the medicines and vaccines that are being reviewed could bring valuable insights to inform EML development and decisions. The IFPMA believes appointing suitable and appropriate industry-nominated representatives to these

¹⁴ World Health Organization, ‘Essential Medicines’, webpage, http://www.who.int/medicines/services/essmedicines_def/en/ (accessed 31/10/2018).

advisory working groups is consistent with, and envisaged by, the WHO's Framework for Engagement with Non-State Actors. As the FENSA states:

“Private sector entities may provide their up-to-date information and knowledge on technical issues, and share their experience with WHO, as appropriate, subject to the provisions of the overarching framework, and this specific policy and operational procedures, and other applicable WHO rules, policies and procedures. Such contribution should be made publicly available, as appropriate, wherever possible. Scientific evidence generated should be made publicly available.”¹⁵

Conclusion

The development of each EML update, and the WHO narrative around the list, should be framed to encourage constructive dialogue and collaboration amongst health system actors, including the pharmaceutical industry, about the purpose and utility of the EML, the compendium of essential medicines and how access and uptake are appropriately and sustainably expanded. The success of the EML lies in the number of additional patients having access to these essential medicines. The pharmaceutical industry is committed to work with the WHO, other international agencies, governments and all stakeholders to identify strategies to strengthen health systems and expand universal health coverage that will enable long-term sustainable access to and uptake of essential medicines.

The pharmaceutical industry is today developing a range of new medicines that will benefit the global community now and in the future. It is important that stakeholders work together with the pharmaceutical industry to identify the best ways to ensure sustainable, safe, efficient, and effective patient access to current and future innovation.

About IFPMA

The International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) represents over 90 innovative pharmaceutical companies and associations across the globe. Based in Geneva, IFPMA has official relations with the United Nations and contributes industry expertise to help the global health community improve the lives of people everywhere. The industry's two million employees discover, develop, and deliver medicines and vaccines that advance global health.

¹⁵ World Health Organization. 2016. *Framework of Engagement with Non-State Actors*, Adopted in resolution World Health Assembly, WHA 69.10, http://www.who.int/about/collaborations/non-state-actors/A69_R10-FENSA-en.pdf?ua=1, p. 28 (accessed 1/11/2018).