

## IFPMA position paper on the WHO Essential Medicines List (2019)

*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.*

### 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 medicines that meet 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 when combined with broader healthcare system investments 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 and is guided purely by cost containment objectives.
- 5) 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.
- 6) 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 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: as of 2015, between 90% and 95% of medicines on the EML were generic<sup>1</sup>. 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, with more treatments added in areas such as cancer, hepatitis C, cardiovascular disease and a range of vaccines. 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 204 molecules in 1977 to 433 unique molecules in 2017. For example, the 2017 update added 30 medicines for adults and 25 for children and specifies new uses for nine already-listed products.

## The Purpose of the EML

The EML should serve as a global model of reference<sup>2</sup> for countries and procurement agencies making decisions about procurement of medicines. Such decisions, while guided by EML, should also reflect each nation's unique health 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 areas<sup>3</sup>.

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 result<sup>4</sup>, 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 since the more recent additions of newer medicines<sup>5</sup>. Some have raised concerns that these efforts to broaden the EML beyond its original remit of providing a short,

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<sup>1</sup> Beall R. & Attaran, A. 2015 *Patent-based Analysis of the World Health Organization's 2013 Model List of Essential Medicines*, Global Challenges Report, World Intellectual Property Organization, [http://www.wipo.int/edocs/mdocs/mdocs/en/wipo\\_gc\\_ip\\_ge\\_16/wipo\\_gc\\_ip\\_ge\\_16\\_www\\_334437.pdf](http://www.wipo.int/edocs/mdocs/mdocs/en/wipo_gc_ip_ge_16/wipo_gc_ip_ge_16_www_334437.pdf) (accessed 20/7/2018).

<sup>2</sup> World Health Organization, 'Essential Medicines', webpage, [http://www.who.int/medicines/services/essmedicines\\_def/en/](http://www.who.int/medicines/services/essmedicines_def/en/) (accessed 28/4/2016)

<sup>3</sup> 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/>.

<sup>4</sup> 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>.

<sup>5</sup> World Health Organization, 'Essential Medicines', webpage, [http://www.who.int/medicines/services/essmedicines\\_def/en/](http://www.who.int/medicines/services/essmedicines_def/en/) (accessed 31/10/2018).

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”<sup>6</sup>.

The research-based biopharmaceutical industry shares these concerns, and recognizes the objective of establishing a prioritized list of essential medicines, while acknowledging that a short, prioritized list of medicines will most likely leave out valuable medicines and therefore must not be used as an absolute ceiling of what the population 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.

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

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 (on- or off-label) fully informed by available scientific evidence on efficacy and safety. Off-label use can be acceptable in some cases, and it offers treatment options to physicians and patients where no licensed therapies are available. However, the decision to do so should be based on adequate scientific evidence on the efficacy and safety, not for economic reasons. Furthermore, this should be based on a case-by-case benefit/risk assessment by the treating physician, a competent and guided advisory board, and in consultation with patients in situations where specific patients cannot be satisfactorily treated with an authorized medicine and 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 over patient safety as it encourages the use of medicines in indications for which the competent authorities have not performed a benefit/risk assessment.

On the other hand, the strategy of listing medicines 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. As an example, personalized therapies, which comprise 73% of all cancer medicines currently in development<sup>7</sup> or recently-approved medicines, whose entire therapeutic potential is yet to be fully understood, would be excluded from this approach. It is crucial to recognize the potential of these medicines, and the EML should not be used to inadvertently discredit their value 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.

This being said, 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.

### **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 as a first step. In order to ensure that medicines actually reach patients who need them, however, the global and

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

<sup>7</sup> Tufts Center for the Study of Drug Development, “Impact Report,” Volume 17, No.3, May/June 2015,

national dialogue on access should be broadened to include other critical aspects of access, including innovative financing and payment models, health systems strengthening (health workforce, service delivery and data infrastructure, etc.), good governance, patient awareness and need-led demand, etc.

A key problem with patient uptake of essential medicines is that in many countries numerous systemic barriers prevent medicines on the EML reaching patients. These include a lack of sufficient, sustained healthcare funding, insufficiently capacitated regulatory systems, supply chain problems, lack of frontline health workers, lack of sufficient health system infrastructure that can reach every patient, health illiteracy and counterfeit medicines<sup>8</sup>. Listing a medicine on the EML without concomitant investments to address 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 aim at ensuring that their health systems are able to provide such medicines to the people who need them equitably, safely, efficiently and effectively in order to derive the most benefit from their health investment. Many innovative medicines now and in the future will require delivery in specialty 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 – are able to 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, including innovative and specialty medicines, on the EML will result in expanded patient access to new treatment options only if combined with broader activities to support delivery and uptake. 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 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 appropriately deliver these medicines.

### **Innovation supported by intellectual property is essential for the development of, and access to, new medicines**

Intellectual property protection is an important enabler for the development of, and access to, new medicines. Virtually every important medicine of the last 150 years — including antibiotics, vaccines, HIV and HCV treatments, cancer and cardiovascular medicines — owes its existence to the R&D activities of the biopharmaceutical industry. Strong IP protection enables the needed investments and supports continued innovation. IP incentivizes not only the discovery and development of new medicines but also the optimization of existing medicines (developing

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<sup>8</sup> Mattke, 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](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>

paediatric formulations, for instance), including those which may address global unmet medical needs.

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 or compulsory acquisition of the rights to essential medicines from companies. 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.

### **Intellectual property 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 technologies<sup>9</sup>. Although generic competition may broaden access to some extent, the persistence of access gaps to the generic medicines that comprise the bulk of the EML shows that broader health system issues, not IP, remain the key barriers to access to medicines by patients. Listing decisions should consider the capacity of health systems globally to deliver these treatments appropriately.

As an example, all cancer medicines included in the EML are listed under the complementary section. 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 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. This holds true for many or all cancer medicines listed on the Complementary List. For these medicines in particular, 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 populations.

WHO also asserts that medicines can also be added to this list on the basis of “consistent higher costs” or less attractive cost-effectiveness. This approach however should acknowledge that a universal 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.

Complementary options that support appropriate access and uptake have also been listed by WHO, including expediting local regulatory approvals or removing taxes and tariffs on essential medicines<sup>10</sup>.

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<sup>9</sup> 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](http://www.wipo.int/edocs/mdocs/mdocs/en/wipo_gc_ip_ge_16/wipo_gc_ip_ge_16_www_334437.pdf)

<sup>10</sup> WHO guideline on country pharmaceutical pricing policies

<http://apps.who.int/medicinedocs/documents/s21016en/s21016en.pdf>

## **The EML should encourage collaboration to develop solutions**

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 in order to broaden access to and appropriate uptake of needed medicines. These efforts should focus on key issues like health system infrastructure, adequate funding and recognizing the value of medicines.

According to the WHO, the EML,

*“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**”<sup>11</sup>.*

The pharmaceutical industry shares this view and encourages WHO and others to ensure that decisions on what medicines to include on the EML should recognize the importance of supporting the development of new and better medicines for the future rather than dissuading that critical investment in global health.

## **Process for developing EML should be open, inclusive and impartial**

Given the relevance of the EML, it is important that the processes around the updating the EML are sufficiently open, inclusive and impartial. The R&D 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 world’s best practice safety, efficacy and quality standards,
- Be predictable, consistent and use transparent processes that respect appropriate commercial confidentiality
- Allow for collective industry input into developing administrative processes for updating the EML and appointing experts for informal advisory groups.
- Provide the opportunity for individual companies to provide feedback, engage and respond to issues about their medicines before the EML reviews are finalized, and
- 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 wider membership, including NRAs, industry and NSAs in official relations with WHO. These working groups have membership from individuals nominated by patient groups and a few selected NGOs, but suffers from lack of expertise from the industry that has developed, tested and brought to market the medicines and vaccines that are being reviewed. These working groups would also benefit from expertise from regulatory agencies: For innovative medicines in

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<sup>11</sup> World Health Organization, ‘Essential Medicines’, webpage, [http://www.who.int/medicines/services/essmedicines\\_def/en/](http://www.who.int/medicines/services/essmedicines_def/en/) (accessed 31/10/2018).

particular, data submitted to NRAs for granting marketing authorization is often the most detailed source of information regarding these products' safety and efficacy.

The IFPMA believes appointing suitable and appropriate industry–nominated representatives to these 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.”<sup>12</sup>*

## **Conclusion**

The development of each EML update, and the WHO narrative around the list, should be framed to encourage constructive dialogue among 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 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.

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<sup>12</sup> 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](http://www.who.int/about/collaborations/non-state-actors/A69_R10-FENSA-en.pdf?ua=1), p. 28 (accessed 1/11/2018).