WHO shapes priorities for medicines? An examination of the stakeholders and decision makers within the historical evolution of the World Health Organization Model Lists of Essential Medicines

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Summary

The World Health Organization (WHO) recently announced a process to review and potentially update the procedures for selecting essential medicines. This announcement presents an opportunity to reflect on the evolution of the WHO Model Lists of Essential Medicines (EML), including the composition of the stakeholders that shape priorities. We contextualised our findings within the broader history of the WHO EML to support future reforms to improve access to essential medicines. The current system allows individuals to propose a medicine for the WHO EML. This makes the EML reactive to applicant priorities. Almost all medicines (687/700, 98·1%) proposed to the WHO EML between 2003 and 2023 came from applicants in high-income countries. Most applications (210/700; 30·0%) were submitted by universities and research institutions, followed by NGOs (159/700; 22·7%), the UN system (158/700; 22·6%), professional associations (98/700; 14·0%), and the pharmaceutical industry (75/700; 10·7%). Between 1977 and 2023, over half of the Expert Committee members were from LMICs, with an increasing proportion in recent EML updates. Mainly, UN agencies acted as observers between 1977 and 2023. One central question emerges when evaluating whether applicants' geographic distribution translates to the WHO EML's intended purpose: For whom are the Model Lists intended? Over the years, the geographic applicability has blurred. Defining a strategic vision for the WHO EML, including articulating a target audience and structured selection process, would strengthen decision-making processes by providing additional clarity, including to those implementing the guidance, mostly in LMICs.

Key messages

1. The WHO EML has evolved substantially since its inception in 1977. Once a tool for low- and middle-income countries (LMICs), changes to the selection procedures in 2001 facilitated the addition of patented, high-priced medicines, broadening the Model Lists' relevance to high-income countries (HICs).
2. Between 2003 and 2023, applicants were nearly all from HICs. Most applications were submitted by universities and research institutions, NGOs, the UN system, professional associations, and the pharmaceutical industry with the lowest proportion.
3. Between 1977 and 2023, over half of the Expert Committee members were from LMICs, with an increasing proportion in recent EML updates, while UN agencies mainly acted as observers.
4. Evaluating the geographic demographics of stakeholders within EML processes raises a question: For whom is the WHO EML intended? Over the years, the geographic applicability has blurred. Clarifying a target audience would decrease decision-making uncertainties.
5. Defining a strategic vision for the WHO EML, including introducing a structured disease-based selection process and clarifying criteria for the selection of essential medicines would strengthen decision-making processes.
6. Member states and WHO leadership should support the Secretariat in undertaking reforms as strengthening the capacities of institutions responsible for essential medicines policies, including the WHO EML, is central to pursuing Universal Health Coverage.

Introduction

The concept of essential medicines was born nearly 50 years ago under the direction of World Health Organization (WHO) Director-General Halfdan Mahler, who announced, at the 1975 World Health Assembly, that there was an urgent need to ensure medicines be available at a reasonable price in developing countries.[1,2] Over the years, the WHO Model Lists of Essential Medicines (EML/Model Lists) gained global visibility and have been widely used by countries to guide national essential medicines lists (NEMLs), clinicians to ensure the rational use of medicines, and the wider global health community to signal that an 'exceptional' medicine must be made available.[3,4] As of 2017, over 150 countries have adopted NEMLs, many based on the WHO EML.[5] The Model Lists also serve as a model for procurement of other global disease programmes and non-governmental organisations (NGOs). Taken together, additions and removals from the list can have far-reaching implications.

In late 2023, WHO announced a process to review and update the procedures for selecting essential medicines, representing the second major procedural change since its inception.[6,7] This announcement presents an opportunity to reflect on the evolution of the WHO EML, including the composition of the stakeholders that shape priorities. To understand who shapes decisions about the world's most influential list of medicines, we comprehensively analysed the applicants for the WHO EML (2003-2023) as well as the demographics of the EML Expert Committee members (decision makers) and observers present during decision-making since the inception of the WHO EML (1977-2023). We contextualised our findings within the history of the WHO EML to develop specific policy implications and support future reforms to improve access to essential medicines worldwide.[8]

What is the process of updating the WHO Essential Medicines Lists?

While the structure and concept of the WHO EML have remained similar since its inception, the process has changed substantially **(Figure 1)**. Until 2001, costs and patent status were major criteria for inclusion in the WHO EML **(Panel 1)**. This led to an original focus on listing affordable medicines for LMICs. Against the backdrop of the HIV/AIDS epidemic and inaccessibility to antiretrovirals, concerns were raised about excluding several effective yet widely patented and high-priced antiretrovirals.[3,4,9] In 2001, an evidence-based approach was introduced to select essential medicines (Revised Procedures).[10] Costs and patent status criteria were dropped, and the focus became clinical benefit (cost-effectiveness is considered between therapeutic alternatives). The idea was that affordability was no longer a precondition but a result of listing. With these changes, several patented medicines have been added throughout the years, shifting the relevance of the concept of essential medicines (i.e., the evidence-based process of rationalising resources towards high-benefit medicines) to HICs.

The 2001 Revised Procedures guide decision-making today. The WHO EML is updated every two years through an application process which opens approximately a year before the biennial update. The decision-making period culminates in the meeting of the WHO Expert Committee, which occurs over one week.[11] Applications to add, remove, or alter medicines on the WHO EML can be submitted by any individual, member state, academic institution, professional organisation, NGO, or company. When there is a perceived gap in the essential medicines for a therapeutic area, the WHO staff responsible for the EML (Secretariat) may source applications from external stakeholders.

Applications are submitted and internally reviewed before being published on the WHO website. Once the applications are publicly available, WHO Technical Departments, working groups, and the public can submit comments to the Secretariat, which are also uploaded to the website.

Applications and external comments are reviewed by the WHO Expert Committee on the Selection and Use of Essential Medicines (Expert Committee) — a committee of external individuals contracted to make non-binding collective recommendations for the inclusion, change, or deletion of medicines on the WHO EML, which are subject to final approval by the Director-General. The Expert Committee are an independent group selected to represent a range of professional and geographical experiences.[12] The decision-making portion of the biennial meeting of the Expert Committee is private. However, the meeting is preceded by an "open session" for the public to make statements about relevant matters before the Committee. Observers from various organisations are allowed into the private portion of the meeting if authorised by the Director-General.[12] These organisations do not participate in the collective decision-making but can provide input if the Committee requests. An overview of the process and stakeholders is provided in **Figure 2**.

[Insert Panel 2. Methods]

Who are the applicants, which countries and organisations do they represent, and what medicines are submitted?

Overall, 170 applicants proposed 416 unique medicines for 705 indication pairs (referred to as "medicines") across 165 different therapeutic categories to the WHO EML between 2003 and 2023. Five medicines (0·7%) did not specify applicants, i.e., 700 medicines were included in the study cohort for the analysis. Cancer medicines comprised the largest therapeutic area of medicines proposed (194/700; 27·7%) and recommended (148/483; 30·6%) to the EML. The average number of medicines proposed per applicant was 4·1 (IQR 1 to 4). The number of applications has increased tenfold over the past twenty years, from a dozen proposed additions in 2003 to 132 changes

(additions and deletions) in 2023. In 2003, applications were mostly driven by WHO, while in the most recent update in 2023, most applications were submitted by universities and research centres.

Overall, almost all medicines (687/700, 98·1%) proposed to the WHO EML came from applicants in high-income countries (HICs) and 13/700 (1·9%) from applicants in LMICs. Nearly half (303/700; 43·3%) of all applicants were headquartered in Switzerland, followed by 114 of 700 (16·3%) in the United States (US), 67/700 (9·6%) from Canada, 40/700 (5·7%) from the United Kingdom (UK), and 38/700 from Australia (5·4%) **(Figure 3)**. There were no regional differences in the types of medicines requested.

Most applications, approximately one-third of the medicines (210/700; 30·0%) were submitted by individuals representing universities and research institutions (most of them located in Canada, the US and the UK), followed by NGOs (159/700; 22·7%) such as the Union for International Cancer Control, Global Action Fund for Fungal Infection or Médecins Sans Frontières, UN system (158/700; 22·6%), and professional associations (98/700; 14·0%) such as the European Society for Medical Oncology (ESMO) and International Association for Hospice and Palliative Care. The pharmaceutical industry submitted the fewest medicines (75/700; 10·7%). The update of the cancer medicines in 2015 in collaboration with the Union for International Cancer Control[13], a Switzerland-based NGO, and the update of the antibiotic medicines in 2017 in collaboration with McMaster University in Canada contributed to the leading positions of universities and research institutions as well as NGOs (**Figure 4**).

The priorities for suggested medicines differed between the applicants. Overall, universities, research centres, and NGOs submitted most of their applications for medicines to treat cancer disorders. By contrast, the UN system (all from WHO technical departments) focused most of its

applications on medicines for tuberculosis, and the pharmaceutical industry submitted most of its applications for HIV/AIDS (**Table**).

Since 2009, cancer medicines have been the largest therapeutic category proposed to the EML (194/700; 28·1%). This trend remained even when excluding the 2015 update, where several medicines were adopted on the EML. The most common tumour types were non-Hodgkin lymphoma (28/194; 14·4%), breast (26/194; 13·4%), chronic lymphoid leukaemia (20/194; 10·3%), and lung (19/194; 9·7%). Between 2009 and 2013, applications for cancer medicines were submitted mostly by universities and research centres. However, since 2017, this therapeutic category has been driven by professional associations, such as ESMO.

Approximately two-thirds (483/700; 69·0%) of medicines proposed to the list received positive recommendations (**Table**). The distribution of therapeutic areas for medicines recommended by the Expert Committee reflected the applications. Cancer medicines comprised the largest therapeutic categories of positive recommendations (148/483; 30·6%) and negative recommendations (42/172, 24·4%). NGOs experienced the highest success rate (138 positive recommendations of 159 submitted applications; 86·8%), followed by universities and research centres (146/210; 69·5%), the UN system (106 of 158; 67·1%), professional organisations (57/98; 58·2%), and pharmaceutical industry (36/75; 48·0%).

Who are the Expert Committee members, what are their professional backgrounds, and which countries do they represent?

Between 1977 and 2023, 166 individuals participated as Expert Committee members or Technical Advisors. The average participation frequency was 2 (range: 1 to 10), which is aligned with the WHO regulations specifying that the appointments of expert advisory members should not exceed

four years.[12] Nonetheless, 10/166 (6·0%) participated over five (most before 2013). In the most recent EML update, 3/19 (15.8%) participated four consecutive times. The finding that 10 individuals served several terms on the Expert Committee may reflect a condition in the regulations allowing the Director-General to renew appointments if certain programme requirements require.[12]

Of the 166 unique participants, 71 (42·8%) were from HICs, and 95 (58·2%) were from LMICs. Notably, the proportion of individuals from LMICs has always been higher than those from HICs (**Figure 5**). Furthermore, the proportion of Expert Committee members from LMICs was 68·4% (13 of 19 members) at the 2023 Expert Committee, demonstrating alignment with the panel regulations that specify participants ought to represent a variety of geographic and professional expertise.[12] Nearly all Expert Committee members had expertise within medicine (101 of 166; 60·2%) or the pharmaceutical sciences (65 of 166; 39·2%). It may be the case that these individuals have multidisciplinary expertise.[14] However, WHO only provides information on primary affiliation, which could be assumed to be the capacity in which these individuals act.

Who are the observers, and which organisations do they represent?

Between 1977 and 2023, 22 organisations represented by 101 unique individuals acted as observers. All organisations were from HICs in the global north (22/22; 100%), with most (10/22; 44.5%) organisations headquartered in Switzerland. None of the organisations had submitted applications for medicines to be included in the WHO EML.

The most common organisation present during the Expert Committee meeting was the United Nations Children's Fund (UNICEF), followed by the UN Population Fund, and the International Federation of Pharmaceutical Manufacturers & Associations (IFPMA) **(Figure 6).** While

pharmaceutical manufacturers only submitted a small proportion of essential medicines, they engaged as observers during the Expert Committee meetings until 1999.

Policy implications and possible way forward

Over the years, we found increasing applications for the WHO EML, suggesting widespread interest and alignment with the importance of rationalising resources towards high-benefit medicines. However, we also found certain therapeutic areas are better represented than others, raising questions about the strategic direction and selection processes of the WHO EML in the rapidly changing pharmaceutical ecosystem. We provide policy implications contextualised within the historical evolution of the WHO EML.

<u>For whom is the WHO EML intended?</u>

One central question emerges when evaluating whether applicants' geographic distribution translates to the WHO EML's intended purpose: For whom are the Model Lists intended? This question is critical to interpreting our results and managing future challenges. The answer is not straightforward.

In 1977, the WHO EML focused on selecting affordable medicines for developing countries. The original geographic application to LMICs was intentional. The pharmaceutical industry initially protested the concept of essential medicines due to concerns about the impact of a restrictive list of medicines in HICs.[15,16] WHO engaged with industry early and contained the EML's remit to developing nations.[15] Indeed, the consistent representation of IFPMA as observers at Expert Committee meetings may be explained by this early industry oversight over the programme's activities[15,16] (representation ceased abruptly after 1999 due to the revised procedures introduced in 2001, which states that the decision-making portion of the Expert Committee meetings is closed

to the public).[10] Combined with original decision criteria that emphasised costs as a major selection criterion, these original constraints resulted in a list of mostly generic medicines. — a stance heavily criticised for excluding LMICs from medical innovation (i.e. "old drugs for poor countries, new drugs for rich countries.")[9,15,17]

The 2001 Revised Procedures stipulated that price nor patent status cannot be reasons for exclusion from the WHO EML, which facilitated the addition of 12 widely patented antiretrovirals (ARVs). At the time, ARVs (among other medicines for cancer, e.g. imatinib) were prohibitively expensive, which made reimbursement under public insurance plans difficult, even in HICs. The addition of patented ARVs widened the relevance of the WHO EML to high-priced, branded medicines and, by extension, wealthy countries.[15] The discourse about the geographic applicability of essential medicines evolved from being only relevant in resource-constrained settings to a tool for health systems worldwide.[18] The global applicability of the WHO EML was solidified again in 2015 when several high-priced, widely patented medicines were added, including a large update for cancer medicines.[19] This EML update was significant, marking the first major addition of high-priced, branded medicines. The WHO Secretariat reinforced the EML as "a global standard"[20], "equally relevant for high-, middle-, and low-income countries".[21] These views were shared by global health experts, who explained, "For many years, the WHO Model Lists have been viewed by some as applicable only to resource-constrained settings and was assumed to include only the most basic medicines. This is a profound misunderstanding […] The idea of selecting a limited list of essential medicines applies in all countries and a variety of settings."[22] This global perspective may explain a rising number of applications for medicines widely used in HICs, such as immunotherapies for front-line cancer treatment[19] and complex technologies, such as CAR-T.[23] While innovative medicines are equally important in LMICs, their absence from the WHO EML may not be seen as problematic compared to wealthy countries, which would challenge the EML on its

comprehensiveness given these medicines' absence.[24] If the WHO EML is a global list, then a large proportion of applications from HICs may be fine. However, to our knowledge, WHO has not explicitly indicated who the decisions are for and whether this original vision has changed.

Over the years, the geographic relevance of the WHO EML has blurred. Currently, there is limited consensus on whether the list is for HICs, LMICs, or both.[25] On the one hand, the WHO EML has been suggested for high-income countries, including its potential relevance to the US.[26] On the other hand, others have recently argued that while the concept of essential medicines is global, the direct applicability of the list is reserved for LMICs.[27] This distinction between the concept and the applicability of the list is important and rarely made, which adds to the confusion. Historical debates about including certain medicines are, in some ways, a symptom of this confusion. For example, cancer medicines have recently challenged the WHO EML decision-making.[19] Between 2015 and 2019, high-priced medicines were added to the WHO EML (e.g., nivolumab and pembrolizumab for melanoma). However, few cancer medicines for adult indications have been added since due to concerns about access and affordability, diversion of resources, opportunity costs, and diagnostic availability in LMICs.[19] These rejections may signal that the main audience of the WHO EML may be LMICs. However, there remains limited consensus on whether these medicines should be included.[27–29]

The definition of an essential medicine may offer some insights. WHO stipulates that essential medicines "satisfy the priority needs of the population" and are selected "with due regard to their public health relevance, evidence of efficacy and safety, and comparative cost-effectiveness."[10] However, the meaning of "priority needs "and "public health relevance" are unclear. In 2013, the WHO Expert Committee clarified that "public health relevance" could mean incidence, prevalence, burden of disease, region-specific needs, curative impact, and the potential political impact when

identifying a medicine as essential, highlighting a case-by-case approach.[30] However, considering all these metrics globally leaves substantial room for interpretation by applicants and adds uncertainties for the Expert Committee. Diseases with low worldwide incidence and prevalence may be particularly burdensome in certain regions, such as sickle cell disease.[31] Indeed, applying the public health relevance criterion has been especially difficult for WHO with medicines for rare diseases.[27,32–35] Originally, WHO was reluctant to add these medicines, emphasising the list's utilitarian function, "in orphan diseases, which do not constitute a global public health priority, there is no justification for the WHO to list the treatment as essential."[34] This view was repeated recently by authors close to WHO EML processes, stating, "Medicines that do not yet represent a very high public health value should not be listed as essential."[27] However, since 2001, the number of medicines for rare diseases on the WHO EML has tripled,[36] suggesting inconsistencies with this original stance. Similarly, we found increasing applications for cancer medicines since 2009, with medicines for non-Hodgkin lymphoma and chronic lymphoid leukaemia among the most recommended. In contrast, several effective medicines for lung cancer were not recommended due to their potential financial impact despite the higher burden worldwide[37], while the same medicines were recommended for melanoma. Cyclin-dependant kinase 4/6 inhibitors were not added for hormone receptor-positive or negative advanced breast cancer primarily due to costs (and uncertainties with dosing and treatment duration) despite meaningful overall survival benefits and increased treatment feasibilities (e.g., oral route, lack of required biomarker). These inconsistencies suggest that the definition of "priority needs" and "public health relevance" may not be entirely clear, or other secondary criteria may be used to weigh the decisions that are not publicly transparent.

Single-medicine or a disease-based approach?

While the pharmaceutical industry is key to developing new drugs that provide medical benefits for patients, within the context of the WHO EML and its diffusion to countries, primarily, the applicants (mostly other individuals than the pharmaceutical industry) drive pharmaceutical priorities.

Since its inception, the WHO EML has based its application process on a single-medicine approach. This contrasts with a disease-based process that comprehensively reviews a class of medicines for a therapeutic area, selecting the most efficacious and cost-effective options. On average, we found applications included between one and six medicines. While there are a few notable instances where a disease-based approach has been taken, such as the 2015 and 2017 updates for cancer medicines and antibiotics[38,39] and the 2023 application for multiple sclerosis[40], a systematic disease-focused approach has generally not been the case. Given limited resources to conduct systematic assessments for missing medicines or underrepresented therapeutic areas, the current single-medicine approach makes the WHO EML somewhat reactive to applicant priorities.

A counterargument may be that several applicants were from international organisations. These organisations often have global mandates and frontline experience within LMICs, which may translate into an inherent understanding of which medicines and disease areas should be prioritised in applications. Indeed, we found more than half of the applicants were from Switzerland. This finding is explained by the significant presence of several global health organisations within the country, including UN bodies, prominent NGOs, and professional organisations (e.g. ESMO). While applications from global organisations are justified, given limited resources in LMICs, it is not sufficient to conclude that there are no underrepresented areas on the WHO EML. Certain issues in global health generate more political priority than others, and with them, organisations that represent their causes.[41,42] For the WHO EML, an application may not be submitted for a highly effective medicine if no WHO technical departments or other groups

represent the disease (e.g., gastrointestinal diseases or sickle cell disease).[43] Taken together, it is difficult to conclude whether the skew towards HIC applicants translates into the mission of the WHO EML without an understanding of whom decisions are for and how well these medicines respond to priority needs.

How could the WHO EML move towards a structured and strategic approach?

In 2023, the WHO Expert Committee recommended revising the WHO EML selection procedures.[6,7] We offer two strategies that might complement this process: 1) identify a strategic vision for the WHO EML, and 2) implement a structured process for selection.

A strategic vision, including a clear statement on the purpose and geographic applicability of the WHO EML, could focus applications and support the Expert Committee in complex decisions. WHO must continually reassess the relevance and purpose of the EML in adapting to the rapidly evolving pharmaceutical market. Over the past decade, we found cancer medicines comprise the single largest therapeutic category of applications. Given current market trends, challenges regarding immature data at approval, high prices, marginal survival benefits, and medicines for rare diseases will only intensify.[19,44] Before implementing structured procedures and clarifying decision criteria, we urge WHO to reflect broadly on the EML's role in global priority setting. To determine a strategic vision, the WHO should engage with clinicians and policymakers within countries to understand how the list is used. Additional research is needed to understand the impact of the WHO EML, especially on the utilisation and prices of essential medicines. Stakeholder engagement would allow WHO to identify regions where the list is most impactful, identify a target audience, and directly shape therapeutics prioritised in applications. We urge Member states and WHO leadership to support the Secretariat in undertaking these reforms as strengthening the capacities of institutions

responsible for essential medicines policies, including the WHO EML, is central to pursuing Universal Health Coverage.[2,45]

While a rising number of applications denotes interest and alignment with the goals of the WHO EML, it also complicates decision-making, given there is no systematic approach to prioritise the importance of one medicine (or disease) over another. Indeed, WHO recently acknowledged concerns about this "ad-hoc, volunteer basis application process", stating, "This passive approach exposes selection to potential risks, such as having an up-to-date and comprehensive list in disease areas that attract attention from stakeholders and an incomplete and outdated list in areas that, although important, lack the support or incentive of stakeholders to develop applications."[6] While the WHO Expert Committee has considerable influence on which medicines are adopted and the increasing proportion of LMIC membership would have a positive impact, their power is limited as, to our knowledge, members can only evaluate a submitted application. While further research is needed, our finding that therapeutic categories of medicines recommended by the Expert Committee mirrored the same distribution of the medicines submitted by the applicants indicates an alignment with applicant priorities.

A structured prioritisation process, including moving to a disease-focused approach (rather than the current single-medicine strategy), may aid the selection of essential medicines and increase transparency. This is especially important given the rise of available medicines and increasing evidential uncertainties that often underpin applications, such as immature data or a lack of comparative pricing information.[46] A degree of subjectivity will always remain in decision-making, especially in the absence of relevant data. Indeed, this subjectivity can be seen as an added value and the responsibility of the WHO Expert Committee. Our finding that the WHO includes various geographic representations on the Expert Committee is encouraging and underscores the diverse

experiences within these deliberations. However, too much uncertainty can contribute to inconsistent decision-making — concerns which have been raised about the WHO EML in recent years.[27,29,47–49] Building on a clearer understanding of how countries use the list and its impact, we urge WHO to implement a structured process for prioritising disease areas and medicines recommended to the EML. Furthermore, WHO might improve the connection between the EML and technical guidelines in disease areas where these exist. Currently, there are no WHO guidelines for cancer treatment. Given that cancer medicines comprise the largest category of applications and the increasing burden in LMICs, WHO could develop guidelines to support treatment in resource-constrained settings, which is crucial to improving cancer outcomes worldwide.

Once a strategic vision and a target audience are defined, decision criteria should be clarified, especially public health relevance and cost-effectiveness. This will help to guide the wide epidemiological considerations that leave substantial room for interpretation. Furthermore, "costs" are not considered for inclusion; rather, cost-effectiveness is reserved for within-class comparisons, which has proven difficult for the Expert Committee, as evidenced by inconsistencies in applying economic criteria across recommendations.[50] One suggestion may be to adapt to the prioritisation methods used in the 2015 cancer update for decision-making across therapeutic areas.[19] Cancer medicines were prioritised based on treatment goals (curative being the highest priority) and disease incidence (high incidence being the highest priority). A disease with high incidence with medicines that have curative impact was a top priority (e.g., early-stage breast cancer) over a disease area with low incidence with medicines that offer marginal benefits (e.g., metastatic pancreatic cancer). This method allows the concept of essential medicines to remain centred on clinical benefit and does not neglect rare diseases so long as there are medicines with meaningful or curative impact (e.g., leukaemia and lymphomas). The challenge will be where to draw the line as essential. However, excluding medicines for rare diseases without considering the impact of their

medicines is ethically unjust. Building on the strategic vision and refined target audience, developing ethical considerations within a prioritisation matrix that considers incidence (or prevalence) and treatment goals together may alleviate current tensions, including for rare diseases.

Limitations

First, we relied on publicly available information in the Technical Report Series documents. These documents may not reflect all the nuanced discussions. Second, we recorded the Expert Committee members' broad membership, as indicated in the Technical Report Series document. These individuals likely have diverse experience, including other roles outside primary expertise. Lastly, we did not include comments from external groups such as the public or the WHO Technical Departments. While their feedback is considered in the decision, they are not present in the decision-making portion of the meeting and, therefore, were excluded.

Conclusion

The WHO EML is an influential tool in global priority-setting processes to improve access to essential medicines and achieve universal health coverage. The program has recently announced a process to update the procedures for selecting essential medicines. This announcement provided an opportunity to reflect on the evolution of the WHO EML, including its history and stakeholders that have shaped which medicines are included.

We found that within the context of the WHO EML, the applicants are primarily shaping the priorities for medicines. Most applications were from HICs, universities and research centres, followed by NGOs, UN organisations, professional associations, and the pharmaceutical industry. Observers were from the pharmaceutical industry (before the Revised Procedures) and UN

organisations**.** Since 2009, increasing applications and recommendations have focused on cancer, raising questions about whether this aligns with the WHO EML strategy. Over half of the Expert Committee members were from LMICs, with an increasing proportion in recent EML updates, underscoring the diverse experience within these deliberations.

The current "ad-hoc, volunteer basis application process" may accentuate underrepresented areas on the WHO EML. Defining a strategic vision for the WHO EML, including articulating a target audience and structured prioritisation process, would strengthen decision-making processes by providing additional clarity, including to those implementing the guidance, mainly in LMICs. Our assessment of the evolution of the WHO EML, including an empirical examination of the applicants, decision-makers and observers within the WHO EML processes, could be used to begin this process.

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Figure 1. Major events for applications and WHO procedures from 1977 to 2023
Abbreviations: ARVs: antiretrovirals; hep C: hepatitis C; LMICs: low and middle income countries; TB: tuberculosis; UICC: Union for International Cancer Control; WHO EML: World Health Organization Model Lists of Essential Medicines

Figure 2. Overview of the process of updating the WHO EML and associated stakeholders.

Figure 3. Number of applications for medicines to the WHO EML per country (2003-2023).
Notes: [a]Upper middle income countries were classified as LMICs

Figure 4. Applicants to WHO Essential Medicines List over time (2003-2023).

Figure 5. The geographic distribution of Expert Committee members between 1977 and 2023[a]
Notes: [a]includes Technical Advisors
Abbreviations: HIC: high income country; LMIC: low- and middle-income country; upper middle income country

Figure 6. Representation of organizations present as observers during Expert Committee meetings (1977-2023).

Panel 1. Definition of an essential medicine and decision criteria for the selection of essential medicines

Year	Definition	Decision criteria
1977[51]	Drugs are of the utmost importance and are basic, indispensable and necessary for the health needs of the population.	• Efficacy • Safety • Quality • Total cost
2002[10]	Essential medicines are those that satisfy the priority healthcare needs of the population. They are selected with due regard to public health relevance, evidence on efficacy and safety, and comparative cost-effectiveness. Essential medicines are intended to be available within the context of functioning health systems at all times in adequate amounts, in the appropriate dosage forms, with assured quality and adequate information, and at a price, the individual and the community can afford. The implementation of the concept of essential medicines is intended to be flexible and adaptable to many different situations; exactly which medicines are regarded as essential remains a national responsibility.	• Clinical benefit • Harms and toxicity • Public health relevance • Comparative cost-effectiveness • Regulatory status and market availability of the medicine

Panel 2. Methods

We extracted information on the applicants who proposed medicines to the WHO EML from the WHO Technical Report Series.[52] Due to the public availability of the data on the applicants, we included the period 2003-2023.

When an applicant proposed more than one medicine in one application, the application for each medicine was evaluated individually. Each indication was assessed individually if a medicine was proposed for multiple indications. This approach was used as the EML assesses each medicine based on its indication.

Aligned with previous research,[53] we classified the applicants into five categories: universities and research centres, NGOs, organisations under the UN system, professional associations, and the pharmaceutical industry. We extracted the applicant institute, country, and WHO region from the WHO Technical Report Series. Country income classification was conducted per the World Bank classification at the time of analysis (high, middle, and low-income countries). In cases of multiple applicants from diverse countries, the geographic location and institute of the lead applicant were extracted.

We further extracted information on the Expert Committee members' and observers' demographics and professional backgrounds from the WHO Technical Report Series (year of the meeting, name, institution, country, and professional affiliation). Without explicit disciplinary details, we searched for additional individual information through public search engines, associated institutions, and publications. We considered temporary advisors as Expert Committee members as they fulfil the same role. We further extracted the income classification from the World Bank (April 2023). The

data on Expert Committee members (and technical advisors) was publicly available since the inception of the EML (1977); therefore, this period was included in our analysis.

Descriptive statistics were used to examine characteristics of applicants that proposed medicines to the WHO EML, Expert Committee members, and observers present during decision-making using Excel Version 16·72 (Microsoft) and R Version 4.3.1 (R Foundation for Statistical Computing).

Table. Characteristics of essential medicines receiving positive and negative recommendations (2003-2023).

Characteristic	Type of recommendation			
	Positive n=483 (%)	Removed n=45 (%)	Negative n=172 (%)	Total n=700 (%)
Applicant				
Universities and research	146 (30·2)	17 (37·8)	47 (27·3)	210 (30·0)
NGO	138 (28·6)	1 (2·32)	20 (11·6)	159 (22·7)
UN system	106 (21·9)	19 (42·2)	33 (19·2)	158 (22·6)
Professional association	57 (11·8)	6 (13·3)	35 (20·4)	98 (14·0)
Pharmaceutical industry	36 (7·5)	2 (4·4)	37 (21·5)	75 (10·7)
WHO Region				
European	350 (72·5)	31 (68·9)	105 (61·0)	486 (68·9)
Americas	107 (22·2)	5 (11·1)	41 (23·8)	153 (21·7)
Western Pacific	21 (4·3)	9 (20·0)	22 (12·8)	52 (7·4)
South-East Asia	3 (0·6)	0 (0·0)	3 (1·7)	6 (0·9)
African	1 (0·2)	0 (0·0)	1 (0·6)	2 (0·3)
Eastern Mediterranean	1 (0·2)	0 (0·0)	0 (0·0)	1 (0·1)
World Bank income class				
HIC	478 (99·0)	45 (100·0)	164 (95·3)	687 (98·1)
LMIC	5 (1·0)	0 (0·0)	8 (4·7)	13 (1·9)
Top 3 therapeutic areas per applicant[b]				
Universities and research centres				
	37 (7·7)	4 (8·9)	11 (6·4)	52 (7·4)
Cancer disorders	22 (4·6)	1 (2·2)	3 (1·7)	26 (3·7)
Cardiovascular diseases	11 (2·3)	0 (0·0)	7 (4·1)	18 (2·6)
Mental disorders				
NGO				
Cancer disorders	87 (18·0)	0 (0·0)	5 (2·9)	92 (13·1)
Other infectious diseases[a]	9 (1·9)	0 (0·0)	2 (1·2)	11 (1·6)
Maternal and neonatal disorders	5 (1·0)	0 (0·0)	1 (0·6)	6 (0·9)
Professional association				
Cancer disorders	23 (4·8)	0 (0·0)	17 (9·9)	40 (5·7)
Mental disorders	13 (2·7)	2 (4·4)	6 (3·5)	21 (3·0)
Neurological disorders	3 (0·6)	0 (0·0)	7 (4·1)	10 (1·4)
UN system				
Tuberculosis	18 (3·7)	3 (6·7)	4 (2·3)	25 (3·6)
Other infectious diseases[a]	19 (3·9)	1 (2·2)	4 (2·3)	24 (3·4)
HIV/AIDS	11 (2·3)	2 (4·4)	5 (5·2)	18 (2·6)
Pharmaceutical industry				
HIV/AIDS	4 (0·8)	1 (2·2)	9 (5·2)	14 (2·0)
Neglected tropical diseases and malaria	8 (1·7)	0 (0·0)	2 (1·2)	10 (1·4)
Cancer disorders	0 (0·0)	0 (0·0)	9 (5·2)	9 (1·3)

[a] Other infectious diseases include an assortment of antibiotics to treat a variety of conditions
[b] Top 3 therapeutic areas as a proportion of total positive, negative, or removed recommendations