Agenda item for the 18th Expert Committee on the Selection and Use of Essential Medicines

18th Expert Committee on the Selection and Use of Essential Medicines

Draft for consultation

How to develop a National Essential Medicines List

First steps:

- Ministry of Health (MoH) to specify purpose of the National Essential Medicines List (NEML).
- MoH to decide if procurement and distribution of medicines in the public sector will be limited to the list.
- If procurement and distribution are to be limited to NEML, MoH to put in place appropriate legislation/regulation.
- Grounds for exceptions and methods for their control (either administrative or budgetary) to be clearly stated and the authority in charge of regulation to be specified.
- MOH to appoint a committee to identify medicines for inclusion in the national EML. Medicine selection by committee is the preferred approach. It minimizes the opportunity for private interests to influence the decision-making process.

How to choose members for the Expert Committee for the Selection of Essential Medicines:

Committee members should have relevant backgrounds and previous experience in the procurement, supply and/or use of medicines. They should be honest and dedicated and have integrity. They should not have relationships with any drug manufacturer or distributor, nor be closely related to any person who does. Potential conflicts of interest should be investigated and a system to manage them agreed by the Ministry if Health (see Annex 1).

It is recommended that Committee members serve for several years with staggered terms, so that the committee retains some experienced members each year. It is highly recommended that EML committees have both professional and gender balance.
Suggested representatives to include on the Selection Committee:

- Ministry of Health representatives including personnel from the medicines purchasing/procurement department.
- Professional organizations, such as the national medical and pharmaceutical association.
- Regional and local health facilities (including medical and paramedical prescribers).
- ≥ 1 clinical pharmacologists/clinical pharmacists.
- Internist.
- Infectious disease specialist.
- Paediatrician.
- Anaesthetist.
- Obstetrician.
- ≥ 1 hospital and district pharmacist.
- Hospital director.
- Other specialists as needed.
- Representatives of disease control programmes (e.g. malaria, tuberculosis and AIDS programmes can be co-opted to attend certain meetings.

Responsibilities of the Committee

1) The committee should start by defining a list of common diseases for each level of health care.

- Identify the first-choice treatment for each health problem (this may be limited to one or more medicines or to various forms of non-medicinal treatment).
- This information should be available from the National Standard Treatment Guidelines. It is important to make sure that the STGs are up-to-date and in line with evidence-based international guidelines/WHO guidelines.
- The list of first-choice treatments for the priority health problems will form the basis of the NLEM.

2) If there are no national STGs or the STGs have not been revised recently the 16th WHO Model List of Essential Medicines can be reviewed to inform the new NLEM.

http://www.who.int/selection_medicines/committees/expert/17/WEB_unedited_16th_LIST.pdf
3) **WHO criteria for the selection of Essential Medicines should be applied during the selection process:**

- Essential Medicines are those that satisfy the health care needs of the majority of the population: they should be available at all times in adequate amounts and in the appropriate dosage forms.

- The choice of medicine depends on several factors, such as the pattern of prevalent diseases; the need for special diagnostic or treatment facilities; the training and experience of the available personnel; the financial resources and genetic, demographic, and environmental factors.

- Only medicines for which sound and adequate data on efficacy and safety are available from clinical studies, and for which evidence of performance in general use in a variety of medical settings has been obtained should be selected.

- Each selected drug must be available in a form in which adequate quality, including bioavailability, can be ensured; its stability under the anticipated conditions of storage and use must be established.

- When two or more medicines appear similar in the above respects, the choice between them should be made on the basis of a careful evaluation of their relative efficacy, safety, quality, price, and availability and feasibility of use in a variety of settings, such as the need for special professional skills and/or diagnostic or treatment facilities.

- In cost comparisons between medicines, the cost of the total treatment, not only the unit cost of the medicine must be considered. Cost and cost-effectiveness comparisons may be made among alternative treatments within the same therapeutic group, but not across therapeutic categories (e.g. between treatment of tuberculosis and treatment of malaria). In some cases the choice may also be influenced by other factors, such as the pharmacokinetic properties, or by local considerations such as the availability of facilities for manufacture or storage.

- Most essential medicines should be formulated as single compounds. However, fixed-ratio combination products can be considered for selection in certain circumstances, such as when there is a high pill burden associated with the treatment regimen which can adversely affect compliance. Fixed-ratio combination products should be selected when the combination has proven advantage in therapeutic effect, safety or compliance over single compounds administered separately. Examples of combination medicines that have met these criteria include new formulations for tuberculosis, malaria and HIV/AIDS.
4) The Selection Committee can also critically review the national list of registered medicines to select a much shorter national list of essential drugs.

- Based on this list, drugs and therapeutics committees in individual health facilities can choose a treatment of first choice for that facility or district. When selecting essential medicines for use at a particular level of care within the national health system the need for special professional skills and/or diagnostic or treatment facilities should be taken into consideration.

How to raise awareness of the completed EML:

- Have a launching campaign to give the list national prominence and credibility.
- Involve the highest possible government officials, such as the minister of health or president.
- Intensive media coverage.
- National conference to emphasize topics such as the advantages of the list, the national consensus in defining the health needs of the population and the cost effective use of limited resources.

How to improve acceptance and uptake of the EML:

- In the development stage involve a wide group of national experts and politicians.
- Drug policy framework needs to be in place and the list needs a purpose.
- Selection process needs to be transparent and there needs to be a procedure for suggestions and additions or deletions.
- Selection of medicines needs to be realistic (do not add sophisticated medicines for lower health care levels when resources are scarce).

Developing a system for reviewing amendments to a National Essential Medicines List

After publication of the first national list, the Committee for Selection of Medicines should meet at least every two years to update it. A form for proposing revisions to the National Essential Medicines List should be developed and widely disseminated to prescribers along with the current STG/EML. A process for reviewing these forms at the national level should be put in place.

Proposals for an amendment to the National Essential Medicines List should only be considered if:

- The prescribed form has been fully completed.
- The applicants contact details are provided.
- The drug name has been stated.
- The indication has been clearly stated.
- All relevant comparator drug(s) have been listed.
- There is sufficient evidence to support the proposed amendment.
Proposals can be separated into different categories depending on whether they address a major or minor amendment to the National Essential Medicines List:

### Major amendments can be considered as:
- New indications
- New therapeutic entities
- New therapeutic classes
- Deletion of a medicine from the NEML

All major amendments must be supported by evidence reflecting safety, efficacy and cost of medicine compared to an already listed medicine for the same indication.

A major amendment may also include proposals for medicines not currently listed and/or for conditions not addressed in the EML. In such cases submissions must be supported by demographic data.

### Minor amendments can be considered as:
- New formulations
- Combination therapies of existing essential medicines

For minor amendments the supporting evidence should be relevant to the nature of the amendment.
Suggested information to include on the revision form is:

Section 1: Proposal

a) The name of the proposed medicine should be the International Non-proprietary Name (INN) of the medicine - this identifies a pharmaceutical substance or active pharmaceutical ingredient by a unique name that is globally recognized and is public property. A non-proprietary name is also known as a generic name.

b) Level of Care - to indicate whether the proposed medicine should be listed for use at primary care or hospital level (adapt as appropriate for your country’s health system).

c) Prescriber level - to indicate level of competency required to prescribe the drug.

Section 2: Applicant’s details

The review committee should acknowledge all submissions and communicate decisions with supporting arguments where appropriate. This section therefore forms a vital link between the applicant and the decision making process.

Section 3: Proposed indications

a) Indication points to consider:

• The NEML should target those conditions that are the most prevalent in the country. Where an applicant suggests an indication not currently reflected in the NEML, a brief rationale based upon the country’s epidemiological data must be included as an appendix.

• Stating the indication allows for the identification of the appropriate comparator in the current NEML.

• Many medicines have multiple indications. However, not all are equally cost effective.

b) Proposed regimen

These data can be used for cost comparison and is very important for pharmacoeconomic evaluation.

c) Cost assessment

This information is necessary for the determination of affordability.

d) Evidence

Evidence is a vital component of the submission and review process. Evidence does not constitute a medicine decision; it merely informs the strength of the argument. It forms the basis upon which the decision is made and allows for transparent scrutiny of the decision as well as facilitating the review.
Evidence is required in support of:

- relative efficacy
- relative safety
- pharmacoeconomic benefits

Evidence needs to be relevant to the country context. Multinational or foreign studies must be supported by a description of the relevance of both the outcome measures as well as socio-economic facets to the country in question.

Potential sources of information for a submission to the Review Committee:

- Literature review by applicant - submit with copies of original articles.
- Published systematic review - submit with copies of the original articles.
- Single article - if Randomized Controlled Trial submit copy of original article.
- Information from opinion leader - if references supplied, include with submission.
- Industry recommendation - if references supplied, include with submission.

**Section 4: Drugs on the current NEML for the same indication**

As a principle, the addition of an EML item should replace an existing item. This is of particular importance when safety and economic implications are taken into account.

**Section 5: For use at national level only**

This section is intended to ensure that the submissions have followed the proper process.
Example Application Form for the Inclusion of a Medicine on a National Essential Medicines List

### Section 1

**Name of Proposed Medicine:** [Blank]

**For inclusion on the Essential Medicines List for:** [Blank]

**Prescriber Level:** [Blank]

**Submission Date:** [Blank]

### Section 2

**Applicant's Details**

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### Section 3

**Proposed Indication**

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<th>Proposed Regimen</th>
<th>Cost Assessment</th>
<th>Level of Evidence</th>
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<tbody>
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<td></td>
<td>Dose Route Interval Duration Cost/Unit Cost per day Cost per course/month</td>
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#### Level of Evidence

1. Meta-analysis
2. Randomized controlled trial
3. Controlled study without randomization
4. Comparative, correlation or case control
5. Expert Committee
6. Clinical experience

### Section 4

**Medicines on the Current EML for the same indication**

| Medicine | Indication as per list above | Dose Route Interval Duration Cost/Unit Cost per day Cost per course/month Can be replaced by proposed medicine |
|----------|-----------------------------|--------------------------|--------------------------------------------------|
|          |                             |                          |                                                  |

### Section 5

**Correspondence**

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<th>Evidence</th>
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**For National Evaluation**

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<th>Rejected</th>
<th>Further evidence</th>
<th>Proposal</th>
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Role of the EML Committee in reviewing proposals for amendments to the NEML

All proposals for amendments to the National/State/Provincial Essential Medicine List should be screened by the team responsible for the co-ordination of the EML Committee prior to being considered by the Committee.

The proposals should be screened to ensure:

- Applicants contact details have been included.
- Drug can be identified in terms of the INN.
- Indication has been included.
- Relevant comparator medicines have been identified with corresponding dosing regimens.
- Supporting evidence to substantiate the request has been included.

Accepted submissions should be allocated to a suitably qualified member of the EML Committee for review. The reviewer should compile a technical report which summarizes the data submitted in the proposal in terms of:

- Relative efficacy.
- Relative safety.
- Practice environment - the focus being efficacy relative to current EML medicines.
- Pharmacoeconomic evaluation.

The report should be presented by the reviewer to the EML Committee at the next planned meeting to revise the EML.

The EML Committee may request further information from the proposer or commission a literature search and formal review. Final decision to accept or reject the proposal rests with the EML Committee. The outcome of the discussion should be communicated back to the proposer.

Adding medicines for children to EMLs

Key points:

- Widespread support of child health opinion leaders, relevant government bodies, and professional organizations working in child health is vital to the process of adding medicines for children to the national EML.
- It is essential that the process for selecting the medicines for children is consultative and transparent, the selection criteria are explicit, and the selection of the medicines for children is linked to evidence-based standard clinical guidelines.
- National authorities can use the medicines for children listed on the revised EML to guide resource allocation, import duties, medicines benefits within reimbursement schemes, donations, manufacturing subsidies, and mark-ups for the private sector.
Checklist of activities to ensure that medicines for children are included on national essential medicines lists:

1. **Contact the essential medicines committee and enquire about the list revision process**
   - Identify the national essential medicines committee and contact persons who can provide information on the list revision process.
   - Obtain the national list of essential medicines and standard treatment guidelines (STGs).
   - Determine the application process and requirements for the addition of new medicines to the national essential medicines list (EML).
   - Verify timing of the next EML revision.

2. **Identify child health experts who will provide input into the national EML process**
   - Contact child health stakeholders and develop a child health working group (CHWG) to add medicines for children to the EML.
   - Inform the EML committee about the child health review by the CHWG. Propose to nominate members of the EML committee to integrate into the CHWG and participate in the review.
   - Prepare a plan of action for the review process with the CHWG, including meeting planning and collection of information. Be cognizant of the deadline for submitting proposals to the EML committee before the next revision.

3. **Identify which medicines need to be added to the EML**
   - Explain the EML review process to the CHWG.
   - Review the national EML to identify currently included medicines for children and compare with the WHO Model List of Essential Medicines for Children 2009.
   - Define the gaps/discrepancies according to STGs, local data, and context, and define a list of medicines for children to be added to the national EML. Indicate levels of care recommended for each of the medicines submitted.
   - Collect and organize data, evidence, and information requested for each new submission to the EML committee.
   - Use the revision form proposed by the EML committee to submit your changes, additions, or deletions. Include all information requested for the review.
   - Submit proposals for revision to the EML committee by the deadline set up by the committee.
4. **Implement the new EML**

**By the Ministry of Health (MOH)**

- Launch the updated EML or new separate EMLc and make it widely available.
- Make the revised list of essential medicines and clinical guidelines available in all health care facilities and to all health care providers in printed and electronic versions, if appropriate.
- Verify with procurement services in both public and private sectors and with regulatory authorities that medicines added to the EML are available in the country.

**By the Medicines for Children Working Group**

- Propose issuing an informational leaflet, newsletter, or drug bulletin that summarizes the changes in the area of child health in collaboration with the EML committee and the MOH.
- Inform the general public by publishing articles in newspapers (press releases).
- Advocate for the review of the STGs (if needed) according to the updated national EML.
- If essential medicines are exempt from taxes in the country, verify that the new medicines added are also tax exempt. If not, advocate for tax exemption for all medicines and commodities on the EML.
- Assess and monitor availability and use of the essential medicines for children at all levels of care in the country in collaboration with the MOH and the EML committee.
Annex 1

Managing conflicts of interest in potential committee members

What is a conflict of interest?

Conflict of interest means that the expert or his/her partner ("partner" includes a spouse or other person with whom s/he has a similar close personal relationship), or the administrative unit with which the expert has an employment relationship, has a financial or other interest that could unduly influence the expert’s position with respect to the subject-matter being considered. An apparent conflict of interest exists when an interest would not necessarily influence the expert but could result in the expert’s objectivity being questioned by others. A potential conflict of interest exists with an interest which any reasonable person could be uncertain whether or not should be reported.

Different types of financial or other interests, whether personal or with the administrative unit with which the expert has an employment relationship, can be envisaged and the following list, which is not exhaustive, is provided for your guidance. For example, the following types of situations should be declared:

1. a current proprietary interest in a substance, technology or process (e.g. ownership of a patent), to be considered in - or otherwise related to the subject-matter of - the meeting or work;

2. a current financial interest, e.g. shares or bonds, in a commercial entity with an interest in the subject-matter of the meeting or work (except share holdings through general mutual funds or similar arrangements where the expert has no control over the selection of shares);

3. an employment, consultancy, directorship, or other position during the past 4 years, whether or not paid, in any commercial entity which has an interest in the subject-matter of the meeting/work, or an ongoing negotiation concerning prospective employment or other association with such commercial entity;

4. performance of any paid work or research during the past 4 years commissioned by a commercial entity with interests in the subject-matter of the meetings or work;

5. payment or other support covering a period within the past 4 years, or an expectation of support for the future, from a commercial entity with an interest in the subject-matter of the meetings or work, even if it does not convey any benefit to the expert personally but which benefits his/her position or administrative unit, e.g. a grant or fellowship or other payment, e.g. for the purpose of financing a post or consultancy.
With respect to the above, an interest in a competing substance, technology or process, or an interest in or association with, work for or support by a commercial entity having a direct competitive interest must similarly be disclosed.

The best way to obtain complete and accurate disclosures on financial ties and other competing interests is to develop a specific, detailed and structured "declaration of interest" form that will allow the organization to obtain as much information as possible about the nature and extent of the competing interests. It is recommended that explicit criteria be developed to determine when a disclosed financial tie or other competing interest constitutes a conflict of interest.

When a conflict of interest is identified in a potential selection committee member, possible management strategies include: public disclosure of the financial tie(s) to the essential medicines selection committee as a minimum and in certain instances disqualification of conflicted individuals from participation in the decision making process. For example, when the Selection Committee is discussing the addition of a medicine to the National Essential Medicines List which is manufactured by a company in which a committee member or a member of their immediate family has a financial interest and may personally gain from its inclusion in the National Essential Medicines List, the committee member in question should excuse themselves from the decision making process.

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Example of a Declaration of Interest Form

DECLARATION OF INTERESTS FOR WHO EXPERTS

Title of meeting or work to be performed, including description of subject-matter, substance (compounds and organisms), technology or process to be considered:

Public health considerations have a primary importance in all WHO technical work. Measures need to be taken to ensure that the best possible assessment of scientific evidence is achieved in an independent atmosphere free of either direct or indirect pressures. Thus, to assure the technical integrity and impartiality of WHO’s work, it is necessary to avoid situations in which financial or other interests might affect the outcome of that work.

Each expert is therefore asked to declare any interests that could constitute a real, potential or apparent conflict of interest, with respect to his/her involvement in the meeting or work, between (1) commercial entities and the participant personally, and (2) commercial entities and the administrative unit with which the participant has an employment relationship. “Commercial entity” refers to any company, association (e.g., trade association), organization or any other entity of any nature whatsoever, with commercial interests.

In addition, as a result of WHO’s strong stance against tobacco use, it is considered relevant for the Organization to know whether experts working with it have, or have had, any relationship with any part of what may be called “the tobacco industry”. Nevertheless, declaration of such an interest would not necessarily be considered a reason to disqualify an expert.

What is a conflict of interest?
Conflict of interest means that the expert or his/her partner (“partner” includes a spouse or other person with whom s/he has a similar close personal relationship), or the administrative unit with which the expert has an employment relationship, has a financial or other interest that could unduly influence the expert’s position with respect to the subject-matter being considered. An apparent conflict of interest exists when an interest would not necessarily influence the expert but could result in the expert’s objectivity being questioned by others. A potential conflict of interest exists with an interest which any reasonable person could be uncertain whether or not should be reported.

Different types of financial or other interests, whether personal or with the administrative unit with which the expert has an employment relationship, can be envisaged and the following list, which is not exhaustive, is provided for your guidance. For example, the following types of situations should be declared:

1. a current proprietary interest in a substance, technology or process (e.g. ownership of a patent), to be considered in - or otherwise related to the subject-matter of - the meeting or work;
2. a current financial interest, e.g. shares or bonds, in a commercial entity with an interest in
the subject-matter of the meeting or work (except share holdings through general mutual
funds or similar arrangements where the expert has no control over the selection of
shares);

3. an employment, consultancy, directorship, or other position during the past 4 years,
whether or not paid, in any commercial entity which has an interest in the subject-matter
of the meeting/work, or an ongoing negotiation concerning prospective employment or
other association with such commercial entity;

4. performance of any paid work or research during the past 4 years commissioned by a
commercial entity with interests in the subject-matter of the meetings or work;

5. payment or other support covering a period within the past 4 years, or an expectation of
support for the future, from a commercial entity with an interest in the subject-matter of
the meetings or work, even if it does not convey any benefit to the expert personally but
which benefits his/her position or administrative unit, e.g. a grant or fellowship or other
payment, e.g. for the purpose of financing a post or consultancy.

With respect to the above, an interest in a competing substance, technology or process, or an
interest in or association with, work for or support by a commercial entity having a direct
competitive interest must similarly be disclosed.

How to complete this Declaration: Please complete this Declaration and submit it to the
Secretariat. Any financial or other interests that could constitute a real, potential or apparent
conflict of interest should be declared (1) with respect to yourself or partner, as well as (2) with
respect to the administrative unit with which you have an employment relationship. Only the
name of the commercial entity and the nature of the interest is required to be disclosed, no
amounts need to be specified (though they may be, if you consider this information to be relevant
to assessing the interest). With respect to items 1 and 2 in the list above, the interest should only
be declared if it is current. With respect to items 3, 4 and 5, any interest during the past 4 years
should be declared. If the interest is no longer current, please state the year when it ceased. With
respect to item 5, the interest ceases when a financed post or fellowship is no longer occupied, or
when support for an activity ceases.

Assessment and outcome: The information submitted by you will be used to assess whether the
declared interests constitute an appreciable real, potential or apparent conflict of interest. Such
conflict of interest will, depending on the situation, result in (i) you being asked not to take part
in the portion of the discussion or work affecting that interest, (ii) being asked not to take part in
the meeting or work altogether, or (iii) if deemed by WHO to be appropriate to the particular
circumstances, and with your agreement, you taking part in the meeting or work and your
interest being publicly disclosed.

Information disclosed on this Form may be made available to persons outside of WHO only
when the objectivity of the meeting or work has been questioned such that the Director-General
considers disclosure to be in the best interests of the Organization, and then only after
consultation with you.
Declaration: Have you or your partner any financial or other interest in the subject-matter of the meeting or work in which you will be involved, which may be considered as constituting a real, potential or apparent conflict of interest?

Yes: ☐  No: ☐  If yes, please give details in the box below.

Do you have, or have you had during the past 4 years, an employment or other professional relationship with any entity directly involved in the production, manufacture, distribution or sale of tobacco or any tobacco products, or directly representing the interests of any such entity?

Yes: ☐  No: ☐  If yes, please give details in the box below.

<table>
<thead>
<tr>
<th>Type of interest, e.g. patent, shares, employment, association, payment (including details on any compound, work, etc.)</th>
<th>Name of commercial entity</th>
<th>Belongs to you, partner or unit?</th>
<th>Current interest? (or year ceased)</th>
</tr>
</thead>
</table>

Is there anything else that could affect your objectivity or independence in the meeting or work, or the perception by others of your objectivity and independence?

__________________________________________________________________________________

__________________________________________________________________________________

I hereby declare that the disclosed information is correct and that no other situation of real, potential or apparent conflict of interest is known to me. I undertake to inform you of any change in these circumstances, including if an issue arises during the course of the meeting or work itself.

_______________________________  ______________________________
Signature                          Date

_______________________________  ______________________________
Name                                Institution