Essential Medicines List (EML) 2015 – Commented application
Information to be included in an application for inclusion, change or deletion of a medicine in the WHO Model List of Essential Medicines

General items

1. Summary statement of the proposal for inclusion, change or deletion
Briefly describe (1-2 paragraphs) your proposal in terms of clinical indication(s), target population and role in therapy also with respect of the current state of the EML and WHO guidelines or other technical WHO documents.

2. Name of the focal point in WHO submitting or supporting the application (where relevant)
Specify the WHO Technical Department supporting the application (if applicable). It is highly recommended that applicants engage with and seek support from the relevant WHO department working in the field of interest.

3. Name of the organization(s) consulted and/or supporting the application
Specify the affiliation of the applicant and indicate if other organizations have been consulted and/or are supporting the application.

4. International Nonproprietary Name (INN, generic name) of the medicine
The medicine(s) for inclusion must be described by its International Nonproprietary Name. International Nonproprietary Names (INN) facilitates the identification of pharmaceutical substances or active pharmaceutical ingredients. Each INN is a unique name that is globally recognized and is public property. A nonproprietary name is also known as a generic name.

5. Formulation proposed for inclusion; including adult and paediatric (if appropriate)
All applications must evaluate data for both adults and children (when applicable to the medicines considered). If data for certain populations (e.g. children, pregnant women) are not available this must be clearly stated in the application.

6. International availability - sources, of possible manufacturers and trade names
The application must demonstrate that the dosage form(s) and strength(s) of the proposed medicine(s) do exist and are available somewhere in the world.

7. Whether listing is requested as an individual medicine or as an example of a therapeutic group
The application must state if the request for inclusion is as an individual medicine or an individual medicine with a square box symbol.

The square box symbol (□) is used to indicate that there are a number of agents within a pharmacological class with similar clinical performance. The listed medicine should be the example of the class for which there is the best evidence for effectiveness and safety. In some cases, this may be the first medicine with marketing authorization; in other instances, subsequently licensed compounds may be safer or more effective.

Where there is no difference in terms of efficacy and safety data, the listed medicine should be the one that is generally available at the lowest price, based on international drug price information sources.

If a square box (□) is being requested for the medicine, the application should identify the therapeutic alternatives that may be considered as similar.

8. Information supporting the public health relevance (epidemiological information on disease burden, assessment of current use, target population)
The application should include information on the public health need for the medicine in terms of disease burden and the likely impact of treatment on the disease.
**9. Treatment details (dosage regimen, duration; reference to existing WHO and other clinical guidelines; need for special diagnostics, treatment or monitoring facilities and skills)**

The application should specify the proposed therapeutic regimen and duration. Reference in particular to existing WHO guidelines is recommended. Other evidence-based guidelines can be mentioned, however potential conflicts of interest issues that may relate to these guidelines should be addressed.

Medicines can be listed in either the core list or the complementary list.

The core list presents a list of minimum medicine needs for a basic healthcare system, listing the most efficacious, safe and cost-effective medicines for priority conditions. Priority conditions are selected on the basis of current and estimated future public health relevance, and potential for safe and cost-effective treatment.

The complementary list presents essential medicines for priority diseases, for which specialized diagnostic or monitoring facilities, and/or specialist medical care, and/or specialist training are needed. In case of doubt medicines may also be listed as complementary on the basis of consistent higher costs or less attractive cost-effectiveness in a variety of settings.

**Public health need and evidence appraisal and synthesis**

**10. Summary of comparative effectiveness in a variety of clinical settings:**
- Identification of clinical evidence (search strategy, systematic reviews identified, reasons for selection/exclusion of particular data)
- Summary of available data (appraisal of quality, outcome measures, summary of results)
- Summary of available estimates of comparative effectiveness

**11. Summary of comparative evidence on safety:**
- Estimate of total patient exposure to date
- Description of the adverse effects/reactions and estimates of their frequency
- Identification of variation in safety that may relate to health systems and patient factors
- Summary of comparative safety against comparators

Items 10 and 11 (comparative effectiveness and safety) are the two most important elements on which the Expert Committee judgments are made. The application must present scientific evidence on comparative effectiveness and safety/harms of the proposed medicine. Summary evidence tables of key trials should be included in the application and the original data (Copies of the key trials) included in the application to support the comparative safety and efficacy of the proposed medicine(s) should be provided electronically in a portable document format (PDF) to the Secretariat and should be available in the public domain. The overall available evidence should be presented separately for benefits (item 10) and harms (item 11) of the intervention/medicine proposed.

Where appropriate evidence of comparative effectiveness and safety should be presented in tabular form using Grading of Recommendations, Assessment, Development and Evaluation (GRADE) tables that can also be obtained from Cochrane systematic reviews.

GRADE website: [http://www.gradeworkinggroup.org/] (http://www.gradeworkinggroup.org/)
Software for producing GRADE tables can be downloaded from the following website:
[http://www.ims.cochrane.org/revman/other-resources/gradepro](http://www.ims.cochrane.org/revman/other-resources/gradepro)

For some initial information regarding GRADE tables refer to the following presentation:
[http://training.cochrane.org/about/newsletters/may-2013](http://training.cochrane.org/about/newsletters/may-2013)
For further information on how to present summary of findings tables (separately for benefits and harms), please refer to:


There are also alternative ways of presenting available evidence either from systematic reviews or single trials. The most relevant comparative trials (randomised controlled trials, RCTs) can be presented showing patients characteristics, baseline risk for the main relevant outcomes in the standard treatment arm, absolute differences and measures of association. If this alternative approach is chosen (especially when only one or two trials are available), ensure there is adequate consideration to the quality of the studies (or risk of bias of individual study) together with comments on applicability and generalizability of the trials data (population, interventions, outcomes chosen).

12. Summary of available data on comparative cost and cost-effectiveness within the pharmacological class or therapeutic group:

- **range of costs of the proposed medicine**
  Show medicine prices from a range of settings where the product is registered. The listing in the MSH International Drug Price Indicator Guide can be an acceptable reference. [http://erc.msh.org/mainpage.cfm?file=1.0.htm&module=DMP&language=English](http://erc.msh.org/mainpage.cfm?file=1.0.htm&module=DMP&language=English)
  If this information is not available, other international sources, such as the WHO, UNICEF and Médecins sans Frontières price information service, can be used. All cost analyses should specify the source of the price information

- **resource use and comparative cost-effectiveness presented as range of cost per routine outcome**
  Applicants should present a range of estimated cost per routine outcome such as cost per case, cost per cure, cost per month of treatment, cost per case prevented, cost per clinical event prevented.
  Applicants may also consider the cost-effectiveness of the intervention to provide general guidance on whether the intervention provides good value for money compared to other drugs.
  Applicants should generally not look at marginal impacts and costs.
  Where possible applicants should also consider the financial impact of making the drug available, in terms of the average cost per patient (globally) and the population in need (average or differences in prevalence) to assist with the development of budget impact calculations.

**Regulatory information**

13. Summary of regulatory status of the medicine (in various countries)

The application must provide a summary of the regulatory status of the medicine(s) proposed for inclusion. This should include the regulatory status in the country of origin and preferably other countries as well. The summary should also specify the indications that the medicine is licensed for.
Status of the proposed medicines should be given regarding the most stringent regulatory authorities\(^1\), including:

- US Food and Drug Administration (FDA)  
- European Medicines Agency (EMA)  
- Australian Government, Department of Health and Ageing, Therapeutic Goods Administration  
- Japan:  
- Health Canada –  

The WHO List of Prequalified Medicinal Products is a list that contains medicinal products used for HIV/AIDS, tuberculosis, malaria and other diseases, and for reproductive health, which have been assessed as part of the WHO Prequalification Programme and found to be acceptable, in principle, for procurement by UN agencies. The list of WHO prequalified medicines can be found at:  
[http://apps.who.int/prequal/info_general/notes.htm](http://apps.who.int/prequal/info_general/notes.htm)


Please verify and list whether the proposed medicine is listed in at least one of the above mentioned Pharmacopoeia.

15. **Proposed (new/adapted) text that could be included in a revised WHO Model Formulary**

Please provide 2-3 short paragraphs summarising the key aspects relating to this medicine and its requested listing on the WHO Model List. This information could provide the basis for a longer monograph that could be adapted for use in a model formulary at a global or national level.

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For further information, please refer to:  
Essential Medicines List Secretariat,  
Medicines Policy, Access and Use Team (PAU),  
Department of Essential Medicines and Health Products (EMP)  
World Health Organization  
20 Avenue Appia  
CH-1211 Geneva 27  
Switzerland  
email: emlsecretariat@who.int

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\(^1\) A stringent regulatory authority is: - the medicines regulatory authority in a country which is: (a) a member of the International Conference on Harmonisation (ICH) (European Union (EU) Japan and the United States of America); or (b) an ICH Observer, being the European Free Trade Association (EFTA) as represented by Swiss Medic and Health Canada (as may be updated from time to time); or (c) a regulatory authority associated with an ICH member through a legally-binding, mutual recognition agreement including Australia, Iceland, Liechtenstein and Norway (as may be updated from time to time); and - only in relation to good manufacturing practices (GMP) inspections: a medicine regulatory authority that is a member of the Pharmaceutical Inspection Co-operation Scheme (PIC/S) as specified on its website.  