

A Case Study on National List of Essential Medicines (NLEM) in India and WHO EML 2015-Overview

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Abstract

Availability of modern medicine increased all over the world due to huge expansion of the global Pharma market. At the same time misuse as well as accessibility of the most of essential drugs to majority of the population was denied due to cost-effectiveness of healthcare delivery combined with poor procurement policies and poor prescribing practices. During the recent years, the national list of India has assumed immense importance to improve access to medicines in India. It is therefore necessary to understand policies and guidelines followed in developing WHO essential drug list and national list of essential medicines. In this review article history of essential drug list and important inclusions in NLEM 2015 and WHO EML 2015 were highlighted.

Keywords: NLEM 2015; WHO EML 2015; Essential drug medicine list

Introduction

Drugs fulfill to the needs and requirements of primary healthcare of population are called as essential drugs, which are available in adequate amounts, in the appropriate dosage forms with assured quality and detailed information providing evidence on efficacy and safety, and comparative cost effectiveness. The Alma-Ata declaration during the International Conference on Primary Health Care in 1978 reaffirms that health is a fundamental human right and the attainment of the highest possible level of health is a most important worldwide social goal. The Alma Ata declaration has outlined the eight essential components of primary health care and provision of essential medicines is one of them [1]. Management of essential medicines results in a higher quality of care with the effective utilization of health resources. WHO maintaining a leader role in development of comprehensive national drug policies and updating model list of essential drugs which sustained the momentum of the revised drug strategy and was a basic element of the validated information for optimal rationalization of drug procurement and supply. WHO introduced the concept of essential medicines in 1977 and since then the list has been revised every 2 years [2,3]. The current one is 19th model essential medicines list released in April 2015 and amended in August 2015.

The concept of essential medicines has been worldwide accepted as a powerful tool for the attainment of the highest possible level of health. Essential medicines are those that satisfy the priority healthcare needs of the population. They are selected with due regard to public health relevance, evidence of 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 appropriate dosage forms, with assured quality and adequate information, and at a price the individual and the community

can afford. Although the WHO has defined the concept of EML and regularly publishes the updated lists, implementation of this concept is intended to be flexible and adaptable. The responsibility of determining exactly which medicines are regarded as essential is left to the discretion of the adopting nations based on their requirements.

Rational drug use is a global versatile health issue, where the healthcare professional's responsibility intensified over the decades in expanding the therapeutic outcomes ideal selection of appropriate medicinal products and proper dispensing is the main goal of clinical and hospital pharmacy activities [4]. The pharmacist's activities can be summarized as below: consulting, drug information, drug use studies and research, selection of drugs pharmacokinetics/therapeutic drug monitoring, formulation and preparation, clinical trials, dispensing and administration, pharmacoeconomy, teaching and training. Overall aim is to reduce the expenditures for medications, maximize the clinical effect, and minimize the risk of treatment-induced adverse events for patients [5].

In developing countries and underdeveloped countries several surveys and thorough evaluation done on prescription audits revealed bitter facts about irrational usage of drugs due to poly-pharmacy, miscommunication problems in conveying the relevant drug information, lack of drug information centres, over prescription (injections), non-adherence to schedule of medication, chronic diseases such as asthma, cardiovascular diseases, hypertension, prescribing towards placebo, gap bridging between physician and patient due to short consultation time and dispensing done improper channels.

WHO Criteria to Guide Selection of an Essential Drug [6]

1. From clinical data available globally drugs safety and efficacy should be determined.

2. Taking in to the consideration of factors such as treatment facilities available for the incidence and pattern of the disease, genetic, demographic factors and financial resources of the patient, including the technical expertise and environmental factors choice of drug is finalized.
 3. When the more options of drugs available under a specific category choice should be made on the basis of relative efficacy, safety, quality, price and availability. Cost benefit ratio remains a major consideration.
 4. Up gradation and reviewing the essential drug list is a regular mandatory continuing process in light of new therapeutic options and changing therapeutic needs.
 5. Choice on essential drug list influenced by pharmacokinetic properties and manufacturing, shelf life and storage facilities.
 6. Most of the cases essential drug list only contains single compounds and rarely fixed dose combination products are prescribed if necessary and specifically when combination has a proven advantage.
 7. Not only should the unit cost of the drug but also the total cost of the treatment be considered.
 8. With the advent of reliable and accurate drug information health care professionals can effectively, safely utilize the essential drugs.
 9. Essential drug list doesn't implicate that only these drugs are useful and others are not, but most of the cases majority of the population will be in a situation to be accessed to the most needed essential medicines list for the health care of the individuals.
- 3) Essential medicines list based on treatments of choice.
 - 4) Drugs and therapeutics committees in districts and hospitals.
 - 5) Problem based learning in pharmacotherapy in undergraduate curricula.
 - 6) Continuing in-service medical education as a licensure requirement.
 - 7) Supervision of health care workers, audit of prescriptions and providing feedback to prescribers.
 - 8) Provision of drug bulletin on medicines.
 - 9) Public education about medicines.
 - 10) Avoidance of perverse financial incentives.
 - 11) Appropriate and enforced regulations.
 - 12) Sufficient government expenditure to ensure availability of medicines and staff.

Implementation of these policies will help prevent to a great extent irrational prescribing and promote rational drug therapy.

Assessment of EML

Based on the national priority and available evidence the "model list" is the source for further evolutions [10].

Addition and deletion of new medicines.

Initiation of correct and fixed dosage strength.

Helpful for the national decision makers in assessment of costs in recognizing the priority medicines which can elevate the major therapeutic benefit of the people.

Depending on WHO EML; which gained worldwide acceptance among the nations where 4 out of 5 countries have initiated the national list (Figure 1).

The importance of the national list is increased in such a way that it became a major source for the national medicine policies. In addition to national list some countries either have provisional or state lists.

The concept of essential medicines has also been adopted by many international organizations, such as united nations children's funds (UNICEF), office of the united nations high commissioner for refugees (UNHCR), doctors without borders (Medicines Sans Frontiers), as well as by NGOs and international non-profit supply agencies.

Among the notable changes in the WHO EML since its inception are the following:

The term pharmaceutical preparations were replaced by medicines in the clinical practice.

The term essential medicines were replaced by essential drugs.

The introduction of national list is based on evidence based instead of being experienced.

Based on research evidence; comparison of benefit and safety of specific medicines lead to evolution of more national selection process.

Evolution from being experience-based to evidence-based.

Earlier the cost of total treatment was taken but now it is replaced by usage of comparative cost effectiveness approach i.e., range of cost per

The Impacts of Essential Drugs [7]

1. To help save lives and improve health by closing the huge gap between the potential that essential drugs have to offer and the reality that for millions of people-particularly the poor and disadvantaged - medicines are unavailable, unaffordable, unsafe or improperly used.
2. Have a profound health impact; effective drug treatment now exists for most leading infectious diseases. Essential life-saving drugs have also been developed for leading non-communicable diseases such as ischemic heart disease and cerebrovascular disease. Essential drugs save lives and reduce suffering, especially for impoverished populations.
3. Essential drugs increase the credibility of a health system and promote patient participation.
4. Effective and transparent drug procurement increases the confidence of governments, ministries of finance and donors in a country's health system.
5. Medicines represent the second largest government public health expenditure and in low-and middle income countries, they represent the largest out-of-pocket household health expenditure. Hence they have economic impact.
6. Increase health system effectiveness and the cost-effectiveness of pharmaceutical Expenditure.

WHO proposed 12 core policies to promote rational use of medicines [8,9], these are:

- 1) Mandated multi-disciplinary body to coordinate medicine use policies.
- 2) Evidence based clinical guidelines.

routine outcome (cost per case, cost per cure, and cost per month of treatment) (Figure 2).

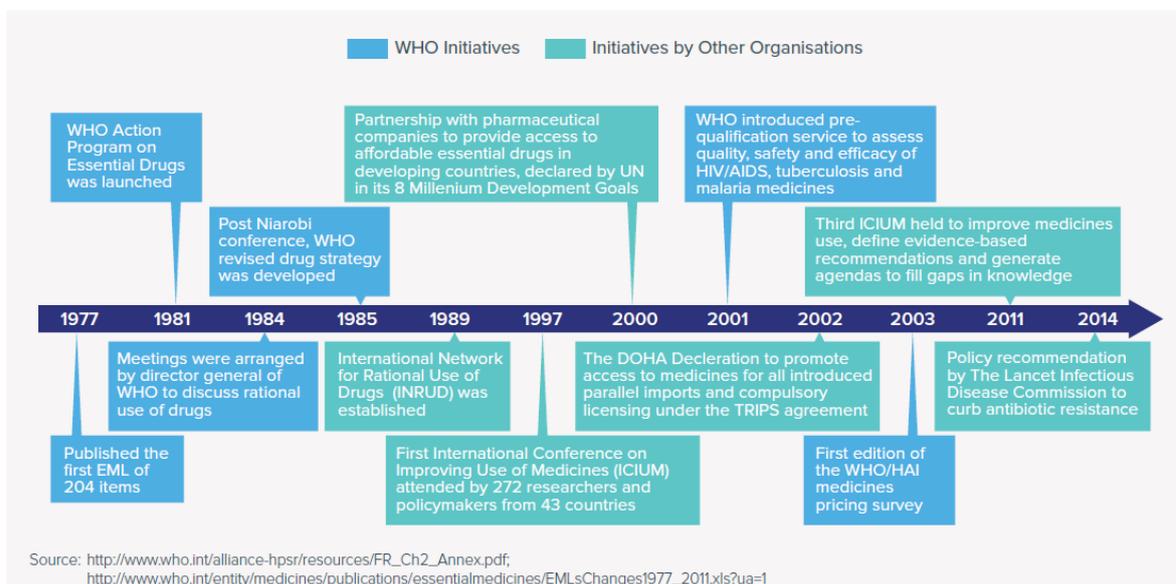


Figure 1: A timeline depicting some important events of essential medicine [11,12].

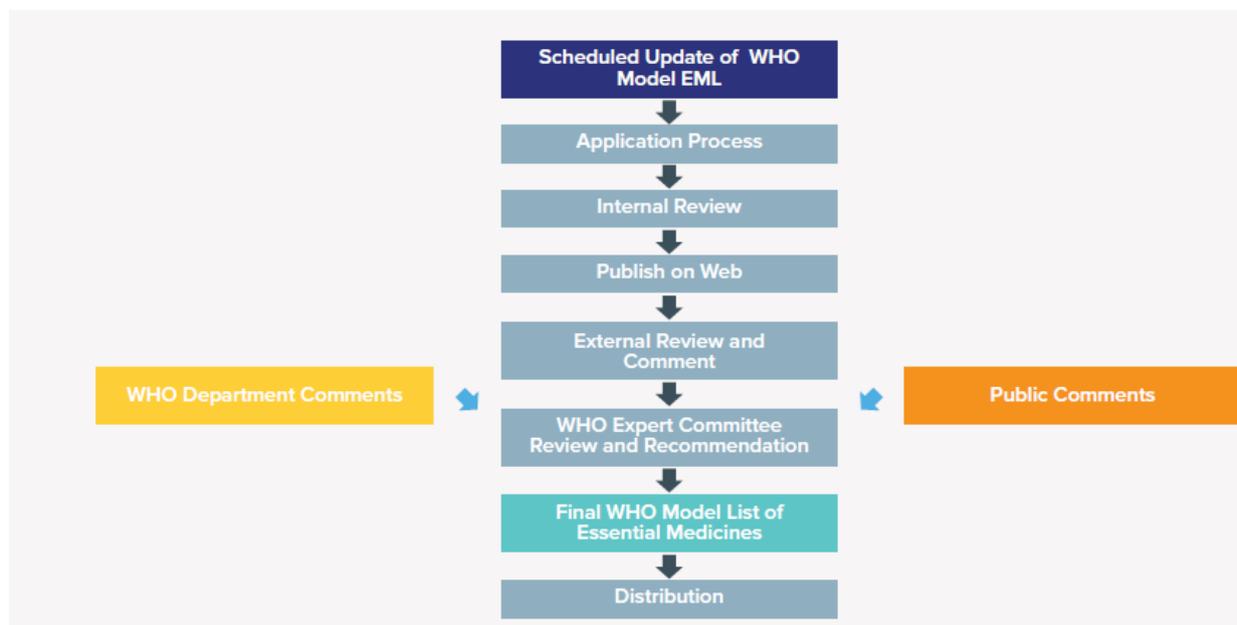


Figure 2: Current process and steps in updating WHO model EML [13].

WHO Model EML Implementation by National Health Systems

For the procurement and supply in the public sector to enable reimbursement schemes for medicine costs and local production, strict government approve selective list of medicines guided in the country's national EML. It strengthened pharmaceutical cares towards effective

treatment of majority of diseases. Increased concerns over Health all around the globe lead to the publication of national EML by almost all developing countries, out of which have updated in the past five years. Even in some countries existence of sub national or state/province national and institutional EML. By keeping in view of certain conditions such as availability of medicines, affordability, treatment of

facilities, personnel, and genetic, demographic and environmental factors.

Some of the factors which ensure optimum utilization of national EML include standard treatment guidelines, national expenditure on essential medicines and procurement practices for adaptation at the national level the modifications made mainly are the changes in the structure of the list and categorization of drugs. Looking upon as example, generally, in Indian national lists and national list of china include anti-diabetic drugs under hormones, other endocrine medicines and contraceptives and "hormones and endocrine agents". While on the other hand WHO EML includes insulin and metformin in the category "medicines used for diabetes". Here the list contains only names of medicines and recommended formulations strengths are mentioned while on the list of some other countries include recommended standard treatment guidelines for specific indication in attempt to align the EML with country specific treatment guidelines.

Status of Essential Drugs in India

The concept of essential drug list was first promoted in Tamilnadu state of India in 1994. Delhi is the initiator in developing a comprehensive policy in 1994 and it was the only Indian state having such a comprehensive policy. For use within the state government health facilities it have developed standard guidelines (STGs). The armed forces medical college (AFMC) has expanded STGs. Three subsequent revisions took place in 2003, 2011 and 2015 where the first national list of essential medicines was introduced in 1996. These lists were neither implemented for obtaining drugs nor were STG's made in India, Delhi model list is considered to be one example for other states [14]. The Government of National Capital Territory of Delhi along with Delhi society for promotion of rational use of drugs (DSPRUD) is providing a lead role of revising the list of essential drugs since 1996, the last being in 2013. It involved widespread participation of doctors from hospitals, dispensaries and health centers. Suggestions received were discussed in eleven sub-committees and finally 406 medicines including 152 for dispensary level were included in the latest list [15].

In NLEM 2011 348 medicines were prepared by 87 expert committee.

They are clearly documented in inputs by experts of various fields in the review committee.

In this the list contains anaesthetic agents; they are non-inclusion pediatric formulations and errors in the strength of formulations [16].

WHO listed some essential drugs but Delhi list missed some essential medicines from that list such as Diabetic, TB, HIV, cancer drugs. Glimpiride and Glicazide are the anti-diabetic medicines which was not found in the list of essential medicines but the list of Delhi (DSPRUD) contains anti diabetic drugs like Glimpiride, Sitagliptin, Vildagliptin, Saxagliptin and some other findings which are Salmeterol and Montelukast these are anti-Asthmatic medicines [17,18].

One of the essential regarding the emergencies of multi drug resistances tuberculosis (MDR-TB).

For the treatment of multi drug resistant tuberculosis the drugs like Capreomycin, Cycloserine, Ethionamide, Kanamycin and Para-amino salicylic acid are included in the WHO model list (EML) [19]. These drugs are not mentioned in NLEM 2011 list, while the WHO list

included 21 vaccines and at the same time NLEM 2011 mentioned only 9 vaccines [20].

NLEM list requires more discussion and revision for the missed drugs and it should have taken under the guidance of National Health programmes and also National formulary of India 2010 [21].

In India academy of pediatrics have many essential drugs for children in the NLEM so, it is advised to review for two year intervals of time.

The government of India made a policy for pricing the essential drugs and the central government has been formed to include more drugs in the essential drugs and also they should available under a price cap [22].

50 essential generic drugs were supposed to be provided free of cost by the ministry of health, government of India from "birth to death" to the people of Indians across the nation.

The programme will be rolled out in phases, beginning with select hospitals across India, with the objective of reaching every citizen. Once the rollout is complete, everyone will get these 50 medicines-that includes traditional treatments for pain, infection, hypertension, diabetes, among others-complimentary on prescription at public hospitals and dispensaries [23].

Process used for India EML

The Indian NLEM is reviewed in consultation with experts for discussion on evidence-based criteria for addition and deletion of medicines from the NLEM. This is followed by therapeutic area wise group Discussion by clinicians, pharmacologists, pharmacists, scientists, and regulators. The updated list is then presented for an open-house discussion, and the draft is forwarded to NLEM for considerations with NLEM core committee after modifications.

Assessment of Current Implementation and Specific Mechanisms Impacting Implementation

The current level of implementation appears to be poor with factors such as poor medicine supply and distribution systems, insufficient health facilities and staff, low investment in health, the high cost of medicines adversely affecting the availability of medicines, and lack of confidence in the quality of medicines supplied through the public healthcare system [23].

Most patients either choose or are forced to seek treatment in private clinics and hospitals due to inadequate healthcare infrastructure. An estimated 80% of outpatient consultations and 60% of inpatient treatments take place in private facilities and only 22% of the population has access to public healthcare. Also, there is a considerable variation between rural and urban areas in terms of healthcare infrastructure and access to healthcare services due to the disparity in healthcare services, which are skewed towards urban centers. Funding issues and shortcomings in procurement and distribution systems result in poor supply of essential medicines. Shortages are a particular issue in public health centers, but also affect availability in government hospitals, where patients are sometimes forced to purchase products from alternative sources.

The Government of India is currently negotiating with the pharmaceutical industry to lower the cost of essential drugs. In 2014, the government extended the price control to products beyond the list of EML for over 100 cardiovascular and diabetes drugs. The

appropriate approach to compulsory licensing-in accordance with the provisions of the agreement on the trade-related aspects of intellectual rights (TRIPS) is also under review and discussion.

The criteria for inclusion of a medicine in NLEM are as follows:

The medicine should be approved/licensed in India.

The medicine should be useful in disease which is a public health problem in India.

The medicine should have proven efficacy and safety profile based on valid scientific evidence. The medicine should be cost effective.

The medicine should be aligned with the current treatment guidelines for the disease.

The medicine should be stable under the storage conditions in India.

When more than one medicine are available from the same therapeutic class, preferably one prototype/medically best suited medicine of that class to be included after due deliberation and careful evaluation of their relative safety, efficacy, cost-effectiveness. Price of total treatment to be considered and not the unit price of a medicine.

Fixed dose combinations (FDCs) are generally not included unless the combination has unequivocally proven advantage over individual ingredients administered separately, in terms of increasing efficacy, reducing adverse effects and/or improving compliance.

The listing of medicine in NLEM is based according to the level of health care, i.e., Primary (P), Secondary (S) and Tertiary (T) because the treatment facilities, training, experience and availability of health care personnel differ at these levels.

The salient features of NLEM 2015:

There were 348 medicines listed in NLEM 2011. A total of 106 medicines have been added, and 70 medicines have been deleted to prepare NLEM 2015 which now contains a total of 376 medicines.

The apparent mismatch in the total number of medicines will be clear by noticing the following points.

In NLEM 2011-

- Prednisolone was counted as 3 items (prednisolone, prednisolone acetate and prednisolone sodium phosphate),
- Lignocaine was counted as 2 items (lignocaine and lignocaine hydrochloride),
- Glucose was counted as 2 items (glucose and dextrose 25%),
- Gentian violet was counted as 2 items (Gentian violet and methylrosalinium chloride).
- Sodium chloride was counted as 3 items (normal saline, N/2 saline and N/5 saline).
- Betamethasone was counted as 2 items (Betamethasone and betamethasone dipropionate).
- Snake venom antiserum was counted as 2 item (Polyvalent antsnake venom and Specific antsnake venom).
- Isosorbide mononitrate and isosorbide dinitrate were counted as 1 item.
- Medicines in NLEM are listed with reference to the levels of healthcare, namely, Primary (P), Secondary (S) and Tertiary (T). There are 209 medicine formulations listed for all levels of health care (P, S, T), 115 medicine formulations for secondary and tertiary levels (S, T) and 79 medicine formulations for the tertiary level (T).

- It is to be noted that formulations of certain medicines are listed at different levels but as item, they are counted as one. The total number of medicines remains 376 (Table 1).
- The essentiality of a medicine has been considered in terms of its dosage form and strength also.

Any dosage form of a medicine, other than the dosage form included in NLEM, but in same strength and route of administration, which does not have significant difference in terms of pharmacokinetics/pharmacodynamics/efficacy-safety profile over the dosage form mentioned in the list will be considered as included. To elaborate, if a tablet is included, other dosage forms like conventional tablets and capsules are considered as included. However, such different dosage forms should be considered differently for purposes such as procurement policy, pricing etc. This principle also applies to all other dosage forms e.g. oral liquid dosage forms, injectables, topical dosage forms etc.

The new formulations developed in novel drug delivery systems, sustained release/controlled release etc. should be considered only if specified in the list against any medicine. Such formulations should be given importance in the procurement policy, pricing etc.

In some of the cases like vaccines, immunoglobulins etc. are listed in NLEM irrespective of their source, composition and strength and all their products are approved by the licensing authority.

In general these medicines have mentioned with respect to their active moieties without mentioning their salts.

If in case any active moiety is found as different isomers/analogues/derivatives these are considered as different/variable entities and inclusion of one does not imply other isomers/analogues/derivatives.

The pack size for single or multi dose has not been mentioned so, this regard must be included as variable moieties for procurement and pricing.

Fixed dose combinations are not included unless it is proven advantage by the people over the administration of individual drugs in terms of its efficacy reducing side effects/adverse effects for improving compliance which in turn improves the quality of life of a patient (Table 2).

Many medicines in various national health programmes are suggested to be included in NLEM.

Any medicine when recommended under National Health programme must occupy in NLEM.

NLEM 2015 has been prepared mainly for the adherence of basic like efficacy, safety, cost effectiveness and main considerations for public health problems.

Year	WHO EML	NLEM
1977	204	-
1979	235	-
1983	243	-
1985	263	-
1988	280	-
1990	293	-

1992	300	-
1995	301	-
1996	-	279
1997	310	-
1998	317	-
2000	322	-
2002	341	-
2003	331	354

2005	319	-
2007	337	-
2009	352	-
2011	358	348
2013	374	-
2015	414	376

Table 1: The number of medicines in WHO EML and NLEM of India.

Section	Therapeutic category	Total in NLEM 2011	Deleted	Added	Total in NLEM 2015
1	Anesthetic agents	18	3	1	16
2	Analgesics, antipyretics, nonsteroidal anti-inflammatory medicines, medicines used to treat gout and disease modifying agents used in rheumatoid disorders	14	0	1	15
3	Antiallergics and medicines used in anaphylaxis	9	2	0	7
4	Antidotes and other substances used in poisonings	14	1	1	14
5	Anticonvulsants/Antiepileptics	7	0	2	9
6.1	Anthelmintics	4	1	1	4
6.2	Anti-bacterial medicines	21	4	5	22
6.2.3	Antileprosy medicines	3	0	0	3
6.2.4	Antituberculosis medicines	6	1	9	14
6.3	Anti-fungal medicines	5	0	0	5
6.4	Antiviral medicines	15	6	14	23
6.5	Antiprotozoal medicines	15	4	4	15
7	Antimigraine medicines	4	1	2	5
8	Antineoplastic, immunosuppressives and medicines used in palliative care	40	6	25	59
9	Antiparkinsonism medicines	3	1	0	2
10	Medicines affecting blood	10	3	6	13
11	Blood products and plasma substitutes	10	4	2	8
12	Cardiovascular medicines	29	5	5	30
13	Medicines used in dementia	NA	NA	1	1
14	Dermatological medicines	16	6	5	15
15	Diagnostic agents	11	6	2	7
16	Dialysis solution	1	0	1	2
17	Disinfectants and antiseptics	12	3	0	9
18	Diuretics	4	0	0	4
19	Ear, nose, throat medicines	NA	NA	4	4

20	Gastrointestinal medicines	16	3	3	16
21	Hormones, other endocrine medicines and contraceptives	24	4	3	23
22	Immunologicals	13	0	4	17
23	Muscle relaxants and cholinesterase Inhibitors	5	1	1	5
24	Medicines used in neonatal care	NA	NA	3	3
25	Ophthalmological medicines	17	5	6	17
26	Oxytocics and antioxytocics	7	1	1	7
27	Psychotherapeutics	11	5	7	13
28	Medicines acting on the respiratory tract	6	3	3	6
29	Solutions correcting water, electrolyte and acid-base disturbances	10	0	0	8
30	Vitamins and Minerals	10	2	1	9

Table 2: The number of medicines deleted and added to NLEM 2011, along with number of medicines in NLEM 2015 [23].

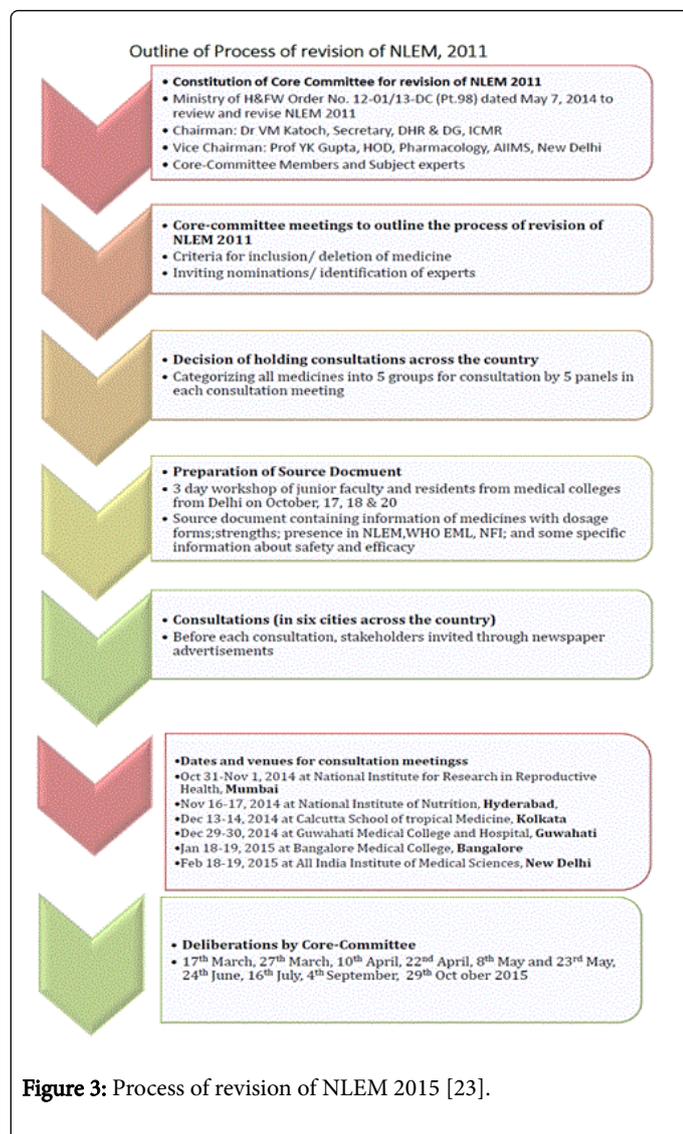


Figure 3: Process of revision of NLEM 2015 [23].

Conclusion

Introduction of new technologies and incremental innovations in drug delivery systems and formulations, wide differences in medical practice pattern in the country, regional variations in health care system etc. made revision of WHO EML a complex process in the light of fast changing concepts in medicines, treatment regimens (Figure 3). WHO EML was also consulted with respect to the country's need. In the light of the above it was difficult to address all the aspects but the basic principle of EML i.e., efficacy, safety, cost; and consideration of diseases as public health problems. The essential drugs concept is a

global concept and health systems of all types, from basic health systems in the poorest countries to highly developed national health insurance schemes in the wealthiest have recognized its therapeutic and economic benefits, which lead to the development of NLEM in India. It was introduced to accelerate the positive impacts of drugs on health status and to provide the best of modern, evidence based and cost-effectiveness healthcare, promotes the need to regularly update drug selections in light of new therapeutic options and changing therapeutic needs, the need to ensure drug quality, and the need for continued development of better drugs, drugs for emerging diseases and drugs for coping with changing resistance patterns.

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