ANNEX 1:
Procedure for Application for Inclusion of Medicines on the Licensed Drugs List of the Ministry of Public Health of Afghanistan[1]

A. General

The Licensed Drugs List selection process is based upon a well-developed procedure that ensures transparency of the licensing process.

Applications for inclusion in the list will only be considered the application form has been fully completed for each proposed drug. There is one application form to be filled out for each proposed drug. In summary, the necessary information required before an application will be considered is as follows:

1. The applicant's contact details are complete;
2. The drug's international non-propriety name (INN) has been stated, including strength, route of administration, and presentation;
3. The indications have been clearly stated;
4. The details of the proposed regimen for each indication are clearly stated;
5. All relevant comparator drugs presently included in the LDL have been listed for each indication;
6. There is sufficient evidence to support the proposed amendment.

B. Types of applications

Applications may address major or minor amendments.

Minor amendments include, but are not limited to:

1. new strengths, presentations or administration forms of drugs already included in the LDL
   E.g. proposing the inhalator form of a bronchodilator that is already included as tablet and/or injection
   E.g. slow-release tablets instead of common tablets
2. combination therapies of drugs already included in the LDL

For minor amendments the required supporting evidence should be relevant to the nature of the amendment, and include cost implications.
E.g. alignment with new WHO recommendations on strengths or combination therapies requires only a copy of the new WHO recommendations.

Major amendments include, but are not limited to:

1. new indications for existing items on the list
   E.g. using a drug included for its anti-hypertension properties as a tocolytic
2. new therapeutic entities

[1] The same format is used for proposing deletions from the list. Often the proposal for inclusion of one drug will also indicate the drug to be replaced with that drug. The drug to be replaced will be deleted. If an exsiting durg should be deleted without replacement, the same format can be used, indicating the drug to be deleted in Section 4 without however proposing a new drug for replacement in Section 3, but mentioning "to be removed" in Section 3.

E.g. a new antibiotic (doxycycline) to replace a previously included one (tetracycline) for the same indication.

3. new therapeutic classes
   E.g. anti-retroviral drugs

All major amendments must be supported by evidence reflecting safety, efficacy and cost of the medicine compared to an already listed drug for the same indication. This usually is one of more article(s) from an unbiased source of globally recognized integrity. A major amendment may also include motivations for drugs not listed and for conditions not yet addressed by the drugs included in the LDL. In such cases, submissions must be supported by demographic/ epidemiologic data.

C. Submittal and screening process

Applications are submitted to the GD Pharmacy of the MOPH. Upon receipt, the GD will acknowledge the receipt of the application in writing.

Applications are screened by the Technical Subcommittee (TSC) of the National Essential Drugs List Committee (NEDLC) at the GD Pharmacy at the MOPH to ensure that:

1. the applicant's contact details are included
2. the drug can be identified in terms of the INN (generic name)
3. at least one indication has been included, with the proposed regimen
4. relevant comparator drug(s) ha(s)(ve) been identified with their corresponding dosing regimen
5. there are supporting references to substantiate the application

TSC will compile a review of the prevailing cost of therapy and allocates the application to a suitably qualified reviewer who compiles a technical report. This **technical report** summarizes a review of the submitted data and supporting references in terms of the following:

1. relative safety – are side-effects acceptable considering the benefits for the patient having the indicated condition
2. relative efficacy – compare treatment results with treatment results of existing drugs for the stated condition
3. practice environment – the focus here being efficacy relative to current LDL drugs
4. pharmaco-economic evaluation – compare the full treatment cost of the proposed drug with the full treatment cost of existing drugs

The report is then presented to the technical subcommittee. The committee may request further information from the applicant before recommending a decision to the NEDLC.

The technical subcommittee will make recommendations to the NEDLC for approval or rejection. Where the NEDLC is of the opinion that a further review is required, the decision will be sent back to the technical subcommittee for further review.
Where the NEDLC is of the opinion that the drug is acceptable, the recommendation for approval will be submitted to the National Medicine Board.
Where the NEDLC is of the opinion that the drug is not acceptable, the applicant will be informed of the rejection and of the reasons for rejection. A rejected drug will not be reconsidered for inclusion within six months of the rejection. Resubmission requires significant additional information and supporting references that address the specific reason(s) for rejection of the original application.

D. Detailed description of the data elements of the application form <*name*>, no. <*number*>

The application submission form is divided into 5 sections.

Section 1: Proposed Drug Identification

a) **Proposed Drug:** The International Nonproprietary 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 nonproprietary name is also known as a generic name. It also includes the presentation form and the strength of the proposed medicine. E.g. Acetylsalicylic acid, tablet, 325 mg.
b) **Level of Care** - indicate whether the proposed medicine should be included in the BPHS, indicating the specific level(s), and/or the EPHS, also indicating the specific level(s). If intended for use by a special program, or specialist MD, indicate the program or MD in the Special: case
C) **Submission date** – the Shamsi calendar date on which the submission is filled out.

Section 2: Applicant's Details

The NEDLC will 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.

a) **Title** – Mr, Mrs, Dr, Pr, etc….
b) **Name** – full name of the applicant. Do not abbreviate: Mohammad, but not Mhd.; Sayyed, but not S.; etc…
c) **Father's Name** - full name of the applicant's father. Do not abbreviate: Mohammad, but not Mhd.; Sayyed, but not S.; etc…
e) **Postal address** – full address where correspondence regarding the application should be sent: house #, street name, village of city *nahia*, district and province
f) **Phone** – Phone number(s) on which the applicant can be contacted.
g) **E-mail** – email address where correspondence regarding the application can be sent
d) **Facility ID** – if applicable, the official MOPH facility code of the facility where the applicant works. If the applicant is a private practitioner, working in a non-registered facility, put "NA" for this entry.

Section 3: Proposed Indications

For each drug submitted for inclusion, at least one indication with proposed regimen needs to be filled out. Up to three indications can be filled out for one drug submitted for inclusion.

a) **Indication** – the applicant can list up to 3 indications (conditions) for using the suggested drug. Points to consider:

i. Where the applicant suggests a new therapeutic class, i.e. a new or emerging disease/condition, a brief motivation based upon Afghan epidemiological data, as well as inclusion status in BPHS/EPHS must be included as an annexure.
ii. The indication should allow for the identification of the appropriate comparator(s) in the current LDL.
iii. Many drugs have multiple indications. However, not all indications are equally cost effective.

b) **Proposed Treatment Regimen:**

Dose – the amount of the drug to be given with each intake/administration
Route – oral, parenteral, topical, etc…
Interval – expressed as one administration every so many hours
Days – number of days for a full treatment. For chronic conditions, write "30"

The above data will be used for cost comparison and is very important for the pharmaco-economic evaluation of the application.

c) **Cost assessment**

Costs are expressed in USD – only this currency should be used. Using USD may facilitate comparisons with drugs available on the international market. The cost assessment of the proposed drug is filled out by the applicant and will be double-checked by the TSC.

Cost/Unit – the cost for one unit of the drug. Clearly indicate the unit for which the cost is given.

Cost/Day – the cost for one day of treatment with the drug.

Cost/Course – the cost for a complete treatment, or for one month's treatment for drugs used in chronic conditions.

The above information is necessary for the determination of affordability. The LDL includes all drugs that are included in the EDL. Drugs on the LDL are commonly prescribed in the private sector, which creates a demand and an implicit expectation that they may be considered for inclusion in the EDL. For this reason, pharmaco-economic data is considered mandatory before deciding to include a drug in the LDL.

d) **Level of evidence**

Indicate for each indication the level of evidence that supports the use of the proposed drug for that indication. The numbers used to indicate the different levels of evidence, in decreasing importance, are:

Ia Meta-analysis: this type of study combines the results of several studies that address a set of related research hypotheses into one study. Ideally should combine results from randomized controlled trials.

Ib Randomized controlled trial (RCT): the patients are randomly allocated to receive either a standard accepted therapeutic or preventive regimen, or an experimental regimen. The purpose of random allocation is to eliminate or minimize bias in the selection of subjects. This greatly enhances the validity of the results. Preferably, the subjects and those observing the trial's results should be unaware of which subjects are receiving the experimental and control regimens The RCT is one of the simplest and most powerful tools in clinical research. Ethical considerations limit the routine application of RCT to all new medicine.

II Controlled study with no randomization: a quantitative, comparative, controlled experiment in which the investigators study two or more interventions in a series of individuals, but without randomization of assigning the intervention. The lack of randomization makes evidence from these trials less convincing than the evidence from a RCT.

III Comparative, correlation or case-control study: can be retro-active or prospective (cohort-study). Basically cases are added as they appear (or as they are found in records), and then a comparison is made between those that followed different therapies. Less convincing evidence, but particularly useful for more rare conditions.

IV Expert committee: expert committees are convened at national or international level to make recommendations on state-of-the-art treatments of diseases. An expert committee formulates an opinion or recommendation, which will be as convincing as the evidence used by the committee to come to that opinion or recommendation

V Clinical experience: the least convincing evidence, clinical experience can be more or less systematically collected.

Section 4: Drugs on the current LDL for the same indication

As a principle, the addition of an LDL item should replace an existing item. This is of particular importance when safety and economic implications are taken into account. For each indication, the applicant will give at least one comparator drug. For new therapeutic classes, this is not required. Details of the comparator drug include:

a) **Drug** – INN (generic name), presentation form and strength.
b) **Indication** – cite (one of) the indication(s) listed in Section 3
b) **Current treatment regimen** – like for the proposed drug
c) **Cost assessment** – the cost assessment of the comparator drugs is done by the TSC
e) **Can be replaced by the proposed drug** – the TSC's conclusion of the comparison between current drug and the proposed drug (Yes/No)

Section 5: Pharmacy Department Only

This section is intended to ensure that the submissions follow the proper process. Dates of steps/decisions will be noted as appropriate. The section will allow the interested parties to quickly review the history of an application.

a) **Correspondence**

Date received – date on which the application was received

Date acknowledged – date on which a message was sent to the initiator confirming receipt

Application for additional evidence – if applicable, date on which a request for more evidence was sent to the applicant. Only one request for more evidence will be sent per application for inclusion. Failure to submit convincing evidence will lead to rejection of the application for inclusion.

Number of articles submitted initially – the number of articles submitted along with the application

Number of articles submitted as additional evidence – the number of articles submitted after application for additional evidence

b) **Advice of TSC** – if "Accept" or "Reject"

c) **Reason for application** – summarizes the reason(s) for the application. More than one option may be circled:

New drug - this is an application for a new drug which is not yet on the LDL

New strength-presentation form – this is an application for a new strength or presentation form of a drug already included in the LDL

New or changed condition – this is an application to extend the use of an existing drug to a condition for which it was previously not used, or the condition it was preciously accepted for has been changed (e.g. split in two or more new conditions)

Change in STG – this an application provoked by a change in Standard Treatment Guidelines or official MOPH protocols

New therapeutic class – this is an application for new drugs that address newly emergent conditions (e.g. HIV/AIDS drugs).

c) **Rejected by NEDLC** – date on which NEDLC rejected the application

d) **Forward to NMB** - date on which NEDLC forwarded the application for final acceptance

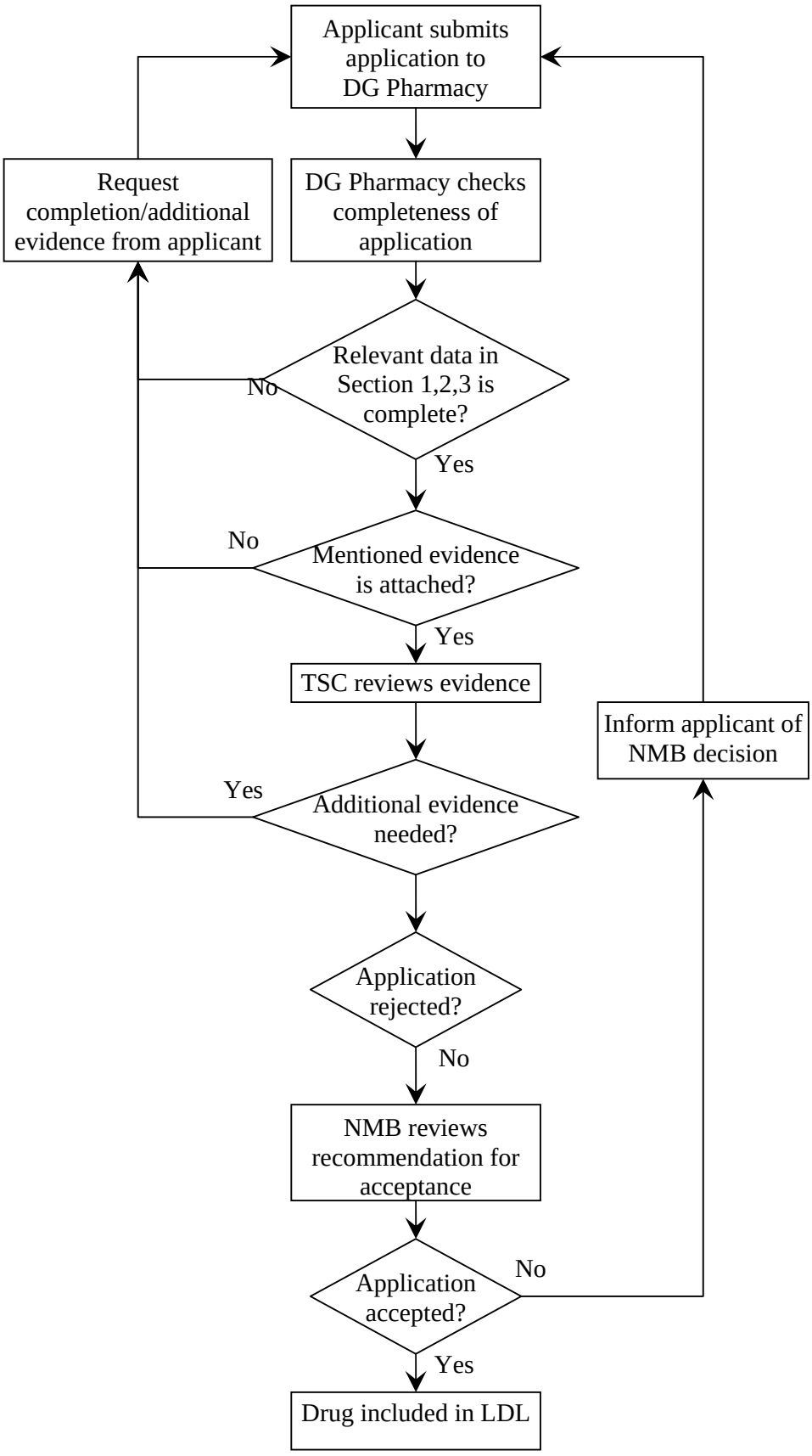
e) **Accepted by NMB** - date on which NMB accepted the drug for inclusion

f) **Rejected by NMB** - date on which NMB rejected the drug for inclusion

e) **Signature and stamp of DG Pharmacy** - (president of NEDLC) and stamp

f) **Signatures and stamp** - signatures of members of the NMB

The applicant will be informed in writing of the final decision.


Applicant submits application to DG Pharmacy
DG Pharmacy checks completeness of application
Relevant data in Section 1,2,3 is complete?
No
Request completion/additional evidence from applicant
Yes
Mentioned evidence is attached?
No
Yes
TSC reviews evidence
Additional evidence needed?
Yes
Application rejected?
No
NMB reviews recommendation for acceptance
Application accepted?
No
Inform applicant of NMB decision
Yes
Drug included in LDL

Notes:

1. Evidence

Evidence is a vital component of the submission and review process. Evidence does not constitute a drug decision and 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*
- *relative safety*
- *pharmacoeconomic benefits*

Evidence needs to be relevant to the Afghan context. Multinational or foreign studies must be supported by a motivation of the relevance of both the outcome measures as well as socio-economic facets to the Afghan context. The inclusion of at least one relevant reference is mandatory.

For application of an existing drug to a new indication, or introduction of a new drug or new class of drugs, a copy of the full journal article should be included in order to expedite the review process.

2. Communication of decision

After processing, the decision regarding an application will be communicated in writing to the initiator. In case of rejection of the application, the exact reasons for rejection will be mentioned.

3. Reconsidering a rejected application

As a rule, a rejected application will not be reconsidered within six months after the rejection. To qualify for reconsideration, compelling additional evidence (see note 1) should accompany the resubmission.

Section 1 – Proposed Drug Identification						**Section 2 - Applicant's details**		
Proposed Drug (INN + form + strength)						Title:	Name:	
						Father's Name:		
Level of Care	BPHS	HP	BHC	CHC	DH	Postal Address:		
	EPHS	DH	PH	RH				
	Special:					Phone:	E-mail:	
Submission Date:						Facility ID:		

Section 3 – Proposed Indications

Indication	Proposed Regimen				Cost assessment			Level of evidence
	Dose	Route	Interval	Duration	Cost/Unit	Cost/Day	Cost/Course	
				days	/			
				days	/			
				days	/			

Level of Evidence: Ia Meta-analysis; Ib Randomized controlled trial; II Controlled study with no randomization; III Comparative, correlation or case control study; IV Expert committee; V Clinical Experience

Section 4 – Drugs on current EDL with the Same Indication

Drug	Indication	Current Regimen				Cost assessment			Can be replaced by proposed drug
		Dose	Route	Interval	Duration	Cost/Unit	Cost/Day	Cost/Course	
					days				
					days				
					days				

Section 5 – For use by Pharmacy Department Only

Correspondence	Date Received	/ /	Acknowledged	/ /	Application for more evidence	/ /
Evidence	Number of Articles submitted initially:		Number of Articles submitted as additional evidence:			
Advice of TSC: Accept / Reject	Reason for application:	New Drug / New strength-form-presentation / New or Changed Condition / Change in Level of Care / New therapeutic class				
Rejected by NEDLC: / /	Forward to NMB: / /	Accepted by NMB: / /	Rejected by NMB: / /			
Signature and stamp of DG Pharm:		Signature and stamp of NMB:				