

Measuring transparency

in the public pharmaceutical sector

Assessment Instrument

Working document for field testing and revision

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Unedited draft

Departments of Medicines Policy and Standards (PSM)
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List of acronyms

COI	Conflict of Interest
CT	Clinical Trials
EML	Essential Medicine List
GCP	Good Clinical Practice
GDP	Good Distribution Practices
GLD	Good Laboratory Practices
GMP	Good Manufacturing Practices
GQCLP	Good Quality control Laboratory Practices
IEC	Independent Ethics Committee
INN	International Nonproprietary Name
IRB	Institutional Review Board
KI	Key Informant
MRA	Medicine Regulatory Authority
NA	National Assessor
NGO	Non-Governmental Organization
NEML	National Essential Medicines List
SOP	Standard Operating Procedure
SPC	Summary Product Characteristics
UNICEF	United Nations Children's Fund
WHO	World Health Organization

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Introduction

Background and rationale

Pharmaceuticals are indispensable to health systems; by complementing other types of health-care services they can reduce morbidity and mortality rates and enhance quality of life. Therefore, access to health-care and essential medicines is increasingly being viewed as a fundamental human right¹. Yet the ability of pharmaceuticals to save lives, reduce suffering and improve health depends on their being of good quality, safe, available, affordable and properly used.

In many countries these conditions are far from being met. It is estimated that today almost 2 billion people (one third of the global population) do not have regular access to essential medicines. In some of the lowest-income countries in Africa and Asia, more than half of the population have no regular access. Furthermore one third of countries have either no regulatory authority or only limited capacity to regulate the medicines market (including registration of medicines, inspections of manufacturers and distributors, or control of medicine promotion). Unreliable supply systems persist, and irrational use of medicines is a major problem worldwide.²

A number of factors contribute to these urgent challenges in the pharmaceutical sector³, including poverty, market failures and government failures. The latter often results, at least in part, from a lack of transparency in the pharmaceutical system⁴– which is *one* of the possible reasons for the medicine gap described above. Lack of transparency in the pharmaceutical system is increasingly becoming an issue of concern because bad practices can waste resources, which in turn reduces the availability of essential medicines and so threatens the well-being of populations.

The pharmaceutical sector and its vulnerabilities

The ‘medicines chain’ involves many different steps. These include: research and development of new medicines; conducting clinical trials; filing patent; their manufacturing; the registration of medicines; selection of essential medicines, their procurement and distribution; inspection of manufacturers and distributors; prescribing; dispensing; pharmacovigilance; and the control of medicine promotion. These are core functions in the pharmaceutical sector. The structures and processes involved in each of these functions must work optimally or access to good quality medicines is compromised.

¹ Hogerzeil HV. Access to essential medicines as a human right. *Essential Medicines Monitor*, 2003;33:26-27.

² WHO Medicines Strategy 2004 - 2007: countries at the core. Geneva, World Health Organization, 2004.

³ Pharmaceutical sector in this document refers to the various actors involved in the area, namely the government, private-for-profit organizations, private not-for-profit organizations, etc., engaged in the research, manufacture, import, export, distribution, retail, etc. of medicines.

⁴ Pharmaceutical system refers to the relationship/interactions between the various actors of the pharmaceutical sector and the way decisions are made in particular in the government.

Each function has different objectives and government has a unique role in each function. For instance, registration is a critical government function ensuring that the medicines registered fulfil quality, efficacy and safety standards. The selection of essential medicines defines government or other institutional clinical and financial priorities for medicine supply, such as determination of limited formularies for reimbursement benefits as part of a health insurance scheme, for example. An effective procurement process ensures the availability of the right medicine in the right quantity, at reasonable prices, and of assured quality standards (medicines may be acquired through purchase or donations). Distribution must ensure that medicines are stored and allocated appropriately, and transported to where medicines are dispensed to patients. Inspection is an important quality assurance activity of the medicines regulatory system whereby staff of the regulatory authority enter premises where medicines are manufactured, stored and distributed to ensure that processes are carried out in accordance with national norms and standards, as well as with national legislation/regulation. Control of medicine promotion will ensure that promotional activities provide accurate information and that material benefits will not be offered to influence the practices of health professionals.

If structures and processes are not transparent and sufficient institutional checks and balances are not in place, each of these functions is vulnerable to corruption. For example, suppliers may bribe government officials to register their medicines without the required information, or government officials may deliberately slow down registration procedures to solicit payments from a supplier. To influence the selection process, special interest groups may offer private incentives to public officials to include particular medicines on the essential medicines list. In the procurement process, suppliers may bribe public officials to gain monopoly positions at the tender stage. Also opportunities for the diversion of goods exist at all stages of the storage and distribution systems.

All these functions need to be protected from unethical or corrupt practices to ensure that patients not only have the medicine they need, but also that the medicine is safe, of assured quality, is sold at a fair price, and has not been purchased or prescribed as a result of undue commercial influence.

Transparency in development work

The World Bank has identified corruption as the single greatest obstacle to social and economic development,¹ keeping millions of people trapped in poverty. Labelled a "cancer" by the same organization, it is a cross-sectoral problem affecting the public and private sectors alike. It also represents a gross departure from fundamental ethical standards.

As mentioned, the pharmaceutical sector is particularly vulnerable to corruption and unethical practices. The commercial reality of the pharmaceutical market tempts the many different - public as well as private - actors involved. The pernicious effects of corruption arise not only from intentional mismanagement by an individual, but also from an inability to identify and ethically manage the conflicts of interest that can occur when institutions and individuals with authority interact. There is also a failure from an organizational position to

¹ <http://www1.worldbank.org/publicsector/anticorrupt/index.cfm>

institutionalize procedures that will prevent corrupt behaviour. Corrupt practices can have a threefold impact:

- a *health impact* as the waste of public resources reduces the government's capacity to provide good quality essential medicines, and unsafe medical products become available on the market;
- an *economic impact* when large amounts of public funds are wasted. Indeed, it is estimated that pharmaceutical expenditures in low-income countries amount to 10-40% of total health-care expenditures,¹ representing potentially major financial loss;
- an *image and trust impact* as inefficiency and lack of transparency reduce public institutions' credibility, decrease donors' trust and lower investments in countries.

Increasingly, aid organizations recognize that, to be efficient and to have long-term impact, development work needs to address lack of transparency and other corruption issues. This is why two of WHO's most recent strategies are committed to improving good governance in the public pharmaceutical sector - the WHO Global Medicines Strategy 2004-2007 and the Regional Strategy for Improving Access to Essential Medicines in the Western Pacific Region (2005-2010). Good governance is currently high on the health research agenda, also. Indeed the Statement on Health Research issued by the Ministerial Summit on Health Research, held in Mexico City in November 2004, identifies as a priority the generation of "relevant knowledge adhering to high ethical standards which can be used to improve the health status of populations in an equitable way."² Transparency International's annual Global Corruption Report in 2006 focuses on the health sector. After almost 10 years' experience in tackling this difficult issue with a cross-sectoral approach, the World Bank is now focusing more specifically on the pharmaceutical sector. In addition, the UK Department for International Development (DFID) has launched a new initiative the Medicines Transparency Alliance (MeTA).

Just as corruption necessarily represents a departure from ethical obligations, transparency is recognized as an essential element of ethical processes for governments (sometimes termed "fair process") as well as a manifestation of such basic human rights as people's right to receive information and to participate in decisions affecting their lives.

The rationale for and development process of this assessment instrument

This document's objective is to help stakeholders carry out assessments to measure the level of transparency and the vulnerability to corruption in selected areas of the public pharmaceutical sector. In order to maximize efforts aimed at improving transparency and good governance, countries may choose to conduct an assessment of the situation to be informed of the depth and extent of the issues, their sources, and their diversity. This document presents an assessment methodology together with a questionnaire for national

¹ WHO Medicines Strategy 2004 - 2007: countries at the core. Geneva, World Health Organization, 2004.

² Report by the Secretariat. WHO Executive Board document EB 115/30, and World Health Assembly Resolution WHA58.34.

assessors to systematically collect information and perceptions through interviews of relevant health professionals in the public and private sectors.

The questions are largely based on earlier work by Cohen, Cercone and Macaya.¹ They have been revised according to existing WHO technical guidelines and have been expanded to include four more regulatory functions: control of medicine promotion, licensing, control of clinical trials, and inspection. Earlier versions went through rounds of field testing and revisions from 2005 to 2007 in 19 various countries from all regions. A comparative analysis of the first round of testing has been published². It is expected to keep the methodology under review in light of experience gained in countries, to revise this document on a regular basis and possibly to expand it to additional functions of the medicine chain.

Additionally, the questions included in this assessment instrument are in line with and complementary to other existing tools aiming to assess various elements of the pharmaceutical sector, such as the WHO Data Collection Tool for Review of National Regulatory Systems.

Transparency assessment: entry point to Good Governance for Medicine programmes³

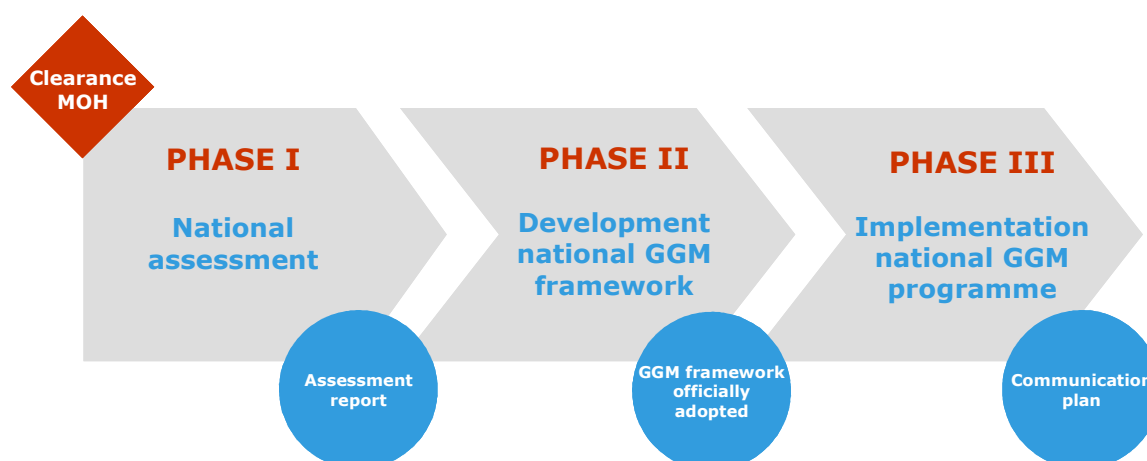
Assessing transparency and potential vulnerability to corruption is not an end in itself. Following the national assessment, the basic components of the GGM programme need to be defined through a nationwide consultation process with key stakeholders and based on experience accumulated in various countries. These components can include: an ethical framework and code of conduct, collaboration mechanisms with other good governance and anti-corruption initiatives, whistle-blowing mechanisms and a GGM implementing task force.

WHO has identified a three-step approach in promoting Good Governance in the pharmaceutical sector, which gives a framework to the project. How these steps are applied can be adapted to suit the specific country situation.

¹ Cohen JC, Cercone J, Macaya R. Improving transparency in the pharmaceutical system: the case of Costa Rica. Unpublished World Bank document, 2002.

² Measuring transparency in medicines registration, selection and procurement. Four country assessment studies. Geneva, World Health Organization, 2006. (WHO/PSM/PAR/2006.7).

³ <http://www.who.int/medicines/ggm/en/>



Content of the assessment instrument

This document presents an overall introduction to the assessment methodology, including how to select national assessors (those who will conduct the assessment) and key informants (those who will be interviewed). It provides best practices for each function, detailed comment for each indicator, describing the rationale for asking the question, a description of the information sought and the way to interpret the results. It includes also a glossary as many terms can be new to national assessors and an annotated content list for drafting the final assessment report.

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Overview of the assessment

Objective

This assessment has been designed to provide countries with a picture of the *level of transparency* and *vulnerability to corruption* in the procedures and structures of eight functions of the pharmaceutical sector, namely:

1. *registration* of medicines
2. *licensing* of pharmaceutical business
3. *inspection* of establishments
4. *medicine promotion*
5. *clinical trials*
6. *selection* of essential medicines¹
7. *procurement* of medicines
8. *distribution* of medicines

The purpose is to probe perceptions of pharmaceutical policy makers and other stakeholders about transparency in a given pharmaceutical system. While this methodology is not exhaustive, it should be viewed as a starting point for investigating weaknesses as well as strengths in a particular pharmaceutical system.

Assumption

Effective functioning of a pharmaceutical system is dependent on transparency of the processes and ability to hold individuals and entities accountable for adhering to standard procedures, norms, laws and regulations in each one of these functions.

There are many different definitions of transparency in the literature. Essentially it means openness in sharing information and that information is publicly and easily accessible for those who need it. Moreover, it is widely agreed that transparency reduces the scope for corruption. Thus the basic assumption is that *the more transparent any system is, the less vulnerable to corruption it will be*.

This tool, based on this assumption, seeks to assess the presence of key documents and procedures necessary to manage pharmaceutical systems, and whether pharmaceutical policy-makers, regulators and managers are aware of their existence. The presence of publicly available and easily accessible documents is considered a sign of transparency and thus the existence of such documents reduces the vulnerability to corruption. On the contrary, their absence will show gaps in the systems that need to be filled in order to make them more resistant to corruption. Likewise, the awareness about the existence of these documents and procedures suggest that they are used and is again a sign of transparency.

¹ The process for selecting essential medicines is similar to the one used for selecting a reimbursement list for insurance purposes, although the objectives are quite different. In some countries measuring the level of transparency in the selection process of medicines for a reimbursement list may be more relevant than doing this for the essential medicines. In such case, the questions included in section 4 of this document "selection of essential medicines" can very well be adapted for the purpose.

On the contrary, a lack of awareness about their existence means that they have not been sufficiently disseminated, that they are not systematically used and there are still some loopholes in the pharmaceutical system that need to be filled.

Methodology and intent

The methodology used in this assessment is not intended to provide only quantitative measurement but rather to collect qualitative information on structural indicators and perceptions by interviewing key informants using a set of questionnaires. The theoretical basis for assigning scores assumes a reverse relation between transparency and vulnerability to corruption. The instrument's underlying hypothesis is thus that high transparency corresponds to low vulnerability to corruption and vice versa (see assumption above).

The instrument is designed for *national assessors* to conduct *semi-structured interviews* and assess the level of transparency in their countries. It provides a list of questions to be answered by *key informants*. Each question is presented in detail in sections 1 to 9, describing the rationale for asking these questions, the information sought and finally some guidance on how to interpret the responses. This methodology should always be tailored to fit particular circumstances and country needs.

Interviews should be loosely structured, based on the list of questions to be discussed (see questionnaires on pages 111 to 157). The method provides information directly from people knowledgeable about the subject; is flexible in that it can explore new ideas; and is generally inexpensive to conduct.

The instrument aims to provide a basis on which to *open dialogue* and further discussion among stakeholders including policy makers with the intention of promoting good governance and enhance the integrity of management practices in the public pharmaceutical field. The instrument does not attempt to measure corruption in a given country.

Moreover, it is important to remember that the *indicators are not unequivocal signs of corruption*. However, they can be used as “red flags” to help policy-makers detect if and where there may be corruption in the pharmaceutical sector, so that further investigation can take place or remedial actions can be implemented. This is done by looking at the level of transparency which is done by using this instrument. In this way access to good quality medicines can be improved.

The scores generated in the assessment are intended for use in conjugation with the qualitative aspects of the questionnaires including the views of key informants, the notes of the national assessors, the evidence obtained throughout the study and other existing empirical evidence. They are not intended for use as a standalone rating method for countries' transparency/vulnerability to corruption.

Box 1 Measuring transparency and institutional weaknesses

Identification of corrupt practices in the pharmaceutical sector can be difficult for a number of reasons. One is that it can be difficult to differentiate corruption to inefficiencies. Corruption can be disguised by inefficiencies and inefficient systems can foster corruption inadvertently. Secondly, people who are being interviewed may be reluctant to admit corruption exists because of fear of retaliation, punishment or shame if directly implicated themselves. Thirdly, corruption is often not documented and thus hard to prove. With this in mind, the series of questions for KIs is intended to help reveal institutional weaknesses in the pharmaceutical and therefore practices that may be susceptible to corruption. The point of these questions is to highlight which practices are working well and which could benefit from reform. The questions are not designed to accuse any person, institution or government agency. Even if corruption is evident in one area it may not occur elsewhere in the pharmaceutical sector.

Key steps prior to assessment**1. Clearance from the Ministry of Health**

It is critical that before starting the assessment and setting up any meeting with key informants, there is clear “buy-in” from the relevant political officials. This involves some initial groundwork before launching the interview process. It will mean briefing senior level officials in the Ministry of Health ideally, the Minister of Health, and other relevant institutions. Clear support should be sought by way of an official letter from the institutions, which sanctions and supports the interview process and encourages officials to participate in the process. This may encourage participants to be more open to meetings and to be more forthcoming during the interview process.

2. Selection and role of national assessors

Two national assessors (NAs) should be selected upon clearance from the Ministry of Health and based on WHO recommendations described below. To ensure objective interpretation of the results, NAs will need to be *from an independent group* outside the Ministry of Health. Ideally they should be senior professionals coming from an academic institution (pharmacy, medicine, etc.), a research institute, a nongovernmental organization (NGO) or a consulting firm. If resources outside the Ministry of Health are not available, then the NA selected should not be directly involved in carrying out any of the functions under review. In any case, they should be *impartial and with no conflict of interest* (COI). Also, to ensure complementarities in perspectives, it is preferable that the NAs are selected from two different institutions and from two different professional backgrounds, although this will not always be possible.

The two assessors will manage the whole assessment exercise. After being introduced to the use of this assessment methodology and the accompanying tools, they will plan the meetings with the key informants, carry out the interviews, compile and analyse the results, and write a report describing the findings of the assessment. An example of the detailed terms of reference for the NAs is included in annex 1.

Selection of key informants

Key informants (KI) are people who *have special knowledge and interest* in the pharmaceutical sector. They will be selected based on their first hand knowledge about the subject and/or their level of involvement in the pharmaceutical sector. The KI should be a

mix of senior, middle managerial and junior level personnel and represent various institutions to get a *multi perspective* answers to the questionnaire. They may include government officials, representatives of the private sector, and of non-governmental organizations, and others with relevant involvement in the pharmaceutical sector. However, not all KIs need to be from the pharmaceutical sector, as it would also be helpful to have cross-checks from KIs active in other areas, such as finance, the judiciary, other organizations that have previous or current interaction with them.

Experience has shown that *10 to 15 interviews for each function* is an optimal number but this may vary according to situation and section. The larger the number of interviews the better, so that more answers could be compared. If fewer interviews are undertaken, an incomplete or biased assessment may result. The goal is to interview enough people until "*saturation*" can be reached (NAs find that no new information is coming from the interviews).

Some KIs *can be interviewed in several functions* and their responses will be tabulated as part of the final score of each function. However, they can only be counted once in the final tally of total KIs. In this way, a minimum number of total KI for the assessment cannot be provided.

Box 2 Suggested list of contact sites for KI interviews

- Ministry of Health (e.g. health service department, pharmaceutical units, national programs for disease controls, medical stores, procurement division, etc.);
- Medicine Regulatory Authority (registration, inspection, control of promotion, licensing and clinic trial units/departments, etc.);
- Procurement agencies, importers and distributors both from the private and the public sector (including tertiary care hospitals, primary-care facilities, pharmaceutical brokers and consolidators, hospital pharmacists, etc.);
- Members of committees such as tender committees, therapeutic committees, selection of essential medicines committees in national and local level;
- Ministries of Finance, Industry and Commerce, Customs and Importation;
- National Quality Control Laboratories;
- Audit departments (internal, external, and state auditors);
- Pharmaceutical industry (multinationals and national) and associations;
- Non-governmental organizations, such as those engaged in health service activities, patient advocacy groups, "watch-dog" organizations;
- International donor organizations, such as WHO, UNICEF and the World Bank
- Academic institutions (national colleges, state universities and research institutes);
- Professional associations (medical association, pharmacologist association, biochemist associations, etc.);
- Media (if knowledgeable about the pharmaceutical sector);
- Ethics committees, institutional review boards.
- Health insurance funds

Interviews of key informants

All participants must be informed about the objectives of the exercise and be contacted officially in writing by the NAs to request an interview (for an example of a model letter see annex 2). It is essential that the responses be kept *confidential and anonymous*, and that participants are assured of this in advance. Files should be kept in a secure location and

locked with numbers and not names assigned to each key informant. After the study is completed and after a reasonable amount of time, could be about 2 years, the files should be destroyed to ensure no breaches of confidentiality take place. Ideally, key informants should sign a consent form which is a standard procedure for any type of research involving human subjects. This consent form acknowledges the confidentiality of the interview as well as ensures that the interviewee is aware that he or she is not obliged to answer any question(s).

Equally important is that questions must be posed in a non-threatening manner. The aim of this exercise is to determine institutional weaknesses and strengths in the pharmaceutical sector so that the appropriate follow-up action can be taken by governments to improve pharmaceutical sector performance in their country.

The semi-structured interviews will generate data that are qualitative as well as quantitative. The questions in the questionnaires deal with structural and process indicators and the extent to which each KI is aware of the existence and application of these indicators. Some other questions capture KIs' perceptions regarding the transparency of the process, and so some of the replies will be subjective.

It is very important, especially for open-ended questions (method 4), to write down exactly what the KI says to avoid subjective interpretations or erroneous translations. It may be useful to use the *probing technique* whenever you feel that the KI is reluctant to give an answer or does not understand the meaning of the question asked. The probing technique requires to allow the KI time to think for a while without interruption (the assessor will need to show patience), then try to help by asking the question in another way (without putting words in the mouth of the KI), or giving examples. For instance, after asking the following method 4 question "in your opinion, what unethical practices are observed in your country?", if the KI does not give an answer after some time, probing can be done using examples on unethical behaviour such as bribery, material gifts, favouritism, COI, political affiliation.

Tips for national assessors

Selecting key informants

- Choose the KIs well (they should be involved in or knowledgeable about the pharmaceutical system)
- Interview as many KIs as possible to enhance the study results
- Remember that these interviews are a learning opportunity for key informants as well
- Plan a wider list than needed, as some KIs will not be available

Preparing for the interviews

- Good preparation is crucial and will make the whole assessment process easier
- Plan a meeting with key officials to brief them on the assessment and ask for key documents under review in this assessment
- Collect in advance as much evidence as possible, it will be useful for you to have the information already while conducting the interviews
- Adapt questionnaires according to the country's system
- Study well all questions and be ready to explain them in more details to KIs

Conducting the interviews

- First remind KIs about the objectives of the exercise.
- Present to the KI a copy of the Ministry of Health clearance.
- Emphasize of the confidentiality and anonymity of their responses
- Reassure participants that questions are not designed to indict or accuse anyone

- Ask questions in a non-threatening manner
- Use "what" and "how" when asking questions, and never "why" as the latter implies the need for a justification
- Two NAs need to be present during each interview
- Take as many notes as possible during the interviews
- Explain questions that are not clear for KIs
- Use the probing technique in open ended questions.
- If a KI is not feel comfortable to use tape recorders, it is necessary to take notes literally to avoid subjective interpretation of what he/she meant

After the interview

- Score results immediately while the discussions are still fresh in the NAs' minds
- Review all notes and complete as needed
- Keep all data strictly confidential and anonymous

Rating indicators and interpretation guidelines

Four methods are used to determine the level of transparency. However only methods 1 and 2 are used to score the vulnerability to corruption for each function, and they are given equal weight in the final scoring. Method 3 allows comparison of the existence of legal provisions, or administrative structures and procedures, with their perceived application. Method 4 use open-ended questions to capture additional information that may not be collected through the questionnaire.

Method 1:

The knowledge of KIs on the presence and absence of publicly available documents is assessed. In order to minimize the subjective interpretation of respondents' answers, the first method consists of a series of questions that require a binary answer (yes/no). Further, interviewers must request documents from key informants in order to validate positive responses.

In this methodology, a "yes" (existence of a document) is given a value of 1 and a "no" (document does not exists) is given a value of 0. A value of 1 represents low vulnerability to corruption (so long as it is supported by the existence of a publicly-available document that describes the process or decision criteria). On the other hand, a rating of 0 represents high vulnerability to corruption, since the absence of a standardized process or documented decision criteria provides decision-makers and others with broad discretion that may be abused.

In summary:

- When the KI responds "yes" and the evidence is found, the score is 1
- When the KI responds "no" and the evidence is found, the score is 0
- When the KI responds "yes" and the evidence is not found, the score is 0
- When the KI responds "no" and the evidence is not found, the score is 0

Method 2:

This method involves questions and a series of sub-questions or criteria. Each of these criteria is formulated to require a binary answer (yes/no). Similarly to method 1, each "yes" is given a 1, and each "no" a 0. If the KI does not know the answer, there is the option of

assigning "D.K." (Don't know). The total "yes" answers are counted and divided by the total of valid answers. The total of "D.K." answers are subtracted from the total of criteria available for each indicator, which will give the total of valid answers. The final rating for the indicator is the total of "yes" responses divided by the total number of valid answers.

For example, indicator 3 "Are there written procedures for applicants on how to submit an application for registration of medicinal products?" includes seven criteria. Let's assume that, based on the answers given by a KI, the NA will fill in the box containing the criteria as follows:

	No	Yes	D.K.
Written procedures	0	①	
Publicly accessible	0	①	
Describe the process to follow in submitting an application	0	①	
Mention timeframe for processing	②	1	
Mention fees	0	①	
Mention data to be submitted	0	1	✓
Mention criteria for registration	0	1	✓
Total			

The scoring of the indicator will then be calculated as follows:

Total yes	4
Total valid answers	5
Scoring (total yes/total valid answers)	0.8

In this type of calculation, each indicator is rated between 1 and 0. As with the method 1 indicators, a value of 1 represents low vulnerability to corruption (so long as it is supported by the existence of a publicly-available document) and a value of 0 represents high vulnerability to corruption. However a figure between 0 and 1 is also feasible in this case.

However if a KI answers "D.K." for the majority of the criteria, then the whole response for that particular indicator and that particular KI will be counted as invalid and will not be taken into account the final scoring. Indeed a majority of "D.K." may give a completely distorted picture of reality.

Method 3:

These are subjective questions which probe the perceptions of the KIs. Asking for their perception provides valuable insight on the transparency level of each of the functions. This method is used as a cross-triangulation technique to verify or refute the data collected with methods 1 and 2.

It is important to remember that *these may be sensitive questions*, and the KI may feel uncomfortable and hesitate to give spontaneous answers. Before asking such questions it may be useful to remind and reassure KIs about the confidentiality of their answers.

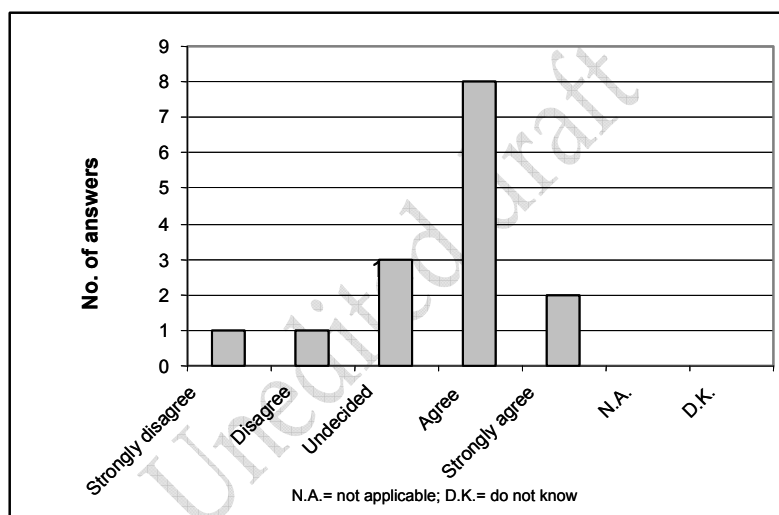
The questions, using the Likert Scale, begin with a statement and the KIs are then asked whether they strongly agree - agree - is undecided - disagree or strongly disagree. For

example, indicator 11 asks the KI to what extent he/she agrees with the statement “The members of the registration committee are systematically selected based on the criteria in force in their country”. The NAs will then tick the answer given by the KI in the box on the questionnaire. For example, after interviewing 15 KIs the following results are obtained:

Answers	Strongly disagree	Disagree	Undecided	Agree	Strongly agree	N.A.	D.K.
Total	1	1	3	8	2	0	0

One way to present this information is to determine the range of results from the KIs using a bar chart as illustrated below. In the example it can be concluded that 10 out of the 15 people interviewed (or 67%) agreed or strongly agreed with the statement, and that in general there was a positive perception of the selection process for the registration committee members. Additional information obtained during the interviews with the KIs who disagreed with the same statement can be added in the narrative text in order to present all perspectives.

Bar chart showing the range of perceptions of key informants



Method 4:

These questions are open questions, and give the opportunity to KIs to provide additional input on the function in general. These contributions will be valuable for the NAs particularly at the time of writing the report and in order to make recommendations for action. They can also capture perceived types of corrupt or unethical behaviour that undermine a well-functioning system. The answers to these questions will not be taken into account in the calculation of the score for each function. They are however important qualitative information, as they will be taken into account in the narrative part of the report and can help confirm findings from methods 1 and 2.

Scoring of each function

Once all of the interviews are completed, a score will be calculated for each function (registration, licensing , inspection, promotion, clinical trials, selection, procurement and

distribution). This final score will be calculated from only those indicators using methods 1 and 2, with the help of score sheets included in Annex 5 (1 score sheet for each function).

First, for each indicator (using methods 1 and 2) an *average rating* should be calculated. This will be calculated by adding all the rates for each indicator and dividing the total by the number of valid answers (remember to always disregard the non-valid answers such as "don't know" or "not applicable"). The average rating for each indicator has a possible range between 0 and 1.

Then, the sum of all the average ratings (for all indicators using methods 1 and 2) is divided by the number of indicators in a given function to obtain the percentage of indicators rated as 1. The resulting percentage is then converted to a 0 to 10 scale by multiplying the resulting percentage by 10, as shown in the example below.

Example: There are 12 indicators related to medicine registration using methods 1 and 2. If the total of the average ratings amounts to 8.60, then scoring for registration will be calculated as follows:

1. $8.60/12 = 0.716$
2. This would then be converted into the 10-point rating system by multiplying 0.716 by a possible rating of 10: $0.716 \times 10 = 7.16$ (corresponding to 'Marginally Vulnerable').

The 10-point rating system is used to indicate the following degrees of vulnerability to corruption:

0.0 -2.0	2.1 -4.0	4.1-6.0	6.1-8.0	8.1 – 10.0
Extremely vulnerable	Very vulnerable	Moderately vulnerable	Marginally vulnerable	Minimally vulnerable

The average rating of responses to individual questions is converted to a 10-point scale for the group average in order to analyse and compare the degree of susceptibility to corruption among the different functions, as well as between functions in different health-care systems. These final numbers are designed to help determine the level of transparency in each function.

The theoretical basis for assigning scores assumes a reverse relation between transparency and vulnerability to corruption. The instrument's underlying hypothesis is thus that high transparency corresponds to low vulnerability to corruption and vice versa.

This quantitative information will be completed in the narrative report together with additional qualitative information related to indicators using methods 1 and 2 that may be shared by KIs during the discussions. The qualitative information collected with the indicators using methods 3 and 4 will also be included.

It is important to keep in mind the value of the qualitative information collected using this methodology. The focus is on learning where the loopholes and institutional weaknesses are, rather than concentrating too much on accurate quantification.

Cross-comparison of indicators

A critical part of the analysis is to compare the results of the indicators assessing the same information but with different methods. For example, indicator I.8 "Are there clear written criteria for selecting the members of the committee" (method 2) assesses the transparency of the procedures adopted to select the members of the registration committee. Indicator I.11, however, "to what extent do you agree with the following statement: the members of the registration committee are systematically and objectively selected based on the written criteria in force in your country" asks for the KI's perception of the application of these selection criteria. It could very well be that in some countries the procedures are in place, and so they will score high with indicator 8, however they are not systematically used, and will score low on indicator 11.

The following table provide a list a comparable indicators, which can be used in the analysis part of the assessment, as well as in the final assessment report.

Table 1 Comparable indicators

Method 1 & 2 indicators	Method 3 indicators
I.8 and I.9	I.11
I.10	I.14
II.3, II.4	II.11
II.6	II.13
III.5, III.6	III.10
III.3, III.6, III.7, III.8	III.11
IV.1	IV.11
IV.3	IV.12
---	IV.13
IV.4	IV.14
V.9	V.13
V.6	V.14
V.1, V.2	V.15
VI.10	VI.2
VI.8, VI.10	VI.6
VII.7	VII.9
VII.1, VII.8	VII.14
VIII.1	VIII.2
most questions (e.g. VIII.6, VIII.8, VIII.11, VIII.16)	VIII.18

Complementary to other methods and assessment tools

This methodology may be complemented with other methods, such as surveys and focus group discussions, as well as other WHO assessment instruments. It is crucial that the findings from these interviews are triangulated with empirical evidence where possible using different methodological approaches, such as objective - outcome based - data to help corroborate or reject findings.

WHO Assessment instruments complementary to this one include:

- WHO Operational package for assessing, monitoring and evaluating country pharmaceutical situations: Guide for coordinators and data collectors (in press)
- WHO Data Collection Tool for Review of National Regulatory Systems
- Medicines Prices: a new approach to measurement
- Questionnaire for Mapping Partners and Financial Flows to Support Medicines Procurement and Supply Management Systems in the Public Health Sector
- Questionnaires for assessing the functioning of national medicine supply agencies

Adaptation to national context

Each country has its own - often unique - systems for managing their pharmaceutical sectors. Countries are also at different levels of development in their pharmaceutical sectors. The methodology is designed in modular way to allow its users to select what areas are most relevant to them. It can also be supplemented for more complex pharmaceutical systems. It is not intended to be a “one-size-fits-all” approach.

Accordingly, some questions or even whole sections may not apply to a certain country. Some questions will need to be adapted based on the nuances of the country's systems and structures. (i.e. presence of a committee instead of a division; presence of a group of responsible people instead of a formal committee; existence of an Ethics committee instead of Institutional Review Board; National Medicine Formulary instead of EML).

It will be the responsibility of the national assessors to adapt the document to their national context prior to (or within the early stages of) conducting the interviews with key informants. Such changes should be clearly stated in the methodology section of their reports.

Limitations

Corruption is a highly sensitive issue. Although the instrument is designed to assess transparency of the system and its vulnerability to corruption, and does not attempt to identify either corrupt practices or those involved in them, it may still be difficult to get *straightforward answers* from KIs or even *appointments* with some. This may limit access to a well balanced list of available KIs.

In some cases a system might not be transparent and not corrupt at the same time. Likewise, a system may have the elements of transparency in place and still have corrupt practices. This would not be reflected in the quantitative indicators but would be addressed in the qualitative indicators measuring the perceptions of KIs and the notes and observations of the national assessors.

Scores may give biased results if KIs are not selected carefully, their findings may be difficult to validate, and interviewer's biases can affect outcomes. *Results will depend on KI's level of knowledge, their awareness of the system and their accuracy/openness in responding to the questions.* The comparison of method 1&2 indicators to corresponding method 3 questions (see Table 1) attempts to minimize this bias. NAs will also need to validate the information on structural indicators with existing evidence in the country (e.g. by finding and checking

documents), and compare the evidence found with the replies of the KIs in the narrative part of their reports.

In some countries human resources with knowledge of the pharmaceutical sector are limited in number and the NA may not *find enough KIs* to complete the questionnaire in certain functions. This should be clearly stated in the methodology section of the report and highlighted in the description of each function.

Furthermore, based on experience in the field, this methodology may generate findings that are *not consistent with outcomes*. In all cases, the findings from the tool should be *triangulated* with other data to determine what information is reliable and to generate policy dialogue about why perceptions of key informants are inconsistent with outcomes. It is also important to note that in the *process of translation*, some inaccuracies may occur. This demands careful attention about how the tool is applied in a country setting.

Unedited draft

General and background information

National anti-corruption efforts

Corruption is a world wide problem affecting both developed and developing countries. Consequently, most countries of the world have formulated different strategies to address the problem of corruption. Examples of such efforts include:

- signing of the UN Convention against corruption;
- signing of the UN convention on human rights;
- promulgation of a national anticorruption law;
- creating a national anticorruption commission;
- enactment of a national law on freedom of information and association;
- a national law on whistle blowing and the protection of whistleblowers;
- formulation, publication and dissemination of ethical principles for civil servants;
- formulation of a code of conduct for civil servants;

Therefore prior to undertaking assessment of the public pharmaceutical sector, it will be necessary to gather general information on the types of measures the government has put in place to address the problem corruption at national level.

Medicine regulation and essentials for good practice

Medicine regulation involves a set of mutually reinforcing regulatory measures, legal, administrative and technical, which governments take in order to - ensure the safety, efficacy and quality of medicines as well as the relevance and accuracy of product information, and to promote fair trade in medicines.

In order to ensure that the goals of medicine regulation are achieved, governments in each country, establish by legislation a national medicine regulatory authority(ies) to regulate medicines. Such a medicine regulatory authority should have at least the following essentials in place to carry out its mandate.

Legislation

Legislation forms the basis for medicine regulation. It gives the authority(ies) power to regulate medicines. Legislation must be comprehensive and enforceable. In general it must:

- Define the type of medical products to be regulated
- State the areas and activities to be regulated
- Create the authority(ies) responsible for regulating the medicines
- Define the roles, responsibilities, rights and functions of all parties involved, including the regulators and those regulated.
- Establish the administrative structure (organization structure) necessary for the implementation of medicine regulation
- Set the standards to be applied in regulating medicines

- Set the terms and conditions under which licenses to import, manufacture, export, distribute, sell, supply and promote medicines will be issued, suspended, revoked or cancelled,
- Define the administrative measures and legal sanctions to be applied when provisions of medicine legislation are violated, and,
- provide to the executive branch of the government the power to formulate the detailed requirements of medicine regulations for the implementation of the legislation, etc.

Regulations

Once legislation is enacted it is necessary to formulate specific regulations which will enable the authority(ies) to implement the provisions of the legislation and carry out the different functions. Examples of such regulations include:

- Regulations for licensing of pharmaceutical establishments
- Regulations for the registration of medicines
- Regulations for the control medicine promotion and advertising
- Regulations for inspection of premises and activities
- Regulations for control of clinical trials, etc.

Official organizational chart (Organigram)

A national regulatory authority(ies) should have an official organizational chart. Such a chart should show the various divisions/departments within the authority that are responsible for the different activities. It should also provide the names of the officials supervising the divisions/departments and the contact address for each. The presence of an official organizational chart will help to make the regulatory system more transparent and show who is accountable for whom and for what. It will also enable clients to know who is responsible for what.

Quality management manual (framework)

The authority should develop a quality management manual which defines the vision, mission and objectives of the authority as well as the responsibilities, policies, procedures, processes, standards, and resources required to deliver quality medicine regulatory services. The manual should outline the day to day principles (customer focused, leadership, staff empowerment, process approach, systematic approach to management, evidence based decision, etc.) and values that guide the organization for better performance of its services, and the ethical principles to be followed by staff. It should have staff development programme and staff recruitment guideline.

Qualified and trained staff

Medicine regulation is a policy, legal, scientific and technical matter that requires people with specialized knowledge and skills to manage it. Staff must be qualified and trained people with integrity and should be paid well, particularly since medicine regulation involves various stakeholders with commercial interests. There should be code of conduct for staff and they should sign conflict of interest form. Recruitment and promotion of staff must be based on merit and there should be written criteria for recruitment. There should be mechanism for human resources development and mechanisms to empower and motivate staff.

Tools

Appropriate standards, guidelines and procedures should be developed and used as tools for the application of all regulatory processes. Tools should be developed in consultation with all stakeholders, printed and made easily accessible to all stakeholders including the public in order to increase the transparency of the authority's operation. The same standards and guidelines should be applied to all clients. The presence of such tools helps to make the process of regulation more transparent and application of regulatory decision less erratic.

Appeal and complaint system

The authority should establish appeals system for clients as well as public complaint mechanism. There should be both administrative and legal appeals system for clients to ensure that there is rule of law and fairness in the regulatory decision making process. Medicine regulation is societal function therefore should be open to societal scrutiny. One way of achieving this is by establishing a public complain system. The presence of appeals and complaint systems ensures that there is transparency and accountability in the system.

A two way-communication system

There should be a two-way (vertical as well as horizontal) communication system within the authority to ensure that there is transparency within the authority. The task of the authority is to protect the public. Its operations must therefore be transparent to both clients and consumers. The authority should establish a routine communication system with clients and consumers. Decisions made by management, minutes of meeting, etc should be easily accessible to all stakeholders including staff.

Audit, monitoring and evaluation system

In order to ensure that objectives set are achieved, the authority should have an internal monitoring and evaluation system. There should also be external audit or peer review system to provide independent opinion on how the system is operating and its weaknesses and strengths.

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Section I: Medicines registration

A) Overview on medicines registration

1. Introduction

Registration of medicinal products (marketing authorization or product licensing) forms one element of the medicine regulatory control system in a country. It is a procedure of release of a medicinal product for marketing after it has undergone a process of evaluation in order to determine its safety, efficacy and quality and the appropriateness of the product information. Its purpose is to provide a system which ensures that only products which have been duly authorized by the national medicine regulatory authority are allowed to be manufactured, imported, distributed or sold/supplied to consumers. In addition, medicine registration may also have additional objectives. Examples are:

- to rationalize medicines on the market in accordance with the prevailing disease patterns;
- to promote competitive conditions from the point of view of quality and price;
- to promote rational use, and
- to facilitate the formulation of essential medicines list, and national formularies.

Registration alone cannot provide adequate safeguards for the supply of safe, effective and good quality medicines. It needs to be supported by suitable inspection and quality control laboratory, and pharmacovigilance services and there should be adequate controls at all stages in the manufacture and distribution of medicines until they reach the end user. For the registration process to be effective the following are essential.

2. Registration essentials

a) Legal basis

There should be provisions within the medicine legislation:

- requiring the registration of medicinal products
- defining the types of medicinal products that should be registered and medicinal products that should be exempted
- requiring defining the criteria for registration of products
- requiring renewal of applications for marketing authorization
- listing requirements for handling variations
- dealing with exemptions to marketing authorization
- setting time limits for processing applications
- setting the fees for registration
- identifying the information that must be publicly released
- defining the appeals system.

b) Written guidelines and procedures

There should be written guidelines and procedures for registration. Such guidelines and procedures will help staff of the registration unit to understand their role in the process. It will also enable applicants to understand the process and the requirements to be met. The

Medicine Regulatory Authority (MRA) should develop and disseminate the following to stakeholders:

- Standard application form for submission of applications
- Guidelines on data and information to be submitted in support of application for marketing authorization (format and content)
- Written criteria for approving a medicinal product for marketing (registration)
- Guidance on exemptions and fast track registration
- Terms of reference and operating procedures for external experts
- Guidelines for assessors on how to assess applications
- Guidance giving instructions, in which situations inspections (all kinds) are organized to verify the data
- Procedures for data archiving, data confidentiality and release for the public
- procedures requiring active monitoring of adverse medicine reactions and reporting findings to the MRA
- Standard format for assessment report
- Guidelines on timeframes for processing applications
- Written criteria for selecting external experts
- Guidelines on meeting with applicants
- Guidance on content of product information leaflets
- Guidelines on conditions attached to issued marketing authorization e.g. validity, post-license trials, prescription only medicine, pharmacy only medicine, etc.
- Guidelines on conflict of interest
- Code of conduct for external experts and internal staff
- Procedures for independent appeals systems
- Certificate of registration/marketing authorization

All guidelines, procedures and guidance materials should be printed, published and made easily accessible to all interested parties. Where possible they should be posted on the MRA website.

c) Qualified and experienced persons

Decisions concerning quality, safety, efficacy and product information should be made by persons with suitable knowledge, training and practical experience of the subject. The MRA should have adequate number of staff with diverse qualifications, such as pharmacy, chemistry, clinical pharmacology, medicine, law. Where such staff is not available internally, the MRA should use external experts with the necessary qualification, technical skills and work experience. Both external and internal persons should sign conflict of interest declaration form and should be fully briefed on written code of conduct.

d) Premises and facilities

Data submitted by applicants need to be stored with sufficient security. There should be adequate office space for staff to store dossiers and related documentation. There should be secured access to computers, Internet, Intranet and other communications systems.

3. The process of assessment for marketing authorization

The process of assessing applications involves the following steps:

- Submission of application dossiers by applicant

- Checking submission for completeness by responsible person within the registration unit
- Entering application into registry book and issuing receipt
- Pre licensing inspection of manufacturing site
- Testing of samples and validation of test methods
- Submission of inspection report and quality control report
- Review of dossiers, inspection report and analytical report by committee of assessors
- Approval/rejection of product for registration by assessors
- Giving decision in writing with reason to applicant
- Posting/publishing registered product on the national Gazette or website together with essential information and making them accessible to all interested parties and the public.
- Appeal by applicant in case of rejection
- Decision of appeals body to applicant and the Medicine Regulatory Authority
- Exceptions (fast track, other medicines, etc.)
- Data archiving and making selected non-confidential information available to the public, etc

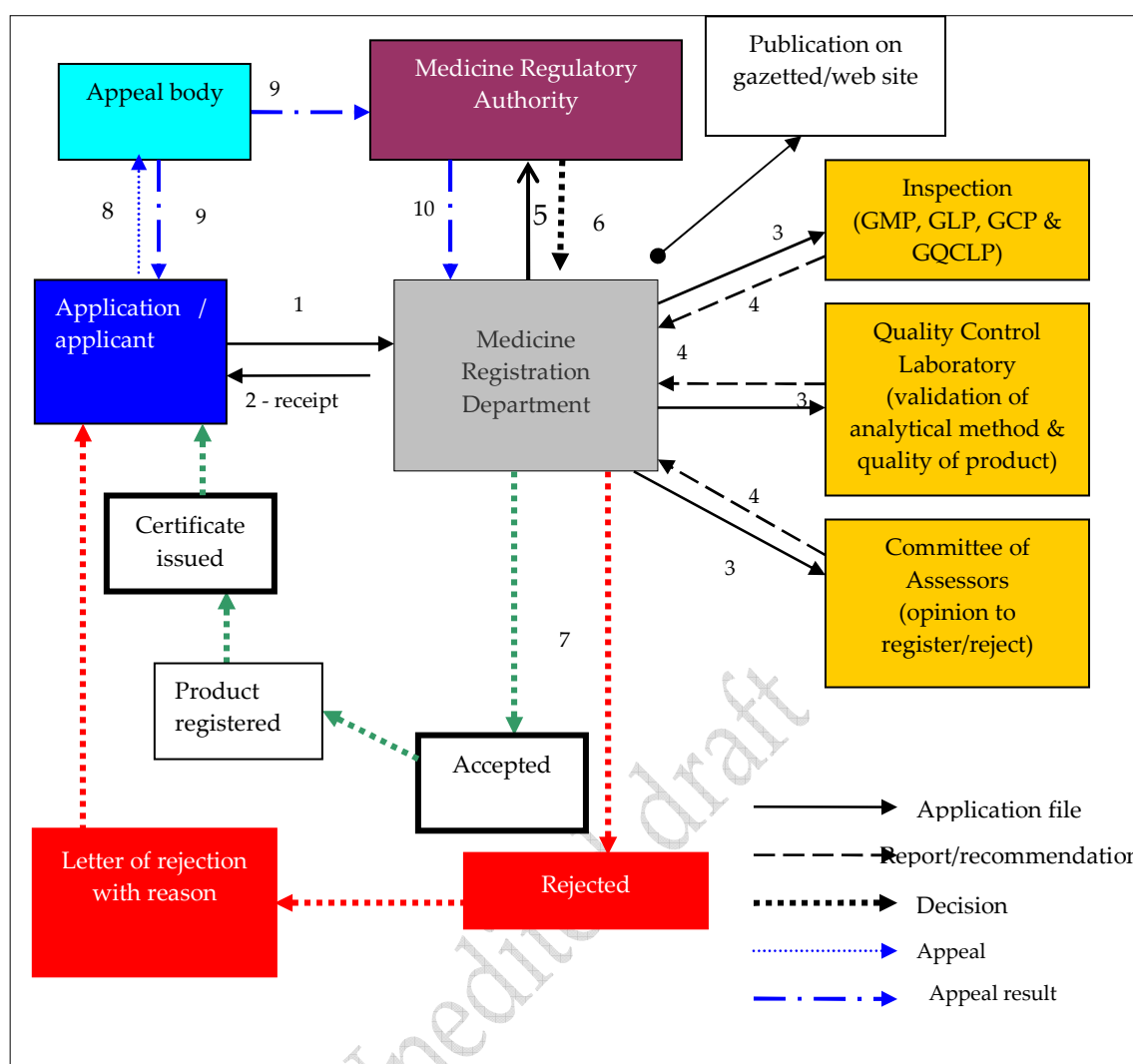
4. Decision making process

To help ensure transparency, fairness and consistency in the registration process the assessment of applications should be done by a committee of experts with the necessary scientific, medical and technical knowledge and skills. The committee should operate in accordance with written guidelines. A product should be approved only if it meets the criteria for registration as stated in the guidelines as well as in the legislation and regulations. Assessors should provide an official written report on the results of their assessment and should indicate whether a product is accepted for registration or rejected. The decision making body (the Registration Department or the MRA) should make decision based on the report of the committee. The presence of written guidelines will discourage inappropriate action on the part of the assessors and allow suppliers and manufacturers to appeal against decisions that appear to be contrary to what the process should have yielded has the procedures been followed. Such guidelines are also crucial to ensure good governance in the assessment process and that decisions by the assessors are based on scientific facts and independent grounds. Having such guidelines publicly available helps to ensure that everyone knows about the process and what the criteria are. The diagram below shows the process of medicine registration commonly applied in countries.

5. Appeal system

The MRA should establish an independent appeal system mechanism for clients to lodge complaints if they are not satisfied with the decision of the authority. The appeal system could be administrative as well as judicial.

Figure 1 Medicine Registration Flow Chart



B) Comments on each indicator

Indicator I.1:

Is there an up-to-date list of all registered pharmaceutical products available in the country?

Rationale: An official and up-to-date list of all registered pharmaceutical¹ products containing accurate and current information can help to indicate how transparent the medicine registration system is about the pharmaceutical products authorized to circulate in the market. It will also ensure that medicines rejected in other countries for safety or efficacy reasons, medicines registered in one country and not yet in other, and medicines produced by manufacturers non-compliant with Good Manufacturing Practices (GMP) are not registered. Thus it also measures the degree to which a

¹ The terms "medicine", "medicinal product", "pharmaceutical", and "pharmaceutical product" are used interchangeably, unless stated otherwise.

government protects its population from low- quality, unsafe and ineffective products. Making the list easily accessible to the public and all stakeholders will help them identify which product is legally approved and which one is illegally sold.

Description: There should be an easily accessible, official, up-to-date list of pharmaceutical products approved for sale or distribution in the country. Medicines not on the official list should be considered non-approved and should not be available in the market for sale or use. Medicine registration must be based on an objective assessment of a medicine's efficacy, safety, quality and the accuracy of the information in the product packaging. The indicator is applicable to all pharmaceutical products mentioned in the national legislation as requiring registration.

Interpretation guidelines: If an up-to-date and official list of all registered pharmaceutical products exists, then the indicator will be rated with a 1. If it does not exist or it has not been updated then the indicator will be rated with a 0. If this list is in the process of being developed or updated, the indicator will also be rated with a 0.

Indicator I.2:

If such a list exists, does it provide a minimum level of information?

Rationale: The list of all pharmaceutical products officially registered in a country should provide a certain level of information as a minimum. This will indicate how transparent the government is in terms of the information obtained for each product. It will also indicate how systematic it is in getting the same information from all companies, and whether any exceptions are made as a result of gifts or any other benefits. Additionally, the availability of such information helps health workers, pharmacists, dispensers and patients to find out if a product is registered with the authorities and what the conditions for registration are.

Description: The list should provide sufficient and accurate information, and include:

- the description of the product including the name of the product;
- packaging and any identifying mark;
- country of manufacture;
- site of the manufacturer;
- the date of registration;
- validity of registration;
- the conditions for registration, for example whether the medicine is prescription-only or can be bought over-the-counter (OTC).

Interpretation guidelines: If there is no evidence of such a list then the indicator will be rated with a 0. If the list exists, rate the indicator as a *method 2* question.

Indicator I.3:

Are there written procedures for applicants on how to submit an application for registration of medicinal products?

Rationale: Consistent and open procedures for medicine registration for all applicants (e.g. manufacturers, importers) are critical for a transparent pharmaceutical system. This ensures that decision-making is based on objective criteria and is not just subjective. It will also ensure consistency and avoid confusion in communications between applicants and registration staff (as everyone will use the same terminology).

Description: The written procedures must be:

- available in writing
- clear and publicly accessible.
- They should describe comprehensively and cogently the processes to follow in submitting an application,
- the data to be submitted,
- the timeframe for processing an application,
- the fees and
- the criteria for medicine registration. There should be no *ad hoc* exceptions to the standard requirements.

Interpretation guidelines: If there is no evidence of such a procedure then the indicator will be rated with a 0. If the procedure exists, rate the indicator as a *method 2* question.

Indicator I.4:

Are there written procedures for assessors on how to assess applications submitted for registration of medicinal products?

Rationale: As with the applicants, assessors will need to follow clear procedures on how to assess an application submitted for registration to ensure that decision-making is based on objective criteria and is not subjective.

Description: Procedures should be:

- available in writing;
- be publicly accessible;
- They should describe the process to follow in assessing submissions;
- give the timeframe for processing an application;
- specify the issues to be considered in assessing submissions; and
- provide guidance on report writing.

Interpretation guidelines: If there is no evidence of such a procedure then the indicator will be rated with a 0. If the procedure exists, rate the indicator as a *method 2* question.

Indicator I.5: Is there a standard application form publicly available for submission of applications for registration of medicinal products?

Rationale: A standard application form is a tool for ensuring consistent registration practices for all applications. It helps to ensure that medicine products are evaluated on objective criteria and that these are applied uniformly, irrespective of the supplier or manufacturer. This is important to foster fair market access.

Description: The document should be:

- publicly accessible
- readily available in the government office.
- As a minimum it should require a description of the product, such as the name of the product (brand name & INN) and the composition per unit dose.
- It should also include a brief summary of the manufacturing method;
- the specifications of active ingredients and excipients;
- the Summary Product Characteristics (SPC), including the pharmacological action, therapeutic classification, indications and contraindications;
- details of the packaging material; and
- labelling.

Interpretation guidelines: If there is no evidence of an application form then the indicator will be rated with a 0. If the application form exists, rate the indicator as a *method 2* question.

Indicator I.6:**Are there written guidelines setting limits on how and where medicines registration officers meet with applicants?**

Rationale: Meetings between the medicines regulatory authorities and applicants can be helpful for both parties as they can clarify issues or misunderstandings. Requests for such meetings should be submitted to the Medicine Regulatory Authority (MRA) and/or registration division in writing, indicating the purpose and who will attend on the applicant's side. The MRA must maintain control over the venue, conduct and content of the meeting. For example, it is useful to have more than one MRA staff member present to avoid any real or perceived conflict of interest in the outcomes of the meetings. Also the minutes of the meetings need to include the names of those who attended, from both the applicant's and MRA's sides.

Description: Such a document should be obtained from the MRAs and MRA staff, applicants and other interested parties should be familiar with it.

Interpretation guidelines: If such a document exists and the KI knows about it then the indicator should be rated with a 1. If it does not exist then the indicator will receive a 0. This document may exist but the KI is unaware of it (in which case it will be rated 0), or the guidelines included may not be systematically applied. In such cases more explanation should be provided in the text of the report.

Indicator I.7:

Is there a functioning formal committee involved in the assessment of the applications for registration of pharmaceutical products?

Rationale: The presence of a formal committee with carefully selected members who will assess applications helps to ensure that evaluations of dossiers are carefully examined and assessed, and that the system is participatory and transparent. Such assessments should not depend on the judgment of a single person, as it is the case in some countries.

Description: This committee should be composed of experts, not of political appointees. This committee should be impartial and ensure that the applications submitted for registration are assessed for efficacy, safety, quality, accuracy and completeness of product information.

Interpretation guidelines: If the committee is formally established and is operational, then this indicator should be rated 1. If the committee exists but is not operational, then this indicator should be rated 0. If committee formation is not formalized, then this indicator should receive a 0.

Indicator I.8:

Are there clear written criteria for selecting the members of the committee?

Rationale: Members of the committee should be selected on the basis of clearly written criteria to ensure that selection is done solely on the grounds of professional expertise, and is free of conflict of interest and favouritism. This will help to ensure that decisions for approving or rejecting a registration application for a product are based on scientific and independent grounds, leading to the circulation of safe, quality assured and efficacious medicines on the market.

Description: Criteria for selecting the members of the committee should be:

- available in writing;
- publicly available;
- define the professional qualifications required;
- define the necessary technical skill and work experience of the experts to be selected;
- require that all members declare any real or perceived conflict of interest (e.g. investment in a pharmaceutical company, spouse working in a pharmaceutical company, payment received from companies or individuals, etc.);
- timeframe to serve as a committee member.

Interpretation guidelines: If there is no evidence of such a criteria then the indicator will be rated with a 0. If the criteria exists, rate the indicator as a *method 2* question.

Indicator I.9:

Is there a written document that describes the composition and terms of reference of the committee?

Rationale: A written document that describes the committee membership, roles and responsibilities helps to ensure transparency in the medicine registration process and the accountability of its committee members.

Description: The document should be:

- up-to-date and
- publicly accessible.
- list committee members by name and their expertise.
- include the roles and responsibilities of its members, as well as
- their accountability and financial benefits given to them, if any.

Interpretation guidelines: If there is no evidence of such a written document then the indicator will be rated with a 0. If the written document exists, rate the indicator as a *method 2* question.

Indicator I.10:

Are there written guidelines on conflicts of interest (COI) with regard to registration activities?

Rationale: Given the potential for conflict of interest that could influence decision-making in the registration process, members of the committee or public officials involved in medicine registration processes, should be aware of what a conflict of interest implies and how it can affect their decision-making process. This would be stated in a COI policy or guideline. They should be obliged to declare officially any potential conflict of interest that could arise in their professional responsibilities.

Description: This question helps to check what systems are in place to identify and manage real or perceived conflict of interest issues. Written and publicly available guidelines on COI should exist, as well as a standardized "declaration of conflict of interest" form (see annex 3 for an example). The guidelines should include as a minimum the following:

- definition of what a COI is;
- rules on accepting gifts;
- rules on reporting COI;
- mechanism protecting informers of COI;
- actions to be taken in case of failure to comply with guidelines;
- evidence of enforcement of these regulations (evidence that these forms are in fact systematically completed and reviewed by the members of the committee and public officials involved in the registration process).

Interpretation guidelines: If there is no evidence of COI guidelines then the indicator will be rated with a 0. If the guidelines exist, rate the indicator as a *method 2* question.

Indicator I.11:

To what extent do you agree with the following statement: "The members of the registration committee are systematically and objectively selected based on the written criteria in force in your country"? (see question I.8)

Rationale and description: Criteria to select the members of the committee may exist and be as comprehensive as those set out in question 8, but in reality they may not be used systematically or they may not be used at all. Asking for KI's perceptions will bring valuable insight on the transparency of the selection process for registration committee members, and on the application (or non-application) of existing rules and regulations in a country.

Interpretation guidelines: *method 3.*

Indicator I.12:

Are there clear and comprehensive guidelines for the committee's decision-making process?

Rationale: To help ensure transparency, fairness and consistency in the decision-making process in registration, the committee should be operating under clear and comprehensive guidelines. In general terms a product should be accepted because it demonstrates quality, efficacy and safety. The committee should provide an official written report on the results of the medicine evaluation, whether the product is accepted or rejected. This procedure discourages inappropriate action on the part of the committee and allows suppliers and manufacturers to appeal decisions, if necessary. This guidance is crucial for helping to ensure good governance of the committee, and that its decisions are based on scientific and independent grounds.

Description: Generally such committee makes recommendations and/or gives advice to a high-level government official (e.g. Minister of Health, Head of MRA, etc.), who will then have the responsibility to take the final decision (he/she will be held accountable for the final decision). However the committee should be given clear guidelines for its decision-making process to make their recommendations. These guidelines should be:

- Available in writing
- Publicly available
- Describe clearly the mandate of the committee
- Specify the number of meetings the committee should convene
- The procedures for reaching decisions
- The committee's reporting structure.
- The review process should have clear time limits; and
- The decisions made at the meetings also need to be made publicly available.

Interpretation guidelines: If there is no evidence of such guidelines then the indicator will be rated with a 0. If the guidelines exist, rate the indicator as a *method 2* question.

Indicator I.13:

Is there an independent and formal appeals system for applicants who have their registration applications rejected?

Rationale: A formal appeals procedure in the registration process can promote transparency by creating a publicly available trail of documentation of how decisions are made by governments.

Description: A formal appeals process or a protest mechanism should be available to manage concerns and complaints from companies and others. Following communication of decisions made after review of an application for registration, firms should be able to file protests based on their view that they were unfairly evaluated and provide reasons and/or supplementary documents, which support the request for a second evaluation.

Interpretation guidelines: If a formal protest mechanism is in operation, then this indicator should receive a rating of 1. If there is no appeals mechanism to speak of, the rating should be 0.

Indicator I.14:

To what extent do you agree with the following statement: "Gifts and other benefits given to the officials in charge of medicines registration have no influence at all on their final decisions"?

Rationale: Despite clear regulation or guidance on the application process, the selection of the registration committee members, and their decision-making process, gifts or other benefits may be offered to public officials or committee members. This information is usually known by those involved in the system, including your KIs. *It is a sensitive question to ask*, and the KIs may feel uncomfortable and hesitate to give a spontaneous answer. Before asking this question it may be useful to remind them and reassure them of the confidentiality of their answers.

Interpretation guidelines: *method 3.*

Indicator I.15

To what extent do you agree with the following statement: "the registration committee meets on regular basis and keeps minutes of its meetings"?

Rationale: Despite clear guidance on holding meetings, the registration committee may not meet on a regular basis or will not keep always the minutes. This information is usually known by those involved in the system, including your KIs. *It is a sensitive question to ask*, and the KIs may feel uncomfortable and hesitate to give a spontaneous answer. Before asking this question it may be useful to remind them and reassure them of the confidentiality of their answers.

Interpretation guidelines: *method 3.*

Indicator I.16:

In your opinion, what types of unethical behaviour are common in the registration system in your country?

Rationale: This indicator captures perceived types of corruption or unethical behaviour that undermine a well-functioning system. Registration office staff and committee members have the responsibility to ensure that the registration process is completed in accordance with national regulations and procedures. It is therefore important that they carry out their activities professionally and with integrity and honesty. They should not place themselves under any financial or other obligation to outside individuals or organizations, or take gifts that might influence them in the performance of their official duties. Their decisions should be based solely on their objective evaluation findings.

Interpretation guidelines: *method 4.*

Indicator I.17:

If you were in a position of highest authority, what would be the first action that you would take to improve the registration process in your country?

Rationale: *method 4*

Unedited draft

Section II: Licensing of pharmaceutical establishments

A) Overview on Licensing of pharmaceutical establishments

1. Introduction

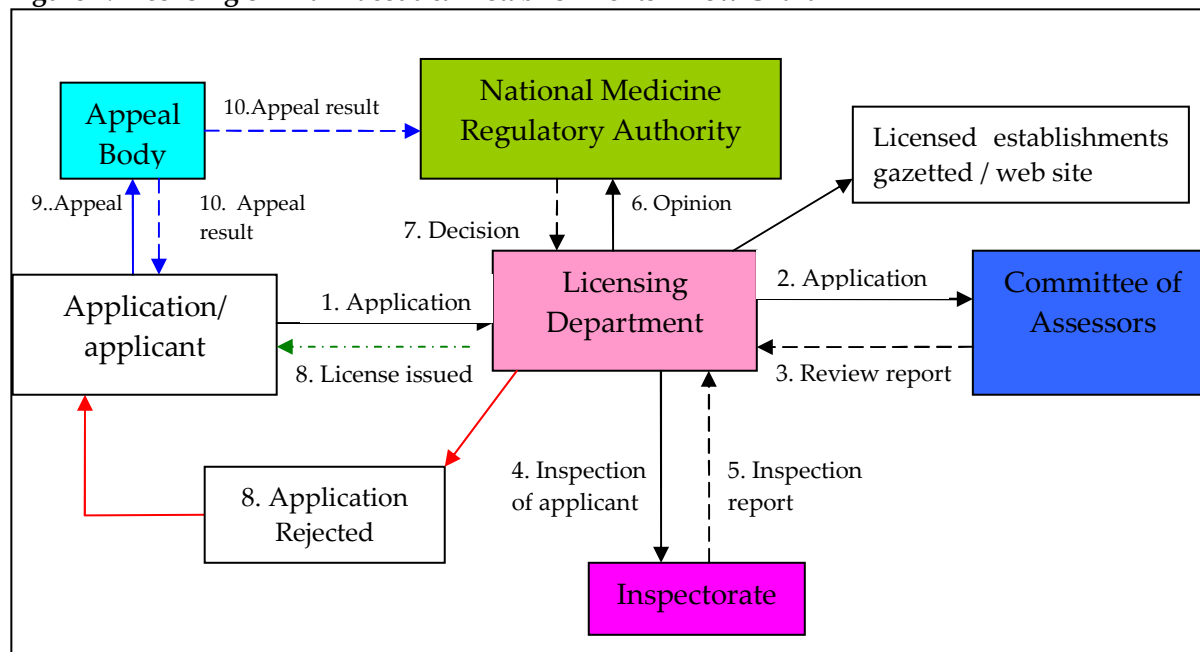
Licensing of pharmaceutical establishments is a regulatory activity of a national medicines regulatory authority (MRA). The primary responsibility of the MRA is to operate a system of administration and enforcement intended to ensure that all medical products subject to its control conform to acceptable standards of quality, safety and efficacy; the promotion and marketing of medicinal products is in accordance with approved product information; the use of medicines is rational, and that all personnel, premises and practices employed to manufacture, store distribute and sell, supply and dispense these products comply with requirements to ensure the continued conformity of the products with these standards until they reach the final user/consumer. These objectives can be effectively achieved only if:

- There is in place a mandatory system of licensing/authorizing of medicinal products; all local medicine manufacturers, importing and exporting agents, distributors (wholesale and retail outlets); all premises and facilities used to manufacture, store or distribute medicines;
- All stages of manufacture and distribution are supervised by appropriately qualified staff;
- The licensing system is complemented by an efficient system of inspection with access to quality control laboratory facilities.

The establishments/areas that need licensing include:

- Manufacturing
- Importing
- Exporting
- Wholesale of medicines
- Retail outlets
- Promoting and advertising,
- Sales representatives, etc.

In its simplified form, the licensing system involves the steps shown in the diagram below:

Figure 2: Licensing of Pharmaceutical Establishments - Flow Chart

2. Essentials for licensing

In order to issue licenses the MRA should have the following in place:

a) Legal provision

The MRA should have legal power in order to issue licenses. The law should clearly define its powers, duties and responsibilities. It should also require compliance with applicable good practices e.g. good manufacturing practices, good storage and good distribution practices, good dispensing practices. There should be provisions within the law defining the validity, renewal and variation of licenses as well as conditions for renewal, suspension and revocation of licenses. Exemption to licensing and criteria for exemption should also be specified in the law or regulations. There should also be provision for control of imports and exports as well as for appeals.

The law and all related regulations should be printed and made easily available to the public, interested parties, so that they know their rights and obligations. Absence of a clear and comprehensive legal provision could be a cause for making arbitrary decisions, bias, favouritism and corruption.

b) Guidelines and procedures

MRA should define standards and develop, print and distribute corresponding guidelines, guidance and procedures describing the administrative and technical requirements that should be met in order to get a license to operate. The presence of such guidelines will make the process transparent and enable applicants to know what is expected of them and regulators to be objective in their decision making. Examples of guidelines, guidance and procedures that need to be developed include the following:

- Standards on conditions to be met in terms of premises, facilities, processes, personnel, equipment, materials, etc in order to get a license;
- Good practices guidelines for the different pharmaceutical operations (good manufacturing practice, good storage practice, good distribution practice, good

dispensing practice/good pharmacy practice, good quality control laboratory practice, good clinical practice, etc);

- Guidelines for appointment and qualification of the qualified person.
- Instruction and format for submission of application for issuance of a license;
- Guidelines for the content of Site Master File
- Guidelines and procedures for the control of imports and exports
- Guidelines on content and format of licenses;
- Procedures for meeting with applicants
- Timeframe for assessing applications
- Procedures for waiving certain requirements or steps

3. System for assessing applications

The MRA should establish a committee composed of members drawn from relevant units within the authority to assess applications. Committee members should declare any conflict of interest. Pre-licensing inspection should be carried out to ensure compliance with the requirements and the inspection report should be part of the application to be assessed. Decisions reached by the committee should be in writing and it should serve as the basis for issuing a license or rejecting application. Such a system will minimize bias or favouritism in assessing application. The following guidelines need to be in place for assessing application:

- Guidelines for assessing of license applications
- Standard checklist for the assessment of application for licensing
- Documented procedures for decision-making and for issuance of license

4. Pre-and post-licensing inspection system

There should be pre-licensing inspection of the site to check compliance with requirements based on standardized inspection protocols. There should also be continued post-licensing inspection to ensure that there is continued conformity to the standards. Inspection reports should serve as one of the criteria in making decisions to issue, renew, suspend or revoke licenses.

5. Appeals system

Clients should have the right to appeal if they are not happy or satisfied with the decision of the licensing body or the MRA. There should be both administrative and judicial appeals systems that are independent of the body that has made the initial decision.

B) Comments on each indicator

Indicator II.1:

Is it a legal requirement to have a licence in order to operate a pharmaceutical establishment?

Rationale: Pharmaceuticals need to be safe, effective and of good quality in order to produce the desired effect. In order to ensure that these requirements are met, the manufacture, storage, distribution, etc of pharmaceuticals should be carried out by people or companies that are licensed. The medicine law should have a provision requiring any one who would like to start a pharmaceutical activity to have a license.

Description: The MRA should have a law which requires a license to operate any pharmaceutical establishment. The law should indicate the requirements to be met in

terms of qualification of personnel, premises, facilities, procedures, etc to operate a pharmaceutical establishment activity.

Interpretation guidelines: If there is a national law requiring pharmaceutical establishments to be operated under license only then this indicator should be rated a one. If licensing is not a requirement then it should be rated a zero.

Indicator II.2:

Does the MRA have a unit responsible for issuing pharmaceutical establishment licences?

Rationale: Applicants need to know where to go, whom to ask and what to comply with in order to get a license. It is therefore necessary for a national medicine regulatory authority to establish a unit within its structure that is responsible for issuing licenses. The unit should have the necessary human resources, facilities, and guidelines and procedures to carry out its functions effectively and in a transparent manner.

Description: The unit should exist, be operational, develop the necessary guidelines, procedures, formats, etc, and make them easily accessible to applicants. The presence of such a unit will make the process transparent, ensure accountability and minimize bureaucracy and corruption.

Interpretation guidelines: If there is a unit within the MRA responsible for licensing, then this indicator should be rated a one. If there is no unit and the unit is not operational, then it should be rated a zero.

Indicator II.3:

Are there written procedures for submission of applications for licensing?

Rationale: Written procedures for licensing of all applicants (e.g. manufacturers, importers, exporters, wholesalers, retailers, dispensers, etc) are critical for a transparent pharmaceutical licensing system. It is a measure of transparency and consistency in the licensing process.

Description: The presence of such procedures will enable applicants to know what is expected of them and also ensures that decision-making is based on objective criteria. It will also ensure consistency and avoid confusion in the communications between applicants and the licensing staff (as everyone will use the same terminology). The written procedures exist in writing and:

- are publicly available
- cover administrative criteria to be met by applicants
- describe the processes to be followed in submitting an application
- describe the requirements to be met in terms of premises, facilities, personnel, etc.
- include the timeframe for processing application
- include the fees.

Interpretation guidelines: If there is no evidence of such a procedure then the indicator will be rated with a 0. If the procedure exists, rate the indicator as a *method 2* question.

Indicator II.4:**Are there written guidelines for assessing applications for a licence?**

Rationale: The MRA should have written guidelines to guide the assessment of applications for licensing. The presence of written guidelines will promote consistency in the decision process and prevent any bias or favoritism.

Description: The MRA should develop guidelines for assessing applications for licensing. The guidelines should be:

- available in writing and easily accessible
- publicly available to all interested parties
- describe the process for assessing
- method for reporting the results of the assessment

Interpretation: If there is no evidence of such guidelines then the indicator will be rated with a 0. If the guidelines exist, rate the indicator as a *method 2* question.

Indicator II.5:**Is the submission of a pre-licensing inspection report one of the requirements for making decisions on whether to issue a licence or not?**

Rationale: Pre-licensing inspection should be carried out by a team of qualified inspectors in order to check whether the site for the intended pharmaceutical establishment complies with the requirements described in the written guidelines and procedures.

Description: Inspectors should inspect the site for the intended establishment and submit report. The committee that assesses an application for licensing should take into account the pre-licensing inspection report in reaching a decision whether to issue a license or not. The inspection report should be retained in the file with the decision.

Interpretation guidelines: If the MRA conducts pre-licensing inspection for all licenses issued and the reports are considered in making decisions then the indicator should be rated a one. If there is no pre-licensing inspection at all or there is pre-licensing inspection but reports are not considered for making decisions or used only sometimes the indicator should be rated a zero.

Indicator II.6:**Is there a functioning formal committee that assesses applications for licensing of a pharmaceutical establishment?**

Rationale: The presence of a formal committee consisting of members with high integrity and knowledge of the pharmaceutical area to assess applications for licensing helps in ensuring that submissions are carefully examined, assessed, and that the system is participatory and transparent.

Description: The committee should be impartial and ensure that the applications submitted for licensing are assessed for conformance with the requirements specified in the guidelines and procedures issued by the MRA as well as the pre-inspection report submitted.

Interpretation guidelines: If the committee is formally established and is operational, then this indicator should be rated a one. If the committee exists but is not operational or if there is no committee at all then the indicator should be rated a zero.

Indicator II.7:

Are there clear written criteria for selecting the members of the committee?

Rationale: Members of the committee should be selected solely on the basis of clearly written criteria to ensure that licenses are provided when applicants meet the guidelines requirements. This will help ensure that decisions are not influenced by gifts, bribes or favouritism.

Description: The criteria should exist in writing and should:

- be publicly available
- require that committee be composed of heads of departments of the MRA
- require that members sign conflict of interest form
- refer to specific code of conduct.

Interpretation guidelines: If there is no evidence of such criteria then the indicator will be rated with a 0. If the criteria exists, rate the indicator as a *method 2* question.

Indicator II.8:

Is there a written document that describes the composition and terms of reference of the committee?

Rationale: A written document that describes the committee membership, roles and responsibilities helps to ensure transparency in the licensing process and the accountability of its members.

Description: The document should be clearly written and be:

- publicly available
- list committee members by name and expertise
- include the role and responsibilities of its members
- accountability of its members and final benefits if any

Interpretation guidelines: If there is no evidence of such document then the indicator will be rated with a 0. If the document exists, rate the indicator as a *method 2* question.

Indicator II.9:

Does the MRA carry out regular (at least every two years) post-licensing inspection of all licensed pharmaceutical establishments?

Rationale: Post-licensing inspection of pharmaceutical establishments is necessary in order to ensure that there is continued compliance with requirements as defined in the specific guidelines, guidance and procedures issued by the MRA. It should be carried out at least every two years and at time of renewal of licenses.

Description: Inspectors should carry out announced or unannounced inspections to ensure that establishment establishments comply with requirements. Renewal, suspension and revocation of licenses should be based on post-licensing inspection.

Interpretation guidelines: If post-licensing inspection is carried on each establishment at least every two year then the indicator should be rated a one. If such inspection is not carried out every two year on all pharmaceutical establishments or only on some of the establishments then the indicator should be rated a zero.

Indicator II.10:

Is there an up-to-date list of all licensed pharmaceutical establishments available in the country?

Rationale: An official and up-to-date list containing accurate and current information can help to indicate how transparent the MRA is about pharmaceutical establishments authorized to operate establishment. It allows the public, patients and consumers to know which establishment is operating officially/legally.

Description: There should be an easily accessible, official, up-to-date list of licensed pharmaceutical establishments in the country. The list should include:

- name and address of premises,
- validity date of licence,
- name of qualified person/contact person,
- last inspection date,
- type of establishment.

Establishments not on the official list should be considered illegal and should be closed. The indicator is applicable to all pharmaceutical establishments mentioned in the national legislation as requiring licensing.

Interpretation guidelines: If there is no evidence of such list then the indicator will be rated with a 0. If the list exists, rate the indicator as a *method 2* question.

Indicator II.11:

To what extent do you agree with the following statement: "The licensing of pharmaceutical establishments is systematically carried out according to policies and procedures"?

Rationale: Despite clear guidelines and procedures on the licensing process, gifts or other benefits may be offered to public officials or committee members. This information is usually known by those involved in the system, including your KIs. *It is a sensitive question to ask*, and the KIs may feel uncomfortable and hesitate to give a spontaneous answer. Before asking this question it may be useful to remind them and reassure them of the confidentiality of their answers.

Interpretation: *Method 3*

Indicator II.12

Is there a independent appeals system for applicants who have their applications for licensing rejected?

Rationale: An independent appeals system in the licensing process (different to the committee that rejected the application) or a protest mechanism will make the licensing system transparent, accountable and ensure the rule of law. Such system should be available to manage concerns and complaints from companies and others not satisfied with the decisions of the licensing body. There should be both administrative and judicial appeal system.

Description: The MRA should have written appeals procedures for clients and the procedures should be printed and made easily accessible to all interested parties. There should be evidence that the system actually work according to the polices and procedures.

Interpretation guidelines: If there is a written appeals and functional procedure then the indicator should be rated a one. If the appeals system is not functional or if there is no written appeals procedure then the indicator should be rated a zero.

Indicator II.13:

To what extent do you agree with the following statement: "the formal committee that assesses applications for licensing of pharmaceutical establishment is fully operational and meets on a regular basis"?

Rationale: Despite the official nomination of the committee and clear TOR, the members may not meet on a regular basis. This will lead to a poorly functional committee and may leave discretion for the decision-making process to one of its member. This information is usually known by those involved in the system, including your KIs. *It is a sensitive question to ask*, and the KIs may feel uncomfortable and hesitate to give a spontaneous answer. Before asking this question it may be useful to remind them and reassure them of the confidentiality of their answers.

Interpretation: *Method 3*

Indicator II.14:

In your opinion, what types of unethical practices commonly occur in the process of licensing pharmaceutical establishments in your country, if any?

Rationale: It is important that the members of the licensing committee carry out their activities professionally and with integrity and honesty. They should not place themselves under any financial or other obligation to outside individuals or organizations, or take gifts that might influence them in the performance of their official duties. Their decisions should be based solely on their assessment findings.

Interpretation: *method 4*

Indicator II.15:

If you were in a position of highest authority, what would be the first action that you would take to improve the licensing process for pharmaceutical establishments in your country?

Interpretation: *method 4*

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Section III: Inspection and market control

A) Overview on inspection and market control

1. Introduction

Inspection of medicine manufacturers, importers, wholesalers, retailers, etc (pharmaceutical establishment) is an essential function of a medicine regulatory authority's inspectorate, the enforcement arm of the authority. The purpose of inspection is to ensure that pharmaceutical operations, such as production, import, export, distribution and promotion, are carried out in accordance with the approved norms, standards and guidelines and with the national medicines legislation and regulations as well. Its goal is to ensure that medicines used by the population are safe, efficacious, and of good quality. In addition to inspection of the formal market, inspectors also carry out surveillance of the informal market as well as the points/ports of entry to the country in order to ensure that there are no illegal activities, such as smuggling of medicines, sale of medicines in open market places or circulation of counterfeit and substandard medicines taking place. For inspection activities to be carried out effectively, a national medicine regulatory authority should have in place the following essentials.

2. Essentials for effective inspection and market control

a) Legal basis

Generally, provisions within the national medicine legislation and regulations give powers to the inspectorate of the MRA and its inspectors to carry out inspection activities. As a minimum, the provisions should give powers:

- to inspectors to enter, at any reasonable time, any place where medicinal products are produced, packaged, stored, distributed, tested or where regulated pharmaceutical activity is carried out;
- to inspectors to take samples and other relevant documents as evidence; and
- define the inspectors' duties, responsibilities and powers to take action in case of violations of provisions of the medicines legislation and regulations;

Inspectors should be provided with special identification documents which they should show when performing inspection. The legislation should also provide appeals system for applicants.

b) Trained and experienced inspectors

Inspectors should have training and/or experience in pharmaceutical manufacturing, quality control, community pharmacy, detecting counterfeits and substandard products, legal procedures, etc. Recruitment should be based on merit and expertise in the area. In any case their training should be in accordance to the internationally accepted guidelines, such as the Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (PIC/s) or the European Compliance Academy (ECA).

Pharmaceutical inspectors deal with products and activities that greatly affect the health and well being of a country's population. They should be able to competently carry out their activities with integrity and honesty. As such, they should not place themselves under any financial or other obligations to outside individuals or organizations or take gifts that might influence them in the performance of their official duties. They should not improperly use or divulge information that is acquired in the performance of their official duties. Their decisions should be solely based on their inspection findings.

c) Written guidelines, procedures and guidance

Inspectors should have reference materials to guide them in carrying out their functions. These include:

- Job descriptions and standard operating procedures (SOPs)
- Guidelines on good manufacturing practice, good clinical practice, good quality control laboratory practice, good storage and distribution practices, good dispensing practice, good pharmacy practice, and guidelines on ethical medicine promotion
- Inspectorate Quality Manual
- Check list or aid-memoir for inspection
- Guidance on writing inspection report
- Guidance on classification of deficiencies in good practices (GMP, GDP, GQCLP, GCP, etc) and measures to be taken to address deficiencies
- Written appeals procedures and guidance on handling appeals
- Code of conduct
- Guidance on conflict of interest and Conflict of interest declaration form.

Guidelines and procedures should be easily accessible to applicants and other interested parties. The use of such reference materials will make the inspection process transparent, ensure consistency in the inspection process and prevent subjectivity. The guidelines will also help the inspected firms to know what is expected of them in terms of complying with the regulatory requirements and the consequences in case of failure to comply with the requirements. The presence of written guidelines will also help the inspectorate to check on inspectors if they are performing their duties according to the guidelines or procedures. The absence of written guidelines and procedures will create conditions for inspectors to make arbitrary decisions or to be influenced by financial or other gifts.

d) Transport and communication system

Inspectors need vehicles for transportation as well as computers to enter data and information on inspections performed. They should have access to Internet, telephone and other communication systems.

3. Inspection process

a) Types of inspections

Inspectors usually perform two types of inspections - pre-licensing and post-licensing inspections. Pre-licensing inspection is carried out before a license is issued to an applicant (manufacturer, importer, distributor, etc) in order to:

- evaluate compliance with the requirements specified in the guidelines in terms of premises, facilities, personnel, processes, equipment, etc.
- evaluate procedures and control methods implemented in the manufacture, import, export, distribution of products, to determine if they conform to the application commitments

- audit the completeness and accuracy of the information submitted with the application

The findings of a pre-licensing inspection serve as an important part of the registration application review and approval process.

Post-licensing inspection is carried out after a license has been issued and the applicant has started operating. Its purpose is to ensure that there is continued conformance to the approved standards, guidelines and procedures and the national medicine legislation and regulations.

b) Methods of inspection

Depending on the objective of the inspection, inspectors apply different methods to inspect pharmaceutical establishments. These include, comprehensive or routine inspection, concise inspection, follow-up inspection, special inspection, investigative inspection. Inspection can be unannounced or announced. Strategies used to make the inspection process more objective and to minimize capture and corruption, in inspection include:

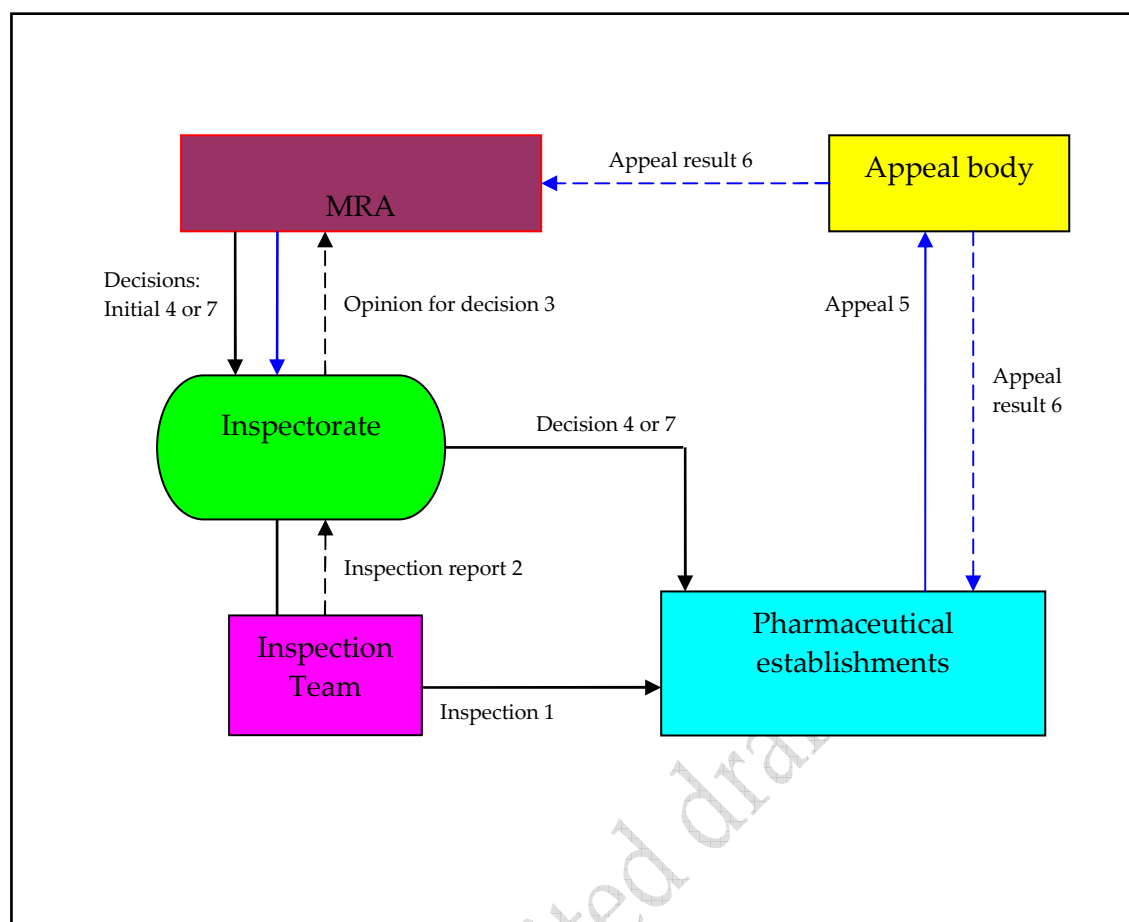
- inspection in teams
- rotation of inspectors (avoiding frequent contact of the same inspector with a particular company)
- peer review
- external audit

Inspectors of pharmaceutical establishments are required to submit their report with recommendations to the head of the inspectorate who will then review the report and the recommendations to ensure that inspection has been carried out in accordance with the guidelines and procedures, and that recommendations do not contradict the findings and that they are not biased. Such a review is also necessary to ensure that inspectors have discussed their findings, including due dates to rectify and comply with recommendations according norms, otherwise appeal, with those responsible for management of the establishment at the end of the inspection

4. Appeal system

Clients should have the right to appeal if they are not happy or satisfied with the decision with regards to the inspection. There should be both administrative and judicial appeals systems that are independent of the body that has made the initial decision.

Figure 3: Inspection of Pharmaceutical Establishments-Flow Chart



B) Comments on each indicator

Indicator III.1:

Is there a provision in the medicines legislation/regulation covering inspection of pharmaceutical establishments?

Rationale: Inspection of medicines manufacturers and distributors (importers, wholesalers and retailers) is an essential regulatory function. Its purpose is to ensure that operations are carried out in accordance with the approved norms, standards and guidelines. Inspections uncover weaknesses and deficiencies as well as actual or potential errors in the production, quality control, storage and distribution of medicines. In order to ensure that the medicines used within the country are safe, effective and efficacious and that there are no illegal activities, such as smuggling and sale of medicines in market places or circulation of counterfeit and substandard medicines, inspectors must inspect both the formal and informal markets, as well as the points of entry to the country. For these activities to be carried out effectively, a national MRA should have, among others, legal powers.

Description: There should be a provision in the medicines legislation or regulations on inspection of pharmaceutical establishments.

Interpretation guidelines: If such a provision exists, then the indicator will be rated 1. If it does not exist, then the indicator should be rated 0. If it is in the process of being developed or updated, it should also be rated 0.

Indicator III.2:

Is the provision on inspection comprehensive enough?

Rationale: The job of inspectors involves entry into any premises (licensed by the medicine regulatory authority or otherwise) where medicines are manufactured, stored, distributed, sold, or where any such related activities are carried out. Therefore, they need to have a strong and comprehensive legal basis that gives them power to carry out their activities. In addition, the law should protect inspectors from any illegal action or abuse by the owners of such premises. The law should state also that any one who hinders inspector from carrying out their lawful activities shall be punishable by court of law.

Description: The provision should as a minimum:

- give the MRA powers to inspect premises and activities;
- give its inspectors the power to enter, at any reasonable time, any place where medicinal products are produced, packaged, stored, distributed or tested in order to carry out an inspection;
- define the inspectors' duties, responsibilities and powers to take action in case of violations of provisions of the medicines legislation and or regulations;
- require inspectors to be provided with a special identification document;
- require that a copy of the provision is available to companies being inspected;

Interpretation guidelines: If there is no evidence of such provision then the indicator will be rated with a 0. If the provision exists, rate the indicator as a *method 2* question.

Indicator III.3:

Are there written guidelines on classifying non-compliance with Good Manufacturing Practices (GMP) that describe the types of deficiencies and the corresponding measures to be taken by the MRA?

Rationale: The use of such guidelines will help inspectors to be objective in their decision-making. It will also make the inspection process more transparent as manufacturers are informed of the measures that will be taken if they fail to comply with GMP. Manufacturers should be able to appeal if inspectors make decisions that are not in accordance with the guidelines. On the other hand, the absence of such guidelines will create conditions for inspectors to make arbitrary decisions or to be influenced by financial or other gifts. The guidelines will also help the supervisory body to check on the inspectors' work.

Description: Such guidelines should be available in writing and easily accessible to all stakeholders. They should include as a minimum:

- a classification system of GMP deficiencies;

- the measures to be taken in case of non-compliance with GMP;
- provisions for an appeals mechanism by companies;
- an appeals system that is independent of the body making the original decision.

Interpretation guidelines: If there is no evidence of such guidelines then the indicator will be rated with a 0. If the guidelines exist, rate the indicator as a *method 2* question.

Indicator III.4:

Are there written guidelines on classifying non-compliance with Good Distribution Practices (GDP) that describe the types of deficiencies and the corresponding measures to be taken by the MRA?

Rationale: The use of such guidelines will help inspectors to be objective in their decision-making. It will also make the inspection process more transparent as distributors are informed of the measures that will be taken if they fail to comply with GDP. Distributors should be able to appeal if inspectors make decisions that are not in accordance with the guidelines. On the other hand, the absence of such guidelines will create conditions for inspectors to make arbitrary decisions or to be influenced by financial or other gifts. The guidelines will also help the supervisory body to check on the inspectors' work.

Description: Such guidelines should be available in writing and easily accessible to all stakeholders. They should include as a minimum:

- a classification system of GDP deficiencies;
- the measures to be taken in case of non-compliance with GDP;
- provisions for an appeals mechanism by companies;
- an appeals system that is independent of the body making the original decision.

Interpretation guidelines: If there is no evidence of such guidelines then the indicator will be rated with a 0. If the guidelines exist, rate the indicator as a *method 2* question.

Indicator III.5:

Are there written procedures/mechanisms to prevent regulatory capture between inspectors and the manufacturers or distributors that he/she inspects?

Rationale: If the same inspector is inspecting the same manufacturer frequently, closeness and friendship may emerge between the inspector and the company. Such a situation, if uncontrolled, may eventually make the inspector susceptible to regulatory capture and corruption. It is therefore necessary for the MRA to have mechanisms to prevent such frequent contact between an inspector and the companies inspected.

Description: Having procedures or mechanisms promoting rotation and peer review will help prevent regulatory capture between the inspectors and manufacturers/distributors inspected. These procedures should be available in writing and require:

- rotation of inspectors, based on a scheduling system;

- a rotation mechanism requiring inspectors from one geographical area to inspect companies in other areas;
- inspectors to visit sites in teams with a team leader;
- inspectors to inspect under the observation of another inspector who will report on what he/she has observed (peer review);
- independent audit of the inspections

Interpretation guidelines: If there is no evidence of such procedures then the indicator will be rated with a 0. If the procedures exist, rate the indicator as a *method 2* question.

Indicator III.6:

Are there written guidelines on conflicts of interest (COI) with regard to inspection activities?

Rationale: Inspectors should not use their official authority for the improper advancement of their own family or friends or for personal or financial interests. They should not engage in any transaction or function or have any financial, commercial or other comparable interest that is incompatible with their functions and duties. They should declare business, commercial and financial interests or activities undertaken for financial gain that may raise a possible conflict of interest while carrying out their official functions. In situations of possible or perceived conflict of interest between the duties and private interests of inspectors, they should inform their supervisors, to eliminate or reduce such conflict of interest. Inspectors should not improperly use or divulge information that is acquired in the performance of their official duties. Inspectors, after leaving their official positions, should not take improper advantage of their previous office. There should be mechanisms to facilitate the reporting of actions perceived to be against the standards set in a code of conduct. Such mechanisms must be in place to effectively protect the personal and professional interests of whistleblowers.

Description: Written guidelines on COI and a COI declaration form should exist and include as a minimum the following:

- definition of what a COI is;
- rules on the acceptance of gifts;
- rules on reporting COI;
- mechanism protecting informers of COI;
- actions to be taken in case of failure to comply with policy;
- evidence of enforcement of these regulations (evidence that COI forms are systematically completed by the inspectors and public officials involved in the inspection process).

Interpretation guidelines: If there is no evidence of such guidelines then the indicator will be rated with a 0. If the guidelines exist, rate the indicator as a *method 2* question.

Indicator III.7:

Are inspection findings and conclusions subject to an internal review?

Rationale: Inspectors of pharmaceutical establishments are required to submit their report with recommendations to the head of the inspectorate. He or she will then review the report and the recommendations to ensure that inspection has been carried out in accordance with the guidelines and procedures, and that recommendations do not contradict the findings and that they are not biased. Such a review is also necessary to ensure that inspectors have discussed their findings with those responsible for management of the establishment at the end of the inspection. The purpose is to ensure that there is transparency in the inspection system.

Description: There should be written inspection guidelines for inspectors, which outline the steps to be followed when conducting inspections of medicine establishments. The interviewers could take samples of inspection reports and check whether:

- the reports have been reviewed by the head of the inspectorate or not
- inspectors have discussed their findings with the management of the establishment or not.

Interpretation guidelines: If internal review of inspection findings and conclusions are systematically carried out, the indicator will be rated with a 1, but if not, then it will be rated with a 0.

Indicator III.8:

Are there written standard operating procedures (SOPs) for inspectors on how to conduct inspections?

Rationale: Inspectors need to have written SOPs to guide them in performing their duties. The presence of such guidelines will help in ensuring that there is consistency in the inspection process, prevent subjectivity and help in checking whether inspectors are performing their activities correctly or not.

Description: These procedures should be:

- available in writing in the form of a checklist or aide-memoire or an equivalent document
- detail the requirements for pre- and post-inspection activities
- detail the scheduling system identifying companies due for inspections within a set timeframe
- detail the format and content of inspection reports.

Interpretation guidelines: If there is no evidence of such SOP then the indicator will be rated with a 0. If the SOP exist, rate the indicator as a *method 2* question.

Indicator III.9:**Are there written criteria for the selection and recruitment of inspectors?**

Rationale: Inspectors should be recruited using clearly written criteria to ensure that selection is done on the basis of professional expertise, and also that the experts are free from any form of conflict of interest. These criteria will help promote transparency in the recruitment process, with selection based on the professional merit of the experts and not on favouritism.

Description: The criteria for selecting and recruiting inspectors should:

- be available in writing and publicly available.
- include at least the professional qualification required (e.g. pharmacist, chemist)
- detail the minimum number of years of work experience in the area.
- recruitment should be based on recommendations from former employers (previous work place, association)
- recruitment should be based successful completion of a training on inspection.

Interpretation guidelines: If there is no evidence of such criteria then the indicator will be rated with a 0. If the criteria exists, rate the indicator as a *method 2* question.

Indicator III.10:

To what extent do you agree with the following statement: "The integrity of inspectors is in no way influenced by personal gain, such as bribes, gifts, or any other benefits, etc."?

Rationale: Despite clear regulation or guidance on the inspection process, gifts or other benefits may be offered to inspectors to influence the findings and recommendations in their reports. This type of information is usually known by those involved in the system, including your KI. *Please remember that it is a sensitive area*, and the KI may feel uncomfortable and find it difficult to give a spontaneous answer. Before asking this question it may be useful to remind them and reassure them of the confidentiality of their answers.

Interpretation guidelines: *method 3.*

Indicator III.11:

To what extent do you agree with the following statement: "Inspection activities are systematically carried out in accordance with the guidelines and procedures to prevent biases (e.g. peer review or rotation) "?

Rationale: Despite clear regulation or guidance on the inspection process, they may not always be followed in practice. This type of information is usually known by those involved in the system, including your KI. *Please remember that it is a sensitive area*, and the KI may feel uncomfortable and find it difficult to give a spontaneous answer. Before asking this question it may be useful to remind them and reassure them of the confidentiality of their answers.

Interpretation guidelines: *method 3.*

Indicator III.12:

In your opinion, what types of unethical behaviour are common in the inspection area in your country? These can include bribery, material gifts, favouritism (family, friends), conflicts of interest (e.g. investments in pharmaceutical companies), etc.

Rationale: Pharmaceutical inspectors have the responsibility to ensure that the manufacture and distribution of medicines are carried out in accordance with national norms and standards. It is therefore important that they carry out their activities professionally and with integrity and honesty. They should not place themselves under any financial or other obligation to outside individuals or organizations, or take gifts that might influence them in the performance of their official duties. Their decisions should be based solely on their inspection findings.

Interpretation guidelines: *method 4.*

Indicator III.13:

If you were in a position of highest authority, what would be the first action that you would take to improve the inspection process in your country?

Rationale: *method 4.*

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Section IV: Medicine promotion control

A) Overview on medicine promotion control

1. Introduction

Medicine information can significantly influence the way medicines are used by consumers and providers of medicines. Regulating medicine information and promotion is therefore necessary to prevent the dissemination of inaccurate and misleading information. The provision of unbiased, truthful medicine information to patients and health professionals by the relevant authorities is crucial to ensure appropriate use of medicines by health care providers and patients.

There are many different types of medicine information designed for different purposes and produced by different sources. Examples are:

- Summary of product characteristics and/or product information supplied by manufacturers as part of the registration dossiers and approved by the MRA
- Product labelling
- Package insert - patient information - leaflet
- Journals, review articles, bibliographic indexes and other published materials
- Reference books, textbooks, formularies, standard treatment guidelines, medicine compendia, medicine bulletins
- Manufacturers' promotion materials.
- On-line advertising

Pharmaceutical manufacturers and suppliers promote and/or advertise their products to health professionals and the general public using a number of methods. These include advertising in journals or other media (television, radio or electronic media), direct mailing, personal selling through sales representatives, provision of gifts and samples, sponsored symposiums, and sponsored publication of information materials. Such promotion aims to influence physicians' prescribing patterns, as well as people's attitudes, beliefs, and behaviour and encourage them to use a particular brand of product.

2. Essentials for controlling medicine promotion and advertising

2.1. Legal provision

The MRA should have legal provision to control medicine promotion and advertising. It should enact rules and regulations for the control of medicinal products promotion and advertising with deterrent sanctions in case of violations.

2.2. National Ethical Criteria for Medicine Promotion and Advertising

The MRA should develop a set of comprehensive Ethical Criteria in conformity with the WHO Ethical Criteria for Medicinal Medicines Promotion for the control of promotion and advertising of medicinal products. The Ethical criteria should cover issues such as:

- Advertising to physicians and health-related professionals
- Advertising to the general public
- Promotion by medical representatives

- Promotion through free medical samples
- Symposia and other scientific meetings
- Information for patients
- Packaging, labeling and package inserts
- Restrictions and monitoring of free samples
- Post-marketing scientific studies
- Speakers fees and consultancies
- Promotion of exported medicines
- Restrictions and limits on gifts, etc.

2.3. Guidelines

The MRA should have written guidelines and/or documented procedures:

- for application and approval of promotion and advertising materials
- for control of the operations of medical representatives
- for the control and approval of promotion and advertising

a) Reviewing and monitoring of promotion and advertising

The MRA should have a system for reviewing and monitoring promotional materials. The system should consist of a committee consisting of staff of the MRA, representatives of health professionals associations, pharmaceutical industry, consumer groups and civic society. The committee should have a conflict of interest (COI) policy. The committee should have written Terms of Reference which will include reviewing and approving of promotional materials. Review should be done against payment of fees. The committee should also monitor the promotion and advertising of medicinal products through media and other means to ensure compliance with the national ethical criteria and national regulations. There should be Standard Operating Procedures (SOPs) to guide the monitoring work of the committee.

The pharmaceutical industry should be encouraged to self-regulate and reinforce its promotional activities but the ultimate responsibility to control promotion and advertising should be that of the national medicine regulatory authority.

b) Standards for the content of information materials

The MRA should set standards for labelling, package inserts and product information. Specifying what information should be included in leaflets and other information materials and giving guidance on the most appropriate format and language can help to ensure that patients are given the necessary information about the medicines they use. Patient information leaflets should include information about:

- therapeutic indications
- contraindications
- information about possible interactions with other medicines or with alcohol, etc
- special warnings including information for the children, pregnant women, the elderly, etc
- instruction for using the medicine
- method, frequency and timing of administration
- duration of treatment
- action to be taken in the event of an overdose or missed doses
- information about possible dependency

3. Reference materials for review of promotional materials

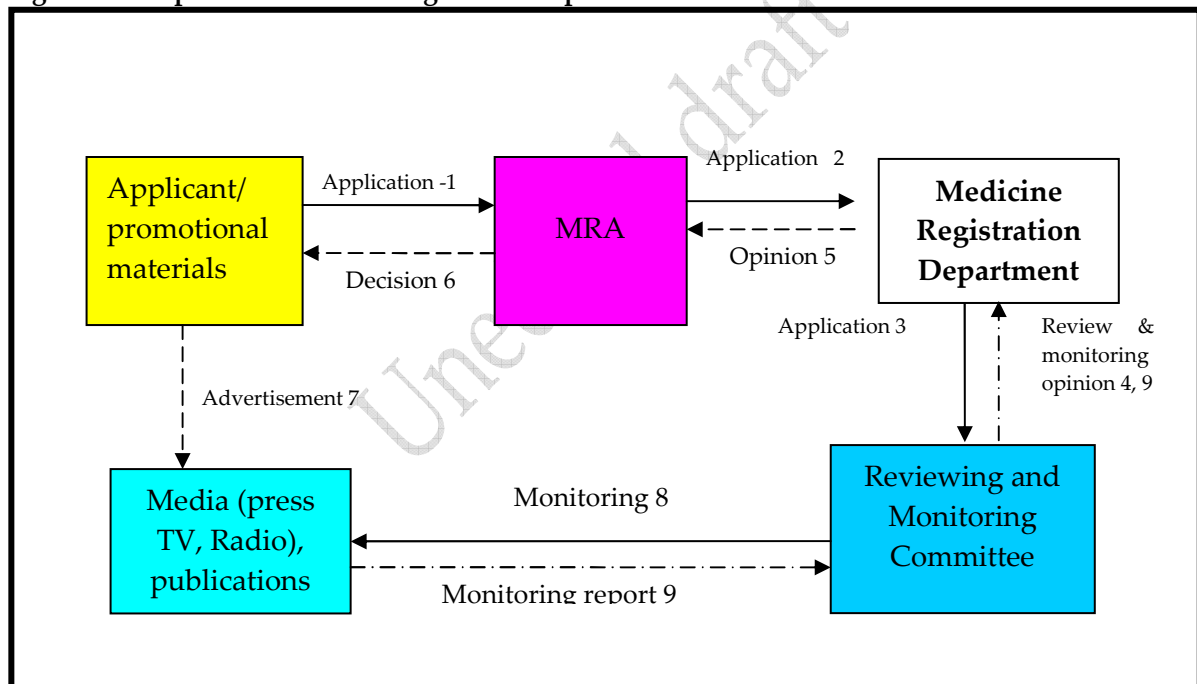
The MRA should have a list of reference materials which will serve as source of unbiased, complete and up-to-date information on medicinal products. The content of promotional materials should be reviewed against these reference materials. Examples of reference materials are:

- Summary of product characteristics/product information supplied by manufacturer as part of the registration dossiers and approved by the MRA
- British National Formulary
- Martindale's the Extra Pharmacopoeia
- United States Pharmacopoeia-Medicine Information (USP-DI)
- Other reputable pharmacopoeia

4. Mechanisms for lodging complaints

The MRA should establish mechanisms for lodging complaints by the public, pharmaceutical industry and any other interested party. Complaints should be reviewed and administrative and legal action taken in case of violation of the National Ethical Criteria and national regulations.

Figure 4: The process of controlling medicine promotion



B) Comments on each indicator

Indicator IV.1:

Is there a provision in the medicines legislation/regulations covering medicine promotion?

Rationale: Promotional activities are usually informational and persuasive and their intention is to induce the prescription, use and purchase of the products promoted. Thus they need to be guided by rigorous legislation and regulations to ensure that the information contained therein is accurate, truthful and not misleading. Medicines are not like any other commodity because of their life-saving but also their life-threatening potential if misused. They therefore require separate legislation/regulation covering their promotion.¹

Description: There could be separate legislation, regulation, or provisions within medicines legislation,² on the promotion of medicines. Details of these should be readily available through government offices or the government website.

Interpretation guidelines: If such provision exists, then the indicator will be rated 1. If it does not exist, then the indicator should be rated 0. If it is in the process of being developed or updated, it should also be rated 0.

Indicator IV.2:

Do the provisions on medicine promotion include explicit mention of the following forms of promotion?

Rationale: Promotional activities can be quite diverse and they target the various types of health professionals (e.g. physicians, pharmacists, nurses) and the public at large. The provisions therefore need to be comprehensive enough to cover all the aspects and targets of promotional activities. The WHO ethical criteria for medicine promotion¹¹ (adopted by the 41st World Health Assembly and prepared by an international group of experts) set out general principles for ethical behaviour in the promotion of medicinal products. They provide a good model for countries to adapt to national circumstances.

Description: The national provisions on promotion of medicines should cover all types of promotional activities carried out by the pharmaceutical industry or suppliers. As a minimum they should cover the following areas:

- Advertisement to professionals
- Advertisement to the public
- Qualification and training of medical representatives
- Restrictions on and monitoring of free samples

¹ WHO Ethical Criteria for Medicinal Medicine Promotion. Geneva, World Health Organization, 1988.

² Only the word "provisions" will be used in the text from this point. Some countries may have separate legislation and regulations on promotion of medicines, but most countries will have provisions within medicine legislation/regulations.

- Symposia and scientific meetings
- Post-marketing scientific studies
- Speakers' fees and consultancies
- Packaging, labelling and package inserts
- Promotion of exported medicines
- Restrictions and limits on gifts and gimmicks
- Products launches

Interpretation guidelines: If there is no evidence of such provision then the indicator will be rated with a 0. If the provision exists, rate the indicator as a *method 2* question.

Indicator IV.3:

Is pre-approval of promotional materials officially required?

Rationale: While self-regulation of medicine promotion by the private sector is highly commendable, to date it has proven insufficient to prevent misleading claims or inadequate information in advertisements. Pre-approval of advertising materials is a more efficient and secure way of ensuring that all advertisements conform to a country's rules and regulations.

Description: A clause included in the provisions or a policy document requiring pre-approval of advertising materials before they are made public should be written and publicly available. It should also mention the minimum information to be included in the application form of the advertising material such as:

- generic (INN) and brand name
- company name
- information on approved indication, dose and administration procedures
- information on expected benefits
- adverse effects
- contraindications
- medicine interactions
- cost

Interpretation guidelines: If there is no evidence of such clause then the indicator will be rated with a 0. If the clause exists, rate the indicator as a *method 2* question.

Indicator IV.4:

Do the provisions foresee an enforcement mechanism on promotion of medicines stating the sanctions in case of violation?

Rationale: The enforcement mechanism should be foreseen in the provision itself, ensuring that safeguards are in place to support ethical promotion of medicines. For example, the existence and application of legal sanctions are powerful in promoting ethical promotion, and can be a measure of a government's commitment to penalize unethical promotion of medicines.

Description: The law should state and express the sanctions and indicate the type of penalties on public officials or pharmaceutical companies for breaching the law.

Interpretation guidelines: If such provision exists, then the indicator will be rated 1. If it does not exist, then the indicator should be rated 0. If it is in the process of being developed or updated, it should also be rated 0.

Indicator IV.5:

Is there a formal complaints procedure to report unethical promotional practices?

Rationale: A formal complaints process can promote ethical promotion by pharmaceutical companies and effective monitoring/enforcement by government officials.

Description: All the key stakeholders (health professionals, competitors, government officials, consumers, etc.) need to be able to report unethical practices of medicine promotion through an established and formal procedure. Written procedures for making complaints need to be publicly available and evidence of their use need to be provided. The results of the complaint will also need to be published.

Interpretation guidelines: If there is no evidence of such clause then the indicator will be rated with a 0. If the clause exists, rate the indicator as a *method 2* question.

Indicator IV.6:

Is there a service or committee responsible for monitoring and enforcing the provisions on medicine promotion?

Rationale: Ensuring the enforcement of laws and regulations in countries remains a challenge if the necessary means and resources are not in place. To ensure that medicine promotional activities in countries are carried out in the framework of the national law and regulations, it is essential to establish a service or committee to monitor these activities. Such a service must be given adequate resources and full authority to guide promotional activities and if necessary implement the appropriate sanctions.

Description: The government service or committee will need to be formally established. Its members should be composed of experts with adequate technical skills and should act in an impartial way.

Interpretation guidelines: If the service or committee is formally established and is operational, then this indicator should be rated 1. If it exists but is not operational, then this indicator should be rated 0. If it is not formally established, then this indicator should receive a 0.

Indicator IV.7:

Are there clear criteria for selecting the members of the service/committee?

Rationale: Members of this service/committee should be selected on the basis of clearly written criteria to ensure that selection is done solely on the ground of professional expertise, and is free of conflict of interest and favouritism. This will help to ensure that

decisions for approving or rejecting a promotional activity or advertisement are based on scientific and independent grounds, leading to ethical promotion of medicines.

Description: Criteria for selecting the members of the service/committee should be available in writing and publicly. They should:

- define professional qualification required
- define necessary technical skills and work experience of the experts to be selected
- require that all members declare any real or perceived conflict of interest

Interpretation guidelines: If there is no evidence of such criteria then the indicator will be rated with a 0. If the criteria exists, rate the indicator as a *method 2* question.

Indicator IV.8:

Is there a written document that describes the composition and terms of reference of the service/committee?

Rationale: A written document that describes the service/committee membership, roles and responsibilities helps to ensure transparency in the process controlling the promotion of medicines, as well as the accountability of its members.

Description: The document should be up-to-date and publicly available. It should:

- list the members by name and their expertise
- include the roles and responsibilities of its members
- specify the frequency of the meetings
- include their accountability of members and financial benefits in any.

Interpretation guidelines: If there is no evidence of such document then the indicator will be rated with a 0. If the document exists, rate the indicator as a *method 2* question.
method 2.

Indicator IV.9:

Are there written and publicly available Standard Operating Procedures (SOPs) guiding the services responsible for pre-approving or monitoring medicine promotion and advertising?

Rationale: Monitoring of promotional materials needs to be standardized and systematic to ensure that all evaluations are processed in a fair manner, with no privileges or favouritism.

Description: Standard Operating Procedures (SOPs) will guide the monitoring work of the government service or committee. The questions they contain will check compliance with the national provisions on medicine promotion, and also that the information in the promotional material complies with the information approved at the time of medicine registration. Additionally the SOPs need to be available in writing and publicly.

Interpretation guidelines: If there is no evidence of such SOP then the indicator will be rated with a 0. If the SOP exists, rate the indicator as a *method 2* question.

Indicator IV.10:

Are there written guidelines on conflicts of interest (COI) with regard to control of medicine promotion activities?

Rationale: Given the potential for conflict of interest that could influence decision-making in the process of controlling promotion of medicines, members of the committee or public officials involved in such activities should be aware of what a conflict of interest implies and how it can affect their decision-making process. This would be stated in a COI policy or guideline. They should be obliged to declare officially any potential conflict of interest that could arise in their professional responsibilities.

Description: This question helps to check what systems are in place to identify and manage real or perceived conflict of interest issues. Written guidelines on COI should exist, as well as a standardized "declaration of conflict of interest" form (see annex 3 for an example). The guidelines should include as a minimum the following:

- definition of what a COI is;
- rules of the acceptance of gifts;
- rules on reporting COI;
- mechanism protecting informers of COI;
- actions to be taken in case of failure to comply with guidelines;
- evidence of enforcement of these regulations (evidence that these forms are in fact systematically completed by the members of the committee and public officials involved in the control of medicines promotion process).

Interpretation guidelines: If there is no evidence of such guidelines then the indicator will be rated with a 0. If the guidelines exist, rate the indicator as a *method 2* question.

Indicator IV.11:

To what extent do you agree with the following statement: "The legal provisions on medicine promotion have been developed in broad consultation with all interested parties"?

Rationale: Provisions developed in documented consultation with key stakeholders involved in medicine promotion (e.g. the pharmaceutical industry, professional and consumer associations) ensure that decisions are made transparently.

Interpretation guidelines: *method 3*.

Indicator IV.12:

To what extent do you agree with the following statement: "Pre-approval of promotional and advertising materials are systematically being obtained before they are made public"?

Rationale: In practice promotion and advertisement of medicines may occur before approval is received, even if pre-approval is required by law. These can have detrimental public health impact, specially for medicines which would not have received approval in any case (e.g. prescription-only medicines).

Interpretation guidelines: *method 3*.

Indicator IV.13:

To what extent do you agree with the following statement: "Civil society/nongovernmental organizations have a great influence on improving the control of medicine promotion in your country"?

Rationale: Independent "watchdog" agencies (civil society/ independent NGOs) can play an important role in promoting transparency and integrity in government practices. Having a neutral and independent organization assess and monitor marketing practices of pharmaceutical products can help reduce the potential harm caused by inappropriate, misleading or unethical pharmaceutical promotion.

Description: Groups and various institutions have taken on the role of monitoring the promotional activities of the pharmaceutical industry. They will identify unethical promotion or misleading information, and ensure that the general public knows about them.

Interpretation guidelines: *method 3.*

Indicator IV.14:

To what extent do you agree with the following statement: "Sanctions foreseen in the provisions on medicine promotion are systematically applied when there is a breach"?

Rationale: Despite clear provisions on how to control medicine promotion and the existence of enforcement mechanisms, unethical medicine promotion practices remain widespread worldwide and often not sanctioned or punished. The perception of KIs can bring new and useful insights. Bear in mind that these types of questions remain sensitive for KIs, and some may feel uncomfortable answering them. As usual, before asking this question it may be useful to remind them and reassure them about the confidentiality of their answers. In this particular situation, it will also be useful to remind them that this is a recognized global problem frequently reported on by the media, including articles in scientific journals.

Interpretation guidelines: *method 3.*

Indicator IV.15:

In your opinion, what types of unethical behaviour are common in the medicine promotion area in your country?

- a) Involving health professionals and health institutions in general
- b) Involving regulatory office staff and committee members responsible for controlling medicine promotion

Rationale: This indicator captures perceived types of corruption or unethical behaviour that undermine a well-functioning system. Regulatory office staff and committee members have the responsibility to ensure that the control of medicine promotional activities is done in accordance with national provisions. It is therefore important that they carry out their activities professionally and with integrity and honesty. They should

not place themselves under any financial or other obligation to outside individuals or organizations or take gifts that might influence them in the performance of their official duties. Their decisions should be based solely on their evaluation findings.

Interpretation guidelines: *method 4.*

Indicator IV.16:

If you were in a position of highest authority, what would be the first action that you would take to improve the medicine promotion process in your country?

Rationale: *method 4.*

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Section V: Clinical trials of medicines

A) Overview on Clinical trials

1. Introduction

A clinical trial is a systematic study carried out on pharmaceutical products in human subjects, patients and other volunteers, in order to discover or verify the effects of and/or identify any adverse reaction to investigational products, and/or to study the absorption, distribution, metabolism and elimination of the products with the object of ascertaining their efficacy and safety. Clinical trials are generally classified into four phases, Phase I to IV.

Phase I

These are the first trials of a new active ingredient or new formulations in man, often carried out in healthy volunteers. Their purpose is to establish a preliminary evaluation of safety, and a first outline of the pharmacokinetic and, where possible, a pharmacodynamic profile of the active ingredient in humans.

Phase II

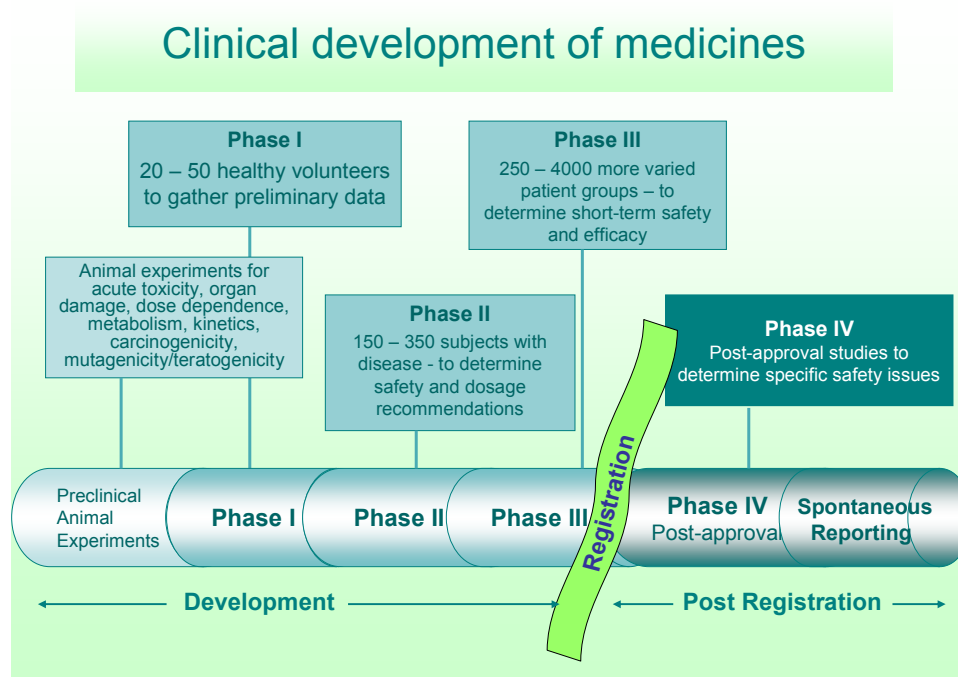
These trials are performed in a limited number of subjects and are often, at a later stage, of a comparative (e.g. placebo-controlled) design. Their purpose is to demonstrate therapeutic activity and to assess short-term safety of the active ingredient in patients suffering from a disease or condition for which the active ingredient is intended. This phase also aims at the determination of appropriate dose ranges or regimens and (if possible) clarification of dose response relationships in order to provide an optimal background for the design of extensive therapeutic trials.

Phase III

Trials in larger (and possibly varied) patient groups with the purpose of determining the short and long-term safety/efficacy balance of formulation(s) of the active ingredient, and of assessing its overall and relative therapeutic value. The pattern and profile of any frequent adverse reactions must be investigated and special features of the product must be explored (e.g. clinically-relevant medicine interactions, factors leading to differences in effect such as age). These trials should preferably be of a randomized double-blind design, but other designs may be acceptable, e.g. long-term safety studies. Generally, the conditions under which these trials are carried out should be as close as possible to normal conditions of use.

Phase IV

Studies performed after marketing of the pharmaceutical product. Trials in phase IV are carried out on the basis of the product characteristics on which the marketing authorization was granted and are normally in the form of post-marketing surveillance, or assessment of therapeutic value or treatment strategies.



2. Regulation of clinical trials

The role of governments is to provide the legal framework for the regulation of clinical trials. The aims are to:

- (i) protect the safety and rights of the subjects participating in clinical trial
- (ii) ensure that trials are adequately designed to meet scientifically sound objectives, and
- (iii) prevent any potential fraud and falsification of clinical data and information

These aims may be met by several means, including by:

- specifying the investigator's qualifications
- requiring for review and approval of the clinical trial protocol by relevant scientific experts and/or ethics committees
- carrying out on-site inspection of clinical trial site
- carrying out audits.

3. Key parties involved in clinical trials

a) Hospitals/clinics/health care facilities

A clinical trial takes place in a hospital, a clinic or a health care facility that has appropriate facilities. In order to undertake any clinical investigation the investigator needs to get permission from the hospital/the health care facility management. The trial site should be adequate to enable the trial to be conducted safely and efficiently.

b) Investigator/principal investigator

The investigator is the person responsible for the trial and for the rights, health and welfare of the subjects participating in the trial. The investigator should have the necessary qualifications and competence in accordance with national laws and regulations to undertake any clinical trial.

c) Sponsor

Sponsor is an individual, company, institution or organization which takes responsibility for the initiation, management and/or financing of the clinical trial. When an investigator initiates and takes full responsibility for a trial, the investigator then also assumes the role of the sponsor. Prior to the trial, the investigator(s) and the sponsor should establish an agreement on the protocol, standard operating procedures (SOP), the monitoring, and auditing of the trial, and the allocation of trial-related responsibilities.

d) Independent Ethics Committee¹

In order to carry out clinical trial there should be an independent ethics committee to:

- verify that the safety, integrity and human rights of subjects participating in a particular trial are protected; and
- consider the general ethics of the trial such as objective of the research and relevance to health priorities in the country) and provide public reassurance.
- Evaluate the ratio risks/benefits, the validity of informed consent process, the modalities to ensure confidentiality of personal data and other ethical aspects

The committee should consist of health professionals as well as social scientists, lawyers, and lay persons, representing the diversity of the community and having the necessary qualifications, skills and integrity. Particular attention must be given to the independency of the committee. The independent ethics committee must be formally established and follow clear standards of procedures.

The investigator must consult the relevant ethics committee(s) regarding the suitability of a proposed clinical trial protocol. The ethics committee has an ongoing responsibility for the ethical conduct of research. Subjects must not be entered into the trial until the relevant ethics committee(s) has issued its favourable opinion on the procedures.

e) Monitor

The monitor is the principal communication link between the sponsor and the investigator and is appointed by the sponsor. S/he is a person appointed by, and responsible to, the sponsor for the monitoring and reporting of progress of the trial and for verification of data. The number of monitors needed to ensure adequate monitoring of the clinical trial will depend on its complexity and the types of centres involved. The monitor is responsible for overseeing progress of the trial and to ensure that the study is conducted and data are handled in accordance with the protocol, Good Clinical Practice, and applicable ethical and regulatory requirements.

4. Essentials for regulating clinical trials

The following are essential in order to regulate clinical trials

a) Legal mandate

The national medicine regulatory authority (MRA) should have legal mandate to authorize and regulate clinical trials. The mandate should provide power to:

- review protocols and require, where necessary, protocol revisions and/or termination of trial,
- protect the safety of subjects

¹ In some countries, the responsible committee may be the Institutional Review Board

- carry out on-site inspections of the quality and reliability of the data obtained, with due concern for confidentiality
- conduct audit trials
- review results of clinical trial reports.

There should be a legal requirement for:

- handling variations /amendments to clinical trial protocols,
- designation of a principal investigator
- enforcing compliance to GCP/GLP
- licensing of manufacturers of investigational products for compliance with GMP
- licensing of importation and exportation of investigational products
- exemptions to clinical trial requirements
- actively monitoring adverse reactions and reporting the medicine regulatory authority

Regulations on clinical trials should specify the procedures for reporting and handling cases of misconduct discovered in connection with clinical trials.

b) Guidelines and procedures

The MRA should develop guidelines and procedures to be followed by sponsors, investigators, independent ethics committees and GCP inspectors, national assessors and those who authorize clinical trials. They should be in line with the major international guidelines on clinical trials including the Declaration of Helsinki, the CIOMS guidelines and various WHO GCP documents. These include guidelines on:

- submission of application for clinical trial
- types and scopes of variations/amendments and documentation required
- the format and content of clinical trial protocol
- good clinical practice, good manufacturing practice, good laboratory practice
- consent form for subjects participating in clinical trials
- review of clinical trial protocols and reports
- evaluation of the adequacy of supervision of the clinical trial by the sponsor's monitor
- on-site inspection of clinical trials
- control of manufacture, importation and exportation of investigational products
- the criteria for selecting the principal investigator and his/her roles and responsibilities
- the roles and responsibilities of independent ethics committee

c) Clinical trial inspectors (GCP inspectors)

The MRA should have inspectors who are qualified and experienced to carry out on-site inspection of clinical trial sites. They should be trained in GCP. As permitted by national regulations, inspectors may carry out inspection routinely, randomly and/or for specific reasons. They should be able to compare the procedures and practices of the investigator with those set out in the protocol and reports submitted to the medicines regulatory authority by the investigator or the sponsor. They should determine whether the investigator has custody of the required records or, if not, who has assumed this responsibility. They

should have easy access to all patient files and raw data used for and generated during the trial, ensuring the confidentiality of the information.

d) MRA review committee and assessment procedure

The MRA should have its own clinical trial review committee composed of people with the necessary scientific and medical knowledge and skills to review protocols and clinical trial reports. Protocols for clinical trials are submitted in advance for review by this Committee in order to establish if they are in accordance with existing national regulations. On the basis of its review of clinical trial protocols and/or reports, the committee may propose revisions or request additional data on a clinical trial or terminate a trial. The committee also evaluates the adequacy of supervision of the trial by reviewing the monitor's reports to the sponsor. In order to guide the assessment process there should be:

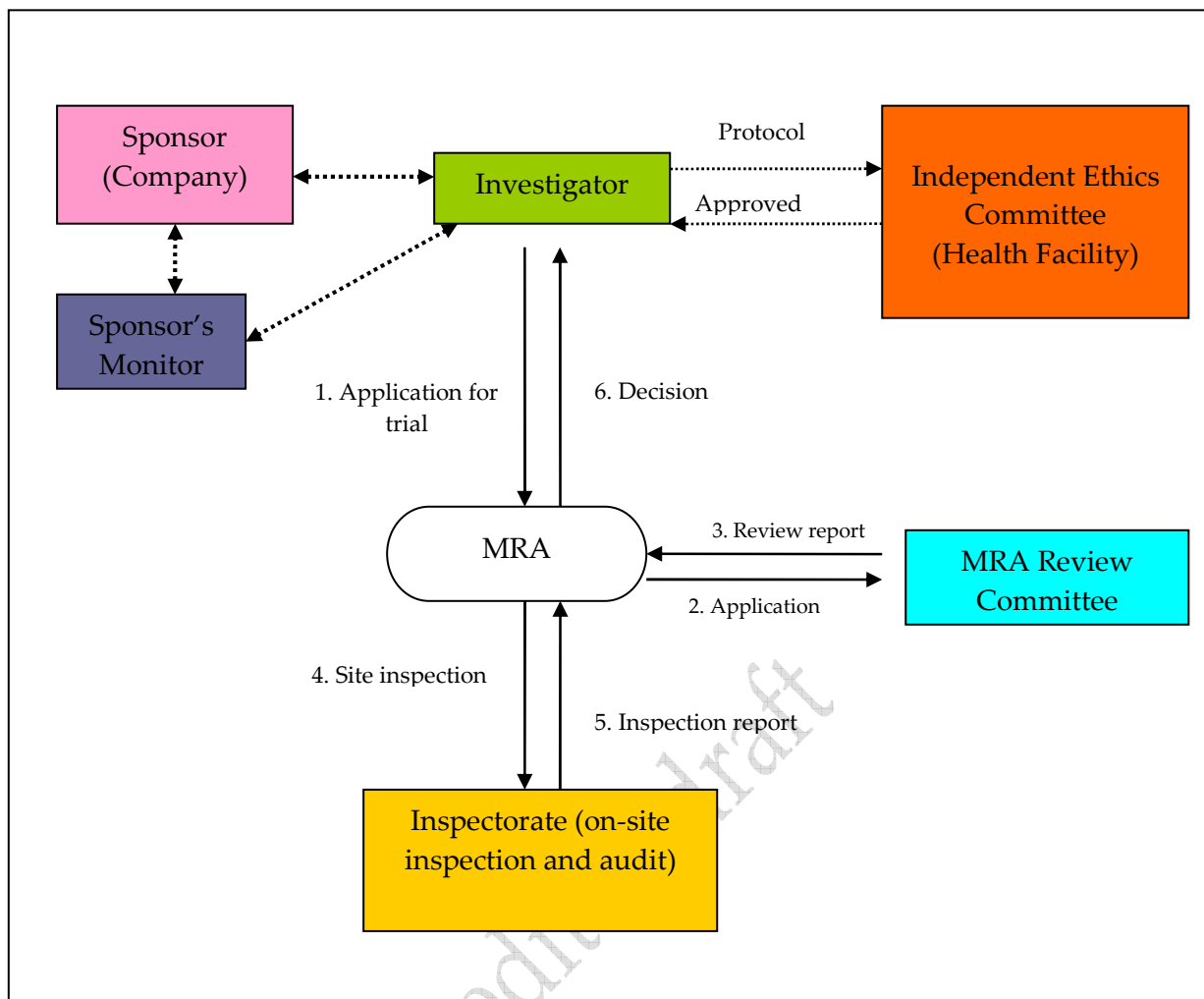
- A written procedure for assessment of CT applications
- A written procedure for assessing applications for variations/amendments
- Documented procedures for management of external experts participating in the evaluation of CT applications
- Documented procedures for decision-making
- A standard format for assessment report
- Time-limit(s) for assessment of applications

e) Information management system

The MRA should have information management system including a data base on all approved and rejected CT applications. The MRA should retain a file of each CT approved, amended and rejected with supporting documentation together with summary of reports.

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Figure 5: Clinical Trial Regulation-Flow Chart



B) Comments on each indicator

Indicator V.1:

Is there a legal provision requiring the regulation of clinical trials (CT)?

Rationale: Clinical trials need to be controlled in order to protect the safety and rights of subjects involved in trials and to ensure that trials are adequately designed to make them scientifically sound and to prevent any potential fraud and falsification of data.

Description: The legislation should give power to the MRA to control clinical trials, carry out on-site inspections or terminate clinical trials if necessary. The law should require the MRA to develop the necessary guidelines, procedures forms and requirements for the control of clinical trials.

Interpretation guidelines: If there is legal provision that gives power to the MRA then the indicator should be rated one. If there is no legal provision or the legal provision is not adequate then the indicator should be rated zero.

Indicator V.2:

Are there written national guidelines on principles of Good Clinical Practice (GCP)?

Rationale: The presence of such guidelines will guide sponsors, investigators, reviewers and those regulating clinical trials to carry out their activities in accordance with the rules and regulations because the standards and expectations will be obvious and transparent

Description: The MRA should develop Good Clinical Practice guidelines. The guidelines should be consistent with internationally accepted standards and they should be easily accessible to all those engaged in clinical trials. The presence of such guidelines will make the process transparent and maintain consistency in decision making by those who are involved in assessing proposal or auditing clinical trials.

Interpretation guidelines: If there are written guidelines covering the technical and ethical aspects of clinical practice that should be complied with by investigators and other involved in clinical trials then the indicator should be rated one. If there are no such guidelines then the indicator should be rated zero.

Indicator V.3:

Is there written and publicly available guideline on submission of application to MRA to conduct clinical trials?

Rationale: The presence of written guidance on submission of applications will help applicants to know what is needed to carry out clinical trials. It will also make the process transparent and prevent any inconsistency on the part of the MRA in decision-making if they are followed.

Description: The MRA should have a clear written guidance for applicants describing the information and data they should provide in order to get permission to conduct

clinical trials. The guidance should be published, be publicly available and made easily accessible to all stakeholders by putting it on MRA website or any other means that the public and clients can access. They should as a minimum provide information on:

- trials' objective and purpose
- trial design
- criteria for inclusion and exclusion of trial subjects
- means of obtaining informed consent
- timeframe for assessing applications

Interpretation guidelines: If there is no evidence of such guideline then the indicator will be rated with a 0. If the guideline exists, rate the indicator as a *method 2* question.

Indicator V.4:

Is there a documented policy or procedure for submission of CT applications to an Independent Ethics Committee (IEC)?

Rationale: The role of the ethics committee is to ensure the protection of the rights and welfare of human subjects participating in clinical trials. The ethics committee should be constituted and operated so that its tasks can be executed free from bias and from any influence of those who are conducting the trial. For this reason the ethics should have clear policy guidelines to make its work transparent and free from undue pressure.

Description: The ethics committee should have documented policies and procedures as a basis for its work, which should include as a minimum:

- The acceptability of the investigator for the proposed trial
- The suitability of the protocol
- The means by which trial subjects will be recruited
- The adequacy and completeness of the information
- Provision for compensation or treatment in the case of death or other loss or injury of a subject
- Form of payment through which the sponsor will remunerate or compensate the organization(s) and/or investigator(s) conducting the trial, and the trial subjects, as required by local laws and regulations.

Interpretation guidelines: If there is no evidence of such policy/procedure then the indicator will be rated with a 0. If the policy/procedure exists, rate the indicator as a *method 2* question.

Indicator V.5:

Are there requirements for the manufacture, importation, exportation and use of investigational products?

Rationale: Investigational products should be safe and of good quality. In order to ensure their safety and quality they should be manufactured according to the principles of good manufacturing practices and their importation and storage and use should be in accordance with good storage and distribution practices and other national regulations.

Description: The MRA should develop regulations and other guidance documents to ensure that investigational products are manufactured in accordance with the principles of GMP and that their importation, exportation, storage and use is according to good storage and distribution practices and other rules and regulations. The presence of such documents will help to ensure that applicants know what the standards are for investigational products.

Interpretation guidelines: If there is no evidence of such regulation/guidance then the indicator will be rated with a 0. If the regulation/guidance exists, rate the indicator as a *method 2* question.

Indicator V.6:

Is there a formal review committee in the MRA responsible for reviewing applications and CT results?

Rationale: The presence of a formal review committee composed of members with relevant expertise and qualification ensures that applications are reviewed effectively and provides the safeguards to protect the safety of subjects.

Description: Medicines regulatory authorities should have a committee with the mandate to review protocols and, where necessary, protocol revisions and/or termination of trials. They will allow be responsible for the review of the trials results

Interpretation guidelines: If a review committee is formally established and operational, then the question should be rated with one. If it is not established or is not operational, then it should be rated zero.

Indicator V.7

Are there mechanisms in place to ensure that those involved in the review of applications and CT results have sufficient and current expertise in all required areas.

Rationale: The assessment and authorization of clinical trials protocols requires people with the appropriate medical and scientific knowledge, experience and skills. They should also be free from conflict interest.

Description: The MRA should have written criteria for selecting committee members, which should cover at least:

- the technical qualification
- experience in research and clinical investigation
- declaration of conflict of interest
- timeframe for serving as committee member

Interpretation guidelines: If there is no evidence of such selection criteria then the indicator will be rated with a 0. If the selection criteria exists, rate the indicator as a *method 2* question.

Indicator V.8:

Is there a CT inspection system established and operational?

Rationale: Clinical trials should be carried out in accordance with good clinical practice. To ensure that investigators and others involved in clinical trial activities follow the GCP and other national regulations there should be an effective and efficient inspection system.

Description: The MRA should have operational inspection system with inspectors trained and experienced to carry out CT inspection. There should be written GCP guidelines for inspectors to follow. As permitted by national regulations, inspectors may carry out inspection routinely, randomly and/or for specific reasons.

Interpretation guidelines: If there is CT inspection system that is operational then the indicator should be rated one. If there is no such system or the system is not operational then the indicator should be rated zero.

Indicator V.9:

Do the national guidelines require the establishment of an Independent Ethics Committee (IEC)?

Rationale: Clinical trial protocols should be reviewed and approved by Independent Ethics Committee before they are submitted to the MRA for approval. The role of the Independent Ethics Committee is to ensure the protection of the rights safety and wellbeing of human subjects participating in clinical trials. The IEC has to consider the qualification of the investigator and review ongoing trials at reasonable interval of time.

Description: The Independent Ethics Committee should:

- be officially established
- consist necessary of members that have the qualifications and experience to review the science, medical aspects and ethics of the proposed trial.
- functions according to written operating procedures
- comply with GCP guidelines and with the applicable regulatory requirements.

Interpretation guidelines: If there is no evidence of such committee then the indicator will be rated with a 0. If the committee exists, rate the indicator as a *method 2* question.

Indicator V.10:

Does the review committee have a timeframe for assessing CT?

Rationale: The MRA should review applications for clinical trial as promptly as possible without compromise on quality of review. Setting a timeframe will help in measuring the efficiency of the MRA

Description: In order to prevent undue delay in review of applications and clinical trial reports the MRA should set a timeframe for reviewing application.

Interpretation guidelines: If the MRA has a set timeframe for reviewing application and making decisions which is followed up the indicator will be rated one. If there is no timeframe or the timeframe is not followed then the indicator will be rated zero.

Indicator V.11:

Are there written guidelines on conflicts of interest (COI) with regard to clinical trial activities?

Rationale: Given the potential for conflict of interest that could influence decision-making in the process of reviewing protocols, members of the MRA review committee as well as the IEC should be aware of what a conflict of interest implies and how it can affect their decision-making process. This would be stated in a COI policy or guideline. They should be obliged to declare officially any potential conflict of interest that could arise in their professional responsibilities.

Description: This question helps to check what systems are in place to identify and manage real or perceived conflict of interest issues. Written guidelines on COI should exist, as well as a standardized "declaration of conflict of interest" form (see annex 3 for an example). The guidelines should include as a minimum the following:

- definition of what constitutes a COI;
- rules on the acceptance of gifts;
- rules on reporting COI;
- mechanism protecting informers of COI;
- actions to be taken in case of failure to comply with guidelines;
- evidence of enforcement of these regulations (evidence that these forms are in fact systematically completed by the members of the committee and public officials involved in the control of medicines promotion process).

Interpretation guidelines: If there is no evidence of such guidelines then the indicator will be rated with a 0. If the guidelines exist, rate the indicator as a *method 2* question.

Indicator V.12:

Is there a list/database of all approved and rejected CT applications?

Rationale: The existence of such list or database will help ensure that the system is transparent and that all results, positive and negative, are available in the public domain. This is vital to ensure the safety of patient and that no product that has failed clinical trials will be made available to the public.

Description: The MRA needs to maintain such a list or database which should:

- be publicly available
- indicate all CT approved
- Indicate all CT amended
- Indicate all CT rejected.

Interpretation guidelines: If there is no evidence of such list/database then the indicator will be rated with a 0. If the list/database exists, rate the indicator as a *method 2* question.

Indicator V.13:

To what extent do you agree with the following statement: "The IEC members are systematically selected based on the written selection criteria"?

Rationale: The IEC must be independent of any kind of undue influence. Its responsibility is to ensure the protection of the rights, safety, and well-being of human subjects. It is important that they are selected based on their qualification and experience. Written selection criteria for IEC members may exist, but in practice they may not be followed. This question helps to find out whether the criteria are used or not.

Interpretation guidelines: *method 3.*

Indicator V.14:

To what extent do you agree with the following statement: "The MRA review committee members are selected systematically based on the written selection criteria"?

Rationale: Similarly to indicator V.13, selection criteria for MRA review committee may not be always used in practice. This type of information is usually known by those involved in the system, including your KI. *Please remember that it is a sensitive area*, and the KI may feel uncomfortable and find it difficult to give a spontaneous answer. Before asking this question it may be useful to remind them and reassure them of the confidentiality of their answers.

Interpretation guidelines: *method 3.*

Indicator V.15:

To what extent do you agree with the following statement: "The MRA is ensuring that CTs conducted in the country are done in accordance with the regulation and GCP principles"?

Rationale: Regulation and guidelines for GCP may exist officially, but the MRA may not be strictly enforcing the regulations as well as the guidelines. This type of information is usually known by those involved in the system, including your KI. *Please remember that it is a sensitive area*, and the KI may feel uncomfortable and find it difficult to give a spontaneous answer. Before asking this question it may be useful to remind them and reassure them of the confidentiality of their answers.

Interpretation guidelines: *method 3.*

Indicator V.16:

In your opinion, what types of unethical behaviour are common in the clinical trials area in your country?

Rationale: The MRA and the IEC have the responsibility to ensure that the clinical trials are carried out in accordance with national regulations and guidelines. It is therefore important that they carry out their activities professionally and with integrity and honesty. They should not place themselves under any financial or other obligation to

outside individuals or organizations, or take gifts that might influence them in the performance of their official duties. Their decisions should be based solely on their review findings.

Interpretation guidelines: *method 4.*

Indicator V.17:

If you were in a position of highest authority, what would be the first actions that you would take to improve the way clinical trials are carried out in your country?

Rationale: *method 4.*

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Section VI: Selection of medicines¹

A) Overview on selection of medicines

1. Introduction

Advances made in pharmaceutical science and technology during the past few decades has given rise to a plethora of pharmaceutical products in the international market. Currently, it is estimated that as many as 70 percent of the pharmaceutical products circulating in international market are said to be duplicative, “me too”, or nonessential products. Many are minor variations of the original medicine and offer no therapeutic advantage over other medicines that are already available. The presence of too many medicines:

- makes life difficult for health care providers, and pharmacists to up-date themselves with relevant current information on each medicine and to compare alternatives
- contributes to inconsistency in the prescribing manner within the same health care system or health care facility
- lessens the purchasing power significantly as the limited money available is used to buy non essential medicines.

To address the problem of access and equity to medicines, the selection of limited number of essential medicines is of paramount importance in that has a considerable impact on the quality of care and the cost of treatment. Such a list, if used to procure medicines and to guide prescribing practices, can leads to help improved supply of medicines, more rational prescribing and lower cost.

2. Criteria for selection of essential medicines

Essential medicines are those that are deemed to satisfy the health care needs of the majority of the population and that should be available in the appropriate dosage forms and strengths at all times. The choice of a limited number of essential medicines depends on many factors such as: the relevance to the pattern of prevalent diseases; the treatment facilities; the training and experience of the available personnel; the financial resources; genetic, demographic and environmental factors.

For these reasons:

- Should be selected only medicines for which sound and adequate evidence of safety and efficacy is available from clinical studies and for which evidence of performance in general use in a variety of medical settings has been obtained
- Where two or more medicines appear to be within the same therapeutic category, the choice between them should be made on the basis of a careful evaluation of their relative efficacy, safety, quality price, and availability.

¹ As mentioned in an earlier section, depending on the national context and needs, the questions included in this section can very well be adapted for assessing the level of transparency in the selection process of a medicines reimbursement list.

- Each selected medicine must be available in a form in which adequate quality, including bioavailability, can be ensured; its stability under the expected conditions of storage must be determined
- In cost comparison between medicines, the cost of the total treatment, not only the unit cost of the medicine, must be considered
- Preference for medicines whose safety and efficacy have been well defined, with good pharmacokinetic and stability properties or by local considerations, such as the availability of facilities for local manufacture and storage.
- Most essential medicines must be formulated as single compounds. Fixed-ratio combination products are acceptable only when the dosage of each ingredient meets the requirements of a defined population group and when the combination has a proven advantage over single compounds administered separately in therapeutic effect, safety or patient adherence to treatment.

3. Advantages of a limited list of essential medicines

When a limited list of essential medicines represents the consensus of medicine treatments of first choice, its use may improve the quality of care by ensuring that patients receive the treatment of choice as well as similar treatments from different providers

A limited list of essential medicines allows prescribers to become more familiar with a smaller number of medicines and contributes to improved recognition of actual benefits and limitations of specific medicine therapy. It contributes to improved detection and prevention of adverse medicine reactions. Improved effectiveness and efficiency in patient treatment, on the other hand, will lead to lower health care costs.

Another advantage of selecting a limited list is that it enables to concentrate procurement and logistics efforts on a limited number of medicines including reduction in the number of medicines to be stocked, distributed and monitored.

Concentrating on a limited list of medicines to be procured increases the potential for economies of scale, makes easier to ensure the quality of medicines, facilitates efforts to provide medicine information and education, increases adherence to treatment by patients and improves medicine availability.

4. The process of developing an essential medicines list

a) Establishing an independent committee

The Ministry of Health, or the government body responsible for health, should establish an independent therapeutics committee composed of health professionals with appropriate scientific and medical knowledge, experience and skills as well as known for their integrity, honesty, and dedication. Selection should be carried out in accordance with written criteria. The Committee should have Terms of Reference and Standard Operating Procedures (SOPs). All members of the committee should sign a conflict of interest form and should not have any relationship with any medicine manufacturer or distributor.

b) Establishing a list of common diseases and standard treatment guidelines

The committee in consultation with authorities of the ministry of health and health professionals and other interested parties should develop the list of common diseases based on the pattern of prevalent diseases, treatment facilities, the training and experience of available personnel and financial resources. This list of common diseases will then guide the

formulation of standard treatment guidelines. The list of essential medicines to be selected should be those used to treat these diseases.

c) Drafting a list of essential medicines list

Once the diseases are defined the committee will have to select the most cost-effective medicine(s) for each disease and define the dosage form and the strength per unit dose for each medicine. The process of developing an essential medicines list should be transparent and participatory to ensure that it will reflect the needs of the population and that it will be accepted by its users. Decision for inclusion of a medicine in the list should be based on the latest evidence available. Having an open and transparent consultation process will be crucial in ensuring that decisions on the EML will be objective and not subjective, evidence-based, and that they take into account the opinion of all parties, and not the views of those people offering incentives to influence the decision to favour their personal interests.

d) Consensus meeting

In order to make the list acceptable to all interested parties, a consensus meeting should be called to discuss the list. The meeting should involve physicians, academicians, pharmacists, paramedics and other health workers, pharmaceutical manufacturers and distributors, patient groups and civic societies and the government budget and finance group. Once accepted by consensus the list should be published and distributed to all health care facilities and health professionals and other interested parties for implementation.

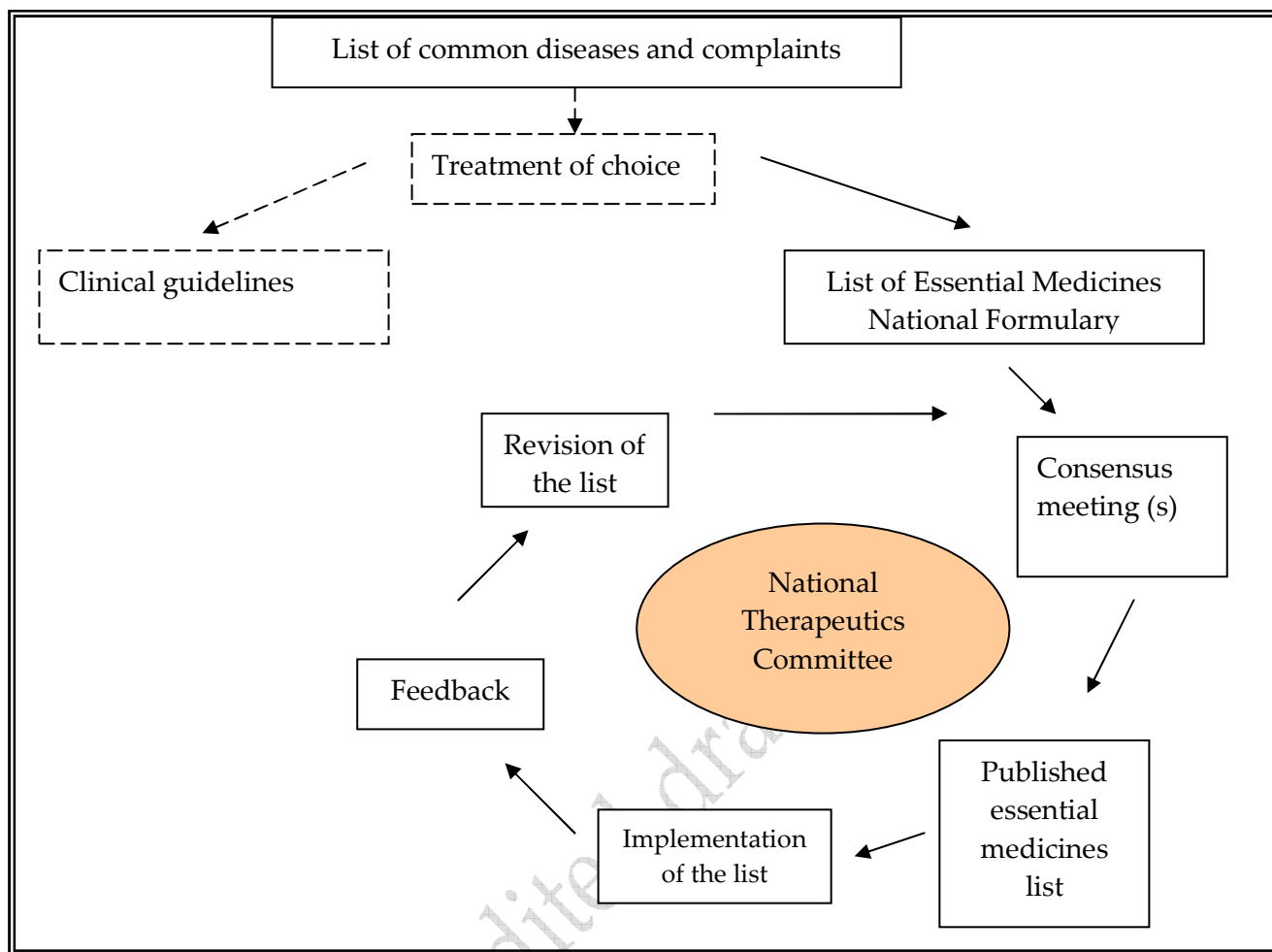
e) Promotion of the list

The list should be promoted through seminars and workshops. Health professionals and other interested parties should be invited to such seminars and explanation on advantages of the essential medicines list should be provided and the development process of the list should be described as well.

f) Revision of the list

The list should be revised after a defined period of time taking into account new developments in the area - pattern of diseases, new treatment approaches, new medicines, etc. Inclusion into and deletion from the list should be based on established criteria and should be carried out in a transparent and open manner.

Figure 6: Essential medicines list development process



B) Comments on each indicator

Indicator VI.1:

Does the government have an officially adopted national essential medicines list (EML) publicly available?

Rationale: An essential medicines list, if used properly, can help to ensure that medicine expenditure is not wasted by the government on unnecessary medicine products that may be promoted by suppliers to governments through the use of legal marketing strategies or illegal payoffs.

Description: An essential medicines list is a published document that identifies those medicines determined by a national authority to be essential for key public health problems in a country and that should be available through the public health system. It is a medicine selection tool that, if prepared well, can help governments purchase appropriate medicines for their population.

Interpretation guidelines: If there is evidence of an essential medicines list and it has been revised in the past five years then this indicator should receive a rating of 1. If it is out of date (more than five years old) or if there is no evidence of an essential medicines list, this indicator should receive a 0.

Indicator VI.2:

To what extent do you agree with the following statement: "The national essential medicines list has been developed in consultation with all interested parties and using an evidence-based approach"?

Rationale: An essential medicines list (EML) should be developed in wide consultation, and in a transparent manner, with all interested parties to ensure that it will reflect the needs of the population and that it will be accepted by its users. Decisions also need to be based on the latest evidence available. Formal and informal consultations may be organized by the responsible government committee (called the selection committee below) with interested parties, including professional bodies and associations, pharmaceutical manufacturers and distributors, consumer organizations and the government budget and finance group. Having an open and transparent consultation process will be crucial in ensuring that decisions on the EML are objective and not subjective, evidence-based, and that they take into account the opinion of all parties, and not the views of those people offering incentives to influence the decision to favour their personal interests.

Interpretation guidelines: *method 3.*

Indicator VI.3:

Are there clearly written and publicly available guidelines for the selection process for including or deleting medicines from the national EML?

Rationale: This indicator can help assess the transparency of the government's decision-making processes relating to the national EML. Rules and criteria for medicines selection can help lessen the likelihood of collusion or payoffs for inclusion on the list and reduces the discretion of selection committee members.

Description: The government should have clear guidelines that specify what criteria are applied for medicines to be included on or deleted from the EML. The inclusion of a new medicine should be based on studies that confirm that the medicine is necessary for the health needs of the population and is cost-effective. It is equally important that the deletion of a medicine from the EML should be based on sound evidence that the medicine is inappropriate or not cost-effective for the population's health needs.

Interpretation guidelines: If there is no evidence of such guidelines then the indicator will be rated with a 0. If the guidelines exist, rate the indicator as a *method 2* question.

Indicator VI.4:

Is the EML in line with WHO procedures?

Rationale: The WHO Model List of Essential Medicines has been developed and updated every two years since 1977, based on a set of principles and recommendations. Following these same principles and recommendations will help to ensure that national EMLs are developed on objective criteria, in a consistent manner and that their use will be promoted widely. For example, the EML should be by generic name and not promote specific branded products. Linking the EML with existing national treatment guidelines will help to ensure that it meets the priority health needs of the population and not commercial priorities.

Description: The EML should be available in a printed format and be easily accessible by all health professionals. To reinforce its impact it needs to be widely disseminated to all relevant health professionals. The products should be listed by generic name and by level of health care. The EML will need to be linked to national treatment guidelines and be revised at least every 5 years.

Interpretation guidelines: If there is no evidence of such procedures then the indicator will be rated with a 0. If the procedure exist, rate the indicator as a *method 2* question.

Indicator VI.5:

Is there a committee responsible for the selection of the national EML?

Rationale: A selection committee should be appointed to give technical advice on the revision and update of the EML. Having a group of experts working together creates a more open and transparent platform for decision-making.

Description: The selection committee should include people from different fields, such as medicine, nursing, pharmacology, pharmacy, public health, consumer groups and health workers at grass roots level.

Interpretation guidelines: If a selection committee exists, then the indicator will be rated with a 1. If there is no formal committee established to advise the government on the development/update of the EML, then the indicator will receive a 0.

Indicator VI.6:

To what extent do you agree with the following statement: "The committee responsible for the selection of the national EML is operating free from external influence"?

Rationale: Despite having clear and written criteria for developing and updating an EML and a formal committee responsible for the selection process, this area can remain vulnerable to unethical practices. Indeed a non-essential medicine may be added as a result of a bribe to a committee member, or because of the pressure a government official may exert for personal benefit (investment in company, spouse in company, etc.).

Interpretation guidelines: *method 3.*

Indicator VI.7:

Are there clear criteria for the selection of members of the selection committee?

Rationale: There should be clearly written criteria for committee member recruitment to ensure that selection is based on professional expertise, and also that the experts are free from any form of conflict of interest. These criteria will help to promote transparency in the selection process. They will also help to ensure that selection is based on the professional merit of the experts and not on favouritism.

Description: The criteria for selecting committee members should be publicly available in writing and easily accessible from the government office. They should define the professional requirements, and the committee should include experts from different fields (medicine, nursing, pharmacology, pharmacy, public health, pharmacoeconomics, consumer affairs, and health workers at the primary health care level. The criteria should require declaration of COI. Membership needs to be time- limited to ensure rotation and so reduce the likelihood of biased decision-making.

Interpretation guidelines: If there is no evidence of such criteria then the indicator will be rated with a 0. If the criteria exists, rate the indicator as a *method 2* question.

Indicator VI.8:

Are there written guidelines on conflicts of interest (COI) with regard to selection of essential medicines?

Rationale: This indicator determines if the government is trying to mitigate conflict of interest and measures a government's commitment to penalizing public officials for not complying with the required procedure.

Description: Written guidelines on COI and a COI declaration form should exist and include as a minimum the following:

- definition of what a COI is;
- rules on the acceptance of gifts;
- rules on reporting COI;
- mechanism protecting informers of COI;
- actions to be taken in case of failure to comply with policy;
- evidence of enforcement of these guidelines (evidence that COI forms are systematically completed by the members of the selection committee and public officials involved in the selection process).

Interpretation guidelines: If there is no evidence of such guidelines then the indicator will be rated with a 0. If the guidelines exist, rate the indicator as a *method 2* question.

Indicator VI.9:

Are there clear terms of reference that describe the role and responsibilities of the selection committee?

Rationale: To help ensure transparency, fairness and consistency in the selection process, the committee should be operating according to written terms of reference (TOR). Moreover, it should not be an ad hoc committee but one that is fully established as an official committee. TOR are crucial for helping to ensure the good governance of the committee.

Description: These TOR should be publicly available and describe clearly the rules for the decision-making process.

Interpretation guidelines: If there is no evidence of such TOR then the indicator will be rated with a 0. If the TOR exist, rate the indicator as a *method 2* question.

Indicator VI.10:

Are there written SOPs for decision-making process of the committee?

Rationale: This is another indicator to measure the amount of checks and balances, which are part of the medicine selection process. It also helps to measure the transparency level in sharing the decisions made by the committee. The decision-making process for medicine selection should reflect the input from a number of individuals and not be made *de facto* by one person. Public information about the selection of medicines decision-making is necessary to lessen the likelihood of decisions that are not based on sound health and economic needs.

Description: The rules for decision-making defined in the SOPs should require at least that:

- decisions are made by all members in a democratic manner;
- minutes of meetings are produced and approved by the members.
- consultations are held with interested parties;
- final decisions for selecting medicines are taken independently;

- decisions on the selection process are made publicly available;
- decisions are disseminated widely.

Interpretation guidelines: If there is no evidence of such SOP then the indicator will be rated with a 0. If the SOP exist, rate the indicator as a *method 2* question.

Indicator VI.11:

In your opinion, what types of unethical behaviour are common in the selection process in your country? These can include bribery, material gifts, favouritism (family, friends), conflicts of interest (e.g. investments in pharmaceutical companies), pressure on consultants by companies, etc.

Rationale: Government officials and other experts responsible for the selection of essential medicines have a duty to ensure that the selection process is done in accordance with national procedures. It is therefore important that they carry out their activities professionally and with integrity and honesty. They should not place themselves under any financial or other obligation to outside individuals or organizations, or take gifts that might influence them in the performance of their official duties.

Interpretation guidelines: *method 4.*

Indicator VI.12:

If you were in a position of highest authority, what would be the first action that you would take to improve medicine selection?

Rationale: *method 4.*

Unedited draft

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Section VII: Procurement of medical products

A) Overview on procurement of medical products

1. Introduction

Procurement is defined as the process of acquiring supplies through purchase from manufacturers or suppliers or distributors. In many countries medicine expenditure constitutes a large proportion of health expenditure. Medicine procurement is therefore a major determinant of medicine availability and total health costs. In most developing countries medicine purchases represent the single largest out-of-pocket health expenditure after personnel costs. Medicines also consume the major share of health related foreign exchange.

2. Operational principles of good procurement system:

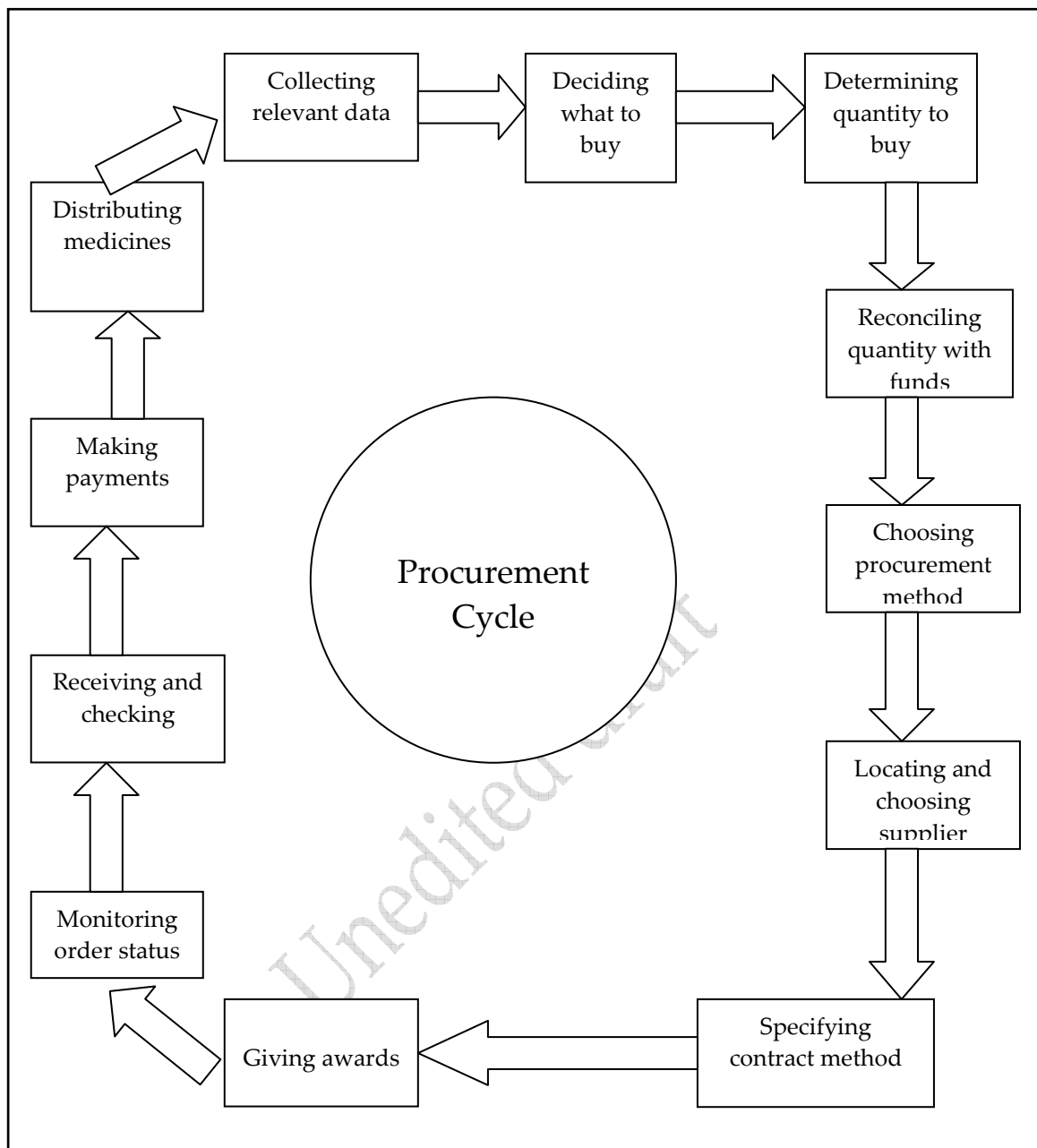
- efficient and transparent management
- different procurement functions should be separated and performed by different offices or committees
- procedure should be transparent following formal written procedures
- should be planned and performance monitored and audited regularly
- should be limited to a national essential medicines list
- order quantities should be based on a reliable estimate of actual need
- mechanisms should be placed to assure reliable financing mechanism
- should be done in the largest possible quantities
- there should be appeals procedures

3. Procurement procedure

A good procurement system should be based on written procedures. The process should be open and transparent. Such system will help in attracting the best suppliers and the best prices. Limiting the number of best suppliers will affect price competition and make procurement prices much higher than the international reference prices. Procurement should be based on the national list of essential medicines. The list should be prepared in INN or generic names. Tenders and contract specification should be publicly advertised. Criteria for adjudication of tender should be part of the tender document and contract awards should be made by the tender committee. Information on tender process and results should be made public and it should also describe the internal process to be followed by the procurement staff on how to process the bids.

Procurement process involves the following steps: deciding what to buy (reviewing the essential medicine list); determining quantities needed; reconciling quantities and funds; choosing procurement method; locating and selecting supplier; specifying contract methods; giving awards; monitoring orders status; receiving and checking medicines; making payment; distributing medicines; collecting consumption information (receiving request for purchase).

Figure 7: Procurement process ¹



a) Types of procurement methods

There are four types of procurement methods used to purchase pharmaceutical products. These are open tender, restricted tender, competitive negotiations, and direct procurement. The procurement method chosen for each product should aim to obtain the lowest possible purchase price for assured quality products and to ensure the supplier's reliability in terms of quality and service. The method should maintain transparency in the process and minimize any potential corruption or favouritism. There should be written guidelines to guide the committee and the staff of the procurement office in deciding which method to use for a given product.

¹ Managing Drug Supply, Management Science for Health, 2nd edition (1997)

b) Setting quantities

There should be established method for deciding quantities to be purchased. In principle it should be based on objective, actual or expected health needs. This is to prevent over or under purchase.

c) Tender committee

There should be a tender awarding committee. Members should be nominated on the bases of their professional expertise and skills. There should clear guidelines specifying the criteria to be applied in selecting the members of the tender committee. There should be written terms of reference that defines the jobs of the committee and membership duration. Members have to sign conflict of interest forms to reduce opportunities for corruption, favoritism or political influence.

c) Information system

There should be management information system for the procurement office and its clients to monitor the medicine procurement process. The system should be able to track the procurement process and signal problems when they arise so they can be easily addressed.

4. Appeals process

There should be a written appeals system for suppliers to lodge their complaints. This will help to make the process transparent and accountable.

5. Inspection of consignments

As soon as goods arrive in the warehouse they should be inspected to verify the quality and quantity of the products received. In addition, physical inspection and laboratory testing of selected products may be carried out to check any quality defects including the presence of counterfeit pharmaceutical products.

Each medicine shipment should be physically inspected. This involves checking adherence to contract specifications. Additionally batch samples should be sent to quality control laboratories (random sampling for known suppliers and systematically for new ones). All documents (inspection report and laboratory testing results) should be archived in the procurement office.

6. Suppliers monitoring system

Monitoring of the procurement process post-tender is critical to ensure that medicine suppliers are honouring their contracts. Poor performers can be identified and “blacklisted” from future tenders.

7. Audits

There should be both internal and external audit system to audit the financial and technical performance of the procurement office. Through audits it is possible to identify if any corruption has occurred or not. Audit reports should be available publicly.

B) Comments on each indicator

Indicator VII.1:

Does the government use transparent and explicit procedures for procurement of pharmaceutical products?

Rationale: Written procurement procedures for procurement of pharmaceutical products can help to ensure that the procurement process is open and transparent. They are also important to attract the best suppliers and the best prices. Secretive procedures create room for cronyism and corruption (whether real or perceived) in the procurement process. Eventually, suppliers, health-care providers and patients may lose their trust in the system. As the pool of applying suppliers decreases to a small set, price competition will decrease as well, and procurement prices may be much higher than the international reference prices.¹

Description: The government should have an explicit document that describes the procurement process for pharmaceutical products clearly. This document should be publicly available and require as a minimum:

- procurement that is based on the national list of essential medicines;
- the use of INN or generic names;
- the advertisement of tenders;
- contract specification are publicly available;
- criteria for adjudication of tender are included as part of the tender package;
- contract awards are made by the tender committee;
- information on the tender process and results are made public (to the extent permitted by the law);
- description of the internal process to be followed by the procurement staff to process the bids.

Interpretation guidelines: If there is no evidence of such procedures then the indicator will be rated with a 0. If the procedures exist, rate the indicator as a *method 2* question.

Indicator VII.2:

Is there written guidance for procurement office staff on the type of procurement method to be used for different types of products?

Rationale: There are several types of procurement methods used to purchase pharmaceutical products, which fall into one of four basic categories: open tender, restricted tender, competitive negotiations and direct procurement.² The procurement

¹ The international reference prices include those found in the *International Medicine Price Indicator Guide* published by Management Sciences for Health and in *Sources and Prices of Selected Medicines and Diagnostics for People Living with HIV/AIDS*, jointly published by UNICEF, UNAIDS, MSF and WHO.

² See definitions in Glossary on page 79.

method chosen for each product should aim to obtain the lowest possible purchase price for assured quality products and to ensure the supplier's reliability in terms of quality and service. Moreover, it should maintain transparency in the process and minimize the opportunity for illicit influence on procurement decisions. In most public sector programmes, the majority of medicines should be purchased through competitive tenders, but depending on the experience of the procurement office and the situation (e.g. emergency), another method may be chosen. Written guidance for procurement office staff on which method to use, depending on the products and situation, are essential to prevent possible personal arrangements with the suppliers, for example by planning a direct procurement instead of a competitive tender to favour a specific supplier.

Description: In many countries, laws and procurement regulations dictate the procurement method to be used, often based on the value of the goods being purchased. There should be clear written guidance for procurement office staff on what procurement method to use for the different types of products to be purchased.

Interpretation guidelines: If written guidelines exist then the indicator will be rated with a 1. If there is no written guidance, then the indicator will receive a 0.

Indicator VII.3:

Is procurement done with an objective quantification method to determine the quantity of pharmaceuticals to be purchased?

Rationale: To reduce the risk of over-supply, under-supply, or unnecessary supply of pharmaceuticals, medicine purchases should be based on objective, actual or expected health needs, and on budget availability. Use of an established methodology for estimating needs reduces vulnerability to unwarranted pressure from pharmaceutical suppliers to make medicine purchases by government officials through the use of kickbacks and other types of payoffs.

Description: There are four major methods for quantifying medicine needs: consumption (based on historical data), morbidity-based, adjusted consumption, and service-level projection. Ideally, a combination of these will be applied to obtain the most accurate estimates.

Interpretation guidelines: If the methodology for quantifying medicine needs is well documented and based on objective criteria, as defined above, then the indicator should receive a rating of one. If there is a non-comprehensive model in place, this indicator should receive a 0. If there is no evidence of a model in use, this indicator should receive a 0.

Indicator VII.4:

Is there a formal appeals process for applicants who have their bids rejected?

Rationale: A formal appeals process in the procurement system helps promote honest behaviour on the part of the governments and suppliers/manufacturers.

Description: A protest mechanism works in the following way. If a firm is unsuccessful in its bid for a tender, a representative from the firm can file a protest based on the firm's view that the tender excludes it unfairly or that the tender process was flawed.

Interpretation guidelines: If there is a protest mechanism in operation and there is evidence of its use, then this indicator should receive a rating of 1. Evidence should support this. If there is a protest mechanism in place but there is little evidence that it is used, then this indicator should receive a rating of 0. If there is no protest mechanism in place, this indicator should receive a rating of 0.

Indicator VII.5:

Is there a tender committee? If so are the key functions of the procurement office and those of the tender committee clearly separated?

Rationale: There are several key procurement functions which in general should be handled by different individuals or committees. These functions include: selection of medicines, quantification of medicine requirements, preparation of product specifications, approval of suppliers (pre-qualification and post-qualification), and adjudication and award of tender. Without separation of functions, the procurement process is much more susceptible to be influenced by special interests. Procurement office staff may be able to influence each of these functions. For example, they may be able to bias selection of medicines, manipulate the orders to increase the quantities of some medicines, prejudice supplier qualification decisions, manipulate the final tender award or slant product specifications to limit competition (e.g. by selecting less common dosage forms). Separation of key functions contributes to professionalism, accountability and avoidance of conflict of interest.

Description: The main role of a tender committee is to review information on suppliers and determine which suppliers should participate in the tender (if a restricted tender is used) and which suppliers receive contracts. Staff from the procurement office (whose main role is to collate information on needs) manage the tender process and monitor suppliers performance.

Interpretation guidelines: If there is no tender committee, then the indicator will be rated with a 0. If there is a tender committee then the indicator will be rated as a *method 2* question.

Indicator VII.6:

To what extent do you agree with the following statement: "Decisions of the Tender Committee are always taken into account in the procurement process."?

Rationale and description: In some circumstances despite the establishment of a Tender Committee that operates efficiently, transparently and with integrity, the committee's decisions may not always be followed by the procurement office. For example, the procurement office may purchase medicines from a suppliers not approved by the tender committee or may purchase quantities in excess of what has been approved by the

Tender Committee. This question will help gain some insight on how things happen in practice.

Interpretation guidelines: *method 3*.

Indicator VII.7:

Are there specific criteria for tender committee membership?

Rationale: Medicine procurement contracting typically involves large amounts of money so there is potential for unethical practices. Clear criteria for selection of tender committee members can help reduce the likelihood of illegal practices and subjective decisions by the committee members. These criteria will help promote transparency in the procurement process. They will also help in ensuring that the selection of tender committee members is based on the professional merit of the experts and not on favouritism or other influence.

Description: The government should have clear guidelines that specify what criteria are applied for selecting the members of the tender committee. The procurement committee should be comprised of members who are appointed for their professional expertise. These members should have skills that complement each other, including senior government officials in departments served by the procurement system, and officials from user facilities. The membership should rotate periodically as it reduces opportunities for unwarranted influence on committee activities. Moreover the criteria should require that each member should declare any conflict of interest.

Interpretation guidelines: If there is no evidence of such criteria then the indicator will be rated with a 0. If the criteria exist, rate the indicator as a *method 2* question.

Indicator VII.8:

Are there written guidelines on conflicts of interest (COI) with regard to the procurement process?

Rationale: This indicator determines if the government is trying to mitigate conflict of interest and measures a government's commitment to penalize public officials for behaviour which breaches the law.

Description: Written guidelines on COI and a COI declaration form should exist and include as a minimum the following:

- definition of what a COI is;
- rules on accepting of gifts;
- rules on reporting COI;
- mechanism protecting informers of COI;
- actions to be taken in case of failure to comply with policy;
- evidence of enforcement of these regulations (evidence that these forms are in fact systematically completed by the members of the tender committee);
- require to be signed by both procurement office staff and tender committee members.

Interpretation guidelines: If there is no evidence of such guidelines then the indicator will be rated with a 0. If the guidelines exist, rate the indicator as a *method 2* question.

Indicator VII.9:

To what extent do you agree with the following statement: "The members of the tender committee are systematically selected based on specific criteria (see question V.6)"?

Rationale and description: Criteria to select the members of the tender committee may exist and be as comprehensive as they are defined in question V.6, but in reality they may not be used systematically or not at all. Asking the perception of KI will bring valuable insight on the transparency of the selection process for tender committee members and on the application (or non-application) of existing rules and regulation in a given country.

Interpretation guidelines: *method 3.*

Indicator VII.10:

Is there a computerized management information system used to report product problems in procurement?

Rationale: One of the most important tools in the procurement office is its management information system. The procurement office and its clients should all use this system to monitor the medicine procurement process. It should track the entire procurement process and signal problems when they arise so they can be easily addressed. This indicator can help to show if the government is making sure that the requisite checks are in place to ensure that the procurement process is seamless and opportunities for corruption are minimized.

Description: The management information system can be computerized or manual. However, a computerized system is preferable as this will make checking for fraud and abuse easier. It should include product records, and monitor supplier and facility performance. It should also record all quality assurance information for products purchased, and track the status for each order, including the quantities actually purchased compared with the original estimates made.

Interpretation guidelines: If there is no evidence of computerized management information system then the indicator will be rated with a 0. If the computerized system exists, rate the indicator as a *method 2* question.

Indicator VII.11:

Are there Standard Operating Procedures (SOPs) for routine inspection of consignments?

Rationale: The quality of the products received needs to be verified as soon as possible after arrival, both by physical inspection of each shipment and by laboratory testing of selected products. This is an indispensable part of the medicine procurement process to check against the risk of counterfeit (both brand-name and generic) or sub-standard pharmaceutical products.

Description: Each medicine shipment should be physically inspected. This involves checking adherence to contract specifications. Additionally batch samples should be sent

to quality control laboratories (random sampling for known suppliers and systematic for new ones). All documents (inspection report and laboratory testing results) should be archived in the procurement office.

Interpretation guidelines: If there is no evidence of such SOP then the indicator will be rated with a 0. If the SOP exist, rate the indicator as a *method 2* question.

Indicator VII.12:

Is there an efficient post-tender system in place to monitor and report on suppliers' performance to the tender committee?

Rationale: Monitoring of the procurement process post-tender is critical to ensure that medicine suppliers are honouring their contracts. Poor performers can be identified and "blacklisted" from future tenders.

Description: The procurement office should monitor supplier performance and compliance with the contract terms. To this end, it needs to track suppliers' lead time, delivery status, shelf-life, and packaging of products. Product quality must also be tracked and suppliers with poor performance blacklisted.

Interpretation guidelines: If there is no evidence of such system then the indicator will be rated with a 0. If the system exists, rate the indicator as a *method 2* question.

Indicator VII.13:

Does the procurement office undergo regular audits?

Rationale: Given that the procurement of pharmaceutical products carries a high risk of corruption, an annual audit of the procurement unit - verifying procurement office accounting records - is indispensable.

Description: The procurement office should undergo an audit (internal or external) at least once a year, and its results should be available publicly. The annual audit should report on the operating costs of the procurement office, pharmaceutical products tendered, quantities of the products procured, and the contracts awarded.

Interpretation guidelines: If there is no evidence of audit then the indicator will be rated with a 0. If the audit is carried out, rate the indicator as a *method 2* question.

Indicator VII.14:

To what extent do you agree with the following statement: "The procurement system in your country is operating in a totally transparent manner"?

Rationale: Despite the fact of having clear and written procurement procedures, a formal tender committee and clear criteria for selection tender committee members, the procurement process remains vulnerable to unethical practices.

Interpretation guidelines: *method 3*.

Indicator VII.15:

In your opinion, what types of unethical behaviour are common in the procurement system in your country? These can include bribery, material gifts, favouritism (family, friends), conflict of interest (e.g. investments in pharmaceutical companies), etc.

Rationale: Procurement office staff and tender committee members have the responsibility to ensure that the procurement of medicines is done in accordance with national procedures. It is therefore important that they carry out their activities professionally and with integrity and honesty. They should not place themselves under any financial or other obligation to outside individuals or organizations or take gifts that might influence them in the performance of their official duties. Their decisions should be solely based on their inspection findings.

Interpretation guidelines: *method 4.*

Indicator VII.16:

If you were in a position of highest authority, what would be the first action that you would take to improve the systems and processes of procurement?

Rationale: *method 4.*

Unedited draft

Section VIII: Distribution of pharmaceuticals

A) Overview on distribution of pharmaceuticals

1. Introduction

Distribution is an important activity in the management of pharmaceuticals and involves the following steps:

- port clearing
- receiving and inspecting
- storage
- inventory management
- requisition of supplies
- dispatch, pick up and transportation
- disposal

There are many different strategies for the distribution of pharmaceuticals. These include multi-tiered models in which supplies cascade and branch out from a central source down to lower levels. Other systems may have direct delivery models in which suppliers deliver directly to the service delivery point. Variations may also be seen between the public and private sector systems in the same country. In general the steps listed above cover all aspects of the distribution of pharmaceutical products, from arrival in the port of entry to the point of supply to health establishments.

Each of the steps listed above can present various opportunities for lack of transparency and therefore invites corruption. In order to prevent any theft, divergence or fraud every activity in the distribution of pharmaceutical products should be carried out according to the principles of good storage practice (GSP)¹ and good distribution practice (GDP)². Published standard operating procedures which specify the roles and responsibilities of all staff involved in each of these steps are important tools that promote transparency and accountability.

2. Port clearing

This step refers only to imported products and port clearing can refer to any port of entry, land or sea. It involves identifying shipments as soon as they arrive in port, processing all importation documents, completing any customs requirements, assuring proper storage of medicines until they are removed from the port, surveying the shipment for damage and collecting the medicines as soon as they have been cleared. Inadequate and inefficient port clearing procedures can result in undue delays, providing extended exposure to potential theft in ports with weak security. Increased efficiency in port clearing minimizes the risk of

¹ WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-seventh Report. Technical Report Series No. 908. Annex 9.

² WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fortieth Report. Technical Report Series No. 937. Annexes 5 and 6.

theft. Port clearance may be conducted by government officials or by contracted clearing agents.

In some countries the process of importing medicines involves additional regulatory requirement, i.e. submission of purchase order to the national medicine regulatory authority prior to placing the order to get permission to import these medicines. Similarly on the arrival of the goods at the port, the importing agency has to submit the invoice of the products to authority who will check against the purchase order and make decision as appropriate. The invoice must indicate all information about product-name of product, name and address of manufacturer, country of manufacture, strength, dosage form, quantity, expiry date and batch number, etc.

3. Receiving and inspecting

When medicines are first delivered to the warehouse, they must be kept separate from other stock until they are inspected by the recipient's/purchaser's representative. The objective of inspection is to assure that the supplier has fulfilled terms of the contract or supply request (could be donation, for example) and to uncover any damage or loss that may have occurred during shipment. Prompt shipment inspection with supporting documentation is part of contract enforcement and helps to resolve disputes with suppliers or handlers.

4. Storage

Proper organization and maintenance of storage facilities ensure that medicine quality is maintained, theft is minimized and medicines are efficiently issued to other facilities. The theft of medicines in warehouses is usually facilitated not only by poor record-keeping but also poor security. Improving security involves analysing the sources of security breaches, developing methods for improving security and comparing the cost of security measures with the financial and public health costs of inadequate security. Prevention mechanisms include:

- limiting access only to approved personnel at all points.
- securing locks and doorways
- actively using an information system from informal sources, such as police informers, to detect theft and trace the point at which the theft occurred
- regular monitoring of medical stores (independent stock-takes or physical inventories).
- using camera(s)
- searching individuals when they are leaving the store.

Poor store management can lead to theft of medicines.

5. Inventory management

Effective inventory management is the basis for ensuring the coordinated and timely flow of medicines through the supply chain. Inventory management includes regular reporting on performance with regard to inventory position, order and back-order status, operating costs and consumption patterns. Stock records are the basic management tool for inventory control activities. Poor record keeping is synonymous with lack of transparency as it makes it difficult for managers to account for supplies received and distributed. It invites accusations of a myriad of abuses, the most common being pilferage (theft).

To minimize this risk, GSP calls for stock records for each item stored that records all transactions for that item, including receipts, issues, orders placed, orders received, and

stock losses. Record-keeping should be detailed enough to provide an audit trail. Accurate records, which provide information on current medicine stocks, are a key component of a well maintained medical store (or warehouse) and are the basis for requisitioning and issuing appropriate medicines and quantities, for financial accounting and for preparing consumption reports necessary for future procurement.

6. Requisition of supplies

Health facilities should have standard form for requesting medicines. The request form should provide minimum information that should describe the medicine to be supplied i.e. name of the medicine, dosage form, strength, quantity. The requisition should be checked by the responsible person, dated and signed. The prepared requisition form will then be submitted to the responsible unit within the central warehouse who will make the decision with regard to the type of medicine and quantities to be supplied and forward the requisition to the appropriate stores for filling the requisition. The appropriate store will fill the requisition and prepare invoice in three copies with the following minimum information on the medicines/products supplied- name of product, dosage form, strength, batch number expiry date and quantity supplied. Quantity supplied is then checked against the invoices in the presence of the representative of the requesting health facility and then properly packed by applying tamper evident seals and labelled with appropriate address and precautions to prevent theft and swapping.

7. Dispatch, pick up and transportation

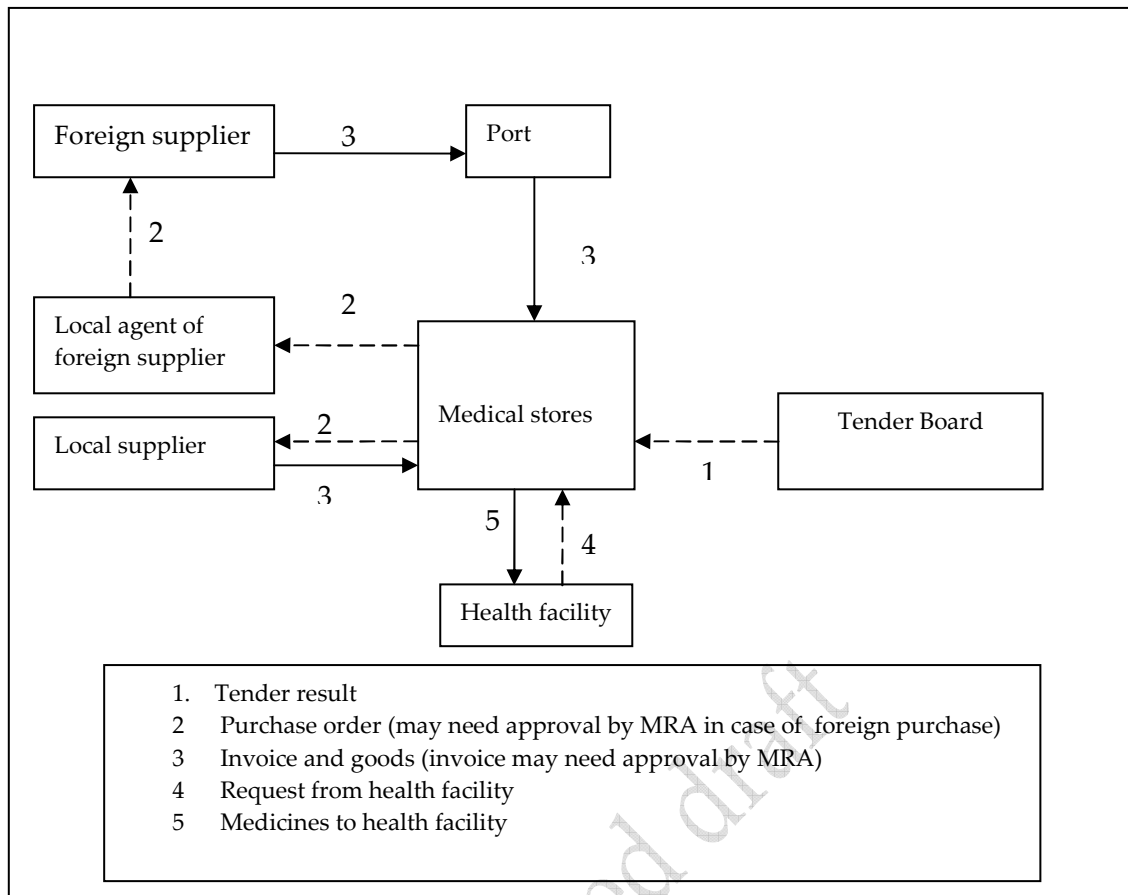
The distribution of medicines through the supply chain involves transportation. Medicines being high-value, small-size products are highly susceptible to theft or diversion by carriers during transportation. Examples of why theft may occur during transportation include:

- stealing some products out of a consignment for personal use,
- diversion of part or all of a consignment and selling it on the illegal market.

8. Disposal of unwanted medicines

At the medical stores and health facilities store level sometimes medicines could expire or get spoiled. In such circumstances the respective store chiefs have to report the case to respective managers who in turn will have to notify the national medicine regulatory authority for appropriate disposal of the medicines . There must be a committee composed of representatives from the regulatory authority (usually inspector), representative of MO Finance, head of the store, and representative of the finance unit of the MS or health facility as the case may be. The committee should supervise the process of disposal and sign minutes confirming the disposal. The minute should be accompanied by the list of products disposed and the following information- name of medicines, dosage form, strength quantity, reason and type of disposal.

Figure 8: Distribution flow chart



B) Comments on each indicator

Indicator VIII.1:

Is there a system in place that can expedite port clearing?

Rationale: Clearing of medicine consignments from ports is a quite time-consuming activity which can lead to many losses. Medicines are highly attractive items to steal. In order to expedite port clearing it is necessary for import managers to assign a person responsible for port clearing. Sometimes port clearance is contracted to a clearing agent. In any event, there should be a manual or computerized information system which is capable of monitoring and reporting on port clearing progress.

Description: The import manager or the person responsible for port clearing should be able to show the information system (documentation) which is used for monitoring port clearing activities. This person should also be cross-checked by another person on a rotating basis to ensure best practices.

Interpretation guidelines: If the Central warehouse has a person or unit that is responsible for port clearing and there is a manual or computerized system to monitor port clearing activities then the indicator should be rated 1. If there is a person or unit but no evidence of an information system for monitoring then the system should be rated 0.

Indicator VIII.2:

To what extent do you agree with the following statement: "Port clearing is done smoothly and there is no need for bribery or gift-giving to expedite the process."?

Rationale: Clearing medicines consignments can be complex and cumbersome and in some countries bribing or giving gifts may be an accepted way of "getting things done". KIs should be able to provide additional insight into common practice in their own country.

Interpretation guidelines: *method 3.*

Indicator VIII.3:

Is there an inspection system to verify that the medicines delivered from the port or directly from a supplier match those that were shipped from the supplier?

Rationale: When medicines are first delivered from the port or directly from a supplier to the warehouse or facility, they are kept separate from other stock until a designated warehouse staff member has performed a complete formal inspection of the shipment. Inspection should uncover loss and assure that the medicines received are consistent with the orders.

Description: There should be a system including:

- A separate space for checking goods on arrival.

- One or more designated person responsible for checking receipts against the packing list when supplies arrive at the warehouse.
- The responsible person should prepare documentation through a Receiving Report on the basis of the invoice specifying the types, quantities and condition of the supplies received.
- There should also be an oversight system to double-check this. This will reveal any possible theft or divergence as long as there is regular and systematic cross-checking.

Interpretation guidelines: If there is no evidence of such system then the indicator will be rated with a 0. If the system exists, rate the indicator as a *method 2* question.

Indicator VIII.4:

Is there a coding system used to identify government medicines?

Rationale: An individual or company caught with stolen medicines may claim to have purchased them. Although the medicines may have been stolen from government stores, it is difficult to prove this without some means of identifying them. Specific government imprints can help identify government supplies and differentiate them from those circulating in the private sector.

Description: Government medicines can be identified in one or more of the following ways:

- imprints on containers and external packaging
- batch number registration
- tablet embossing and capsule imprinting.

Interpretation guidelines: If the government has implemented one of the systems listed above or any other logical and thorough system to identify government medicines, then this indicator should receive a rating of 1. If the coding is not thorough, or if there is no coding on government medicines, then this indicator should receive a rating of 0.

Indicator VIII.5:

Is there systematic and orderly shelving of products in warehouses or storerooms?

Rationale: Systematic and orderly shelving of medicinal products that are regularly updated in warehouses helps to easily identify the medicines and facilitates the detection of unexpected missing stock (see indicator on physical counts. VIII.8).

Description: Products in warehouses should be organized systematically, such as by therapeutic category or alphabetically. There should be a master “map” showing how products are organized and where specific types of products may be located in the warehouse. They should also be shelved by expiry date. Any medicine product should be found with ease if the system works effectively.

Interpretation guidelines: If there is no evidence of such system then the indicator will be rated with a 0. If the system exists, rate the indicator as a *method 2* question.

Indicator VIII.6:

Is there a security management system in place to oversee storage and distribution?

Rationale: Theft control requires secure storage places with limited access, security mechanisms, and the use of alarm systems to detect breaches.

Description: The likelihood of theft can be reduced if there are a few appropriate measures in place in the warehouse, such as those listed below. These include as a minimum the following elements:

- monitoring of entry and exit to warehouses
- controlled substances (such as narcotics) should be separated and secured
- locks with controlled key distribution
- bars on windows, proper roofing, and solid walls and doors, fencing (etc.)
- limited access to unauthorized persons
- alarm system for security breaches
- physical search when leaving the warehouse or dispensary.

Interpretation guidelines: If there is no evidence of such system then the indicator will be rated with a 0. If the system exists, rate the indicator as a *method 2* question.

Indicator VIII.7:

Are there SOPs for stock management at each level of the distribution system?

Rationale: The SOP is necessary to guide the staff working in the distribution chain. They help them to properly manage the stock. If they do not exist or not effectively implemented, there could be stock outs, excess of stocks, expiration of the medicines or simply theft and diversion.

Description: There should be a document of the standard operating procedures for stock management which specify the specific roles and responsibilities of staff with regard to the stock management.

Interpretation guidelines: If the SOP exist in writing and are easily accessible, then this indicator should receive a rating of 1. If the SOP do not exist or are not easily accessible, this indicator should receive a rating of 0.

Indicator VIII.8:

Is there an inventory management system at each level of the distribution system and which provides information as a minimum, on the following elements?

Rationale: The establishment and maintenance of effective inventory records and procedures in storage facilities at the various levels of the distribution system are the basis for coordinating the flow of medicines. Good inventory management is essential for deterring theft from the warehouse. Documentation of the flow of medicines by volume, date, location and signed by a responsible staff member create transparency

and facilitate accountability. Good inventory control systems are required to ensure that medicine purchases are made according to set criteria and plans.

Description: Any inventory control system (manual or computerized records) must provide as a minimum information on the following elements:

- the average working stock
- the amount of safety stock
- the frequency of reordering;
- the quantity of reordering
- the average inventory
- the lead time
- expiry date

Interpretation guidelines: If there is no evidence of such system then the indicator will be rated with a 0. If the system exists, rate the indicator as a *method 2* question.

Indicator VIII.9:

Are stock records reconciled with physical counts at least every 3 months by internal staff?

Rationale: The regular reconciliation of physical counts with stock records is critical for the inventory system and as a means to detect theft from the warehouse. Unannounced physical counts (spot checks) are particularly useful for deterring theft. Designated staff should make unannounced counts on selected items that are likely to be stolen (similar to those done by external auditors) at least every 3 months in order to check if the information shown on stock records matches with the actual quantity in stock.

Description: The warehouse staff should produce the most recent records of current stock levels reconciled with physical count of selected medicines.

Interpretation guidelines: If stock records are checked against physical counts of medicines at least every 6 months, then this indicator should receive a rating of 1. If stock records are reconciled with physical counts of medicines on an ad hoc basis or if there is no evidence of this process, this indicator should receive a rating of 0.

Indicator VIII.10:

Are there independent audits of warehouses by external inspectors or auditors?

Rationale: A well managed medicine warehouse should be subject to unannounced external auditing (e.g. Ministry of Health auditors or private auditors) at regular intervals, and results compared with the medicine receipts and issues. Such third-party audits of warehouses can facilitate the detection of irregular activity and act as a deterrent to corrupt behaviour.

Description: When asked, the warehouse supervisor should be able to provide the date of the last audit that was conducted and show:

- evidence/report of warehouse audit
- audit is carried out at least once a year

- audit carried out by an independent party.

Interpretation guidelines: If there is no evidence of audits then the indicator will be rated with a 0. If the audits are conducted, rate the indicator as a *method 2* question.

Indicator VIII.11:

Is there a system (computerized or manual, historical or current) in place to track the movement of pharmaceuticals from a warehouse to a health facility?

Rationale: An information system that can track the movement of pharmaceuticals from the warehouse to a health facility can help prevent theft.

Description: At each level in the flow of medicines from a warehouse to a health facility records should exist to indicate how much of each medicine was received, who received it (and verified the amounts), and from whom the medicines were received, and the time and date that the medicines arrived at the appropriate health facility. Information on medicine issues should also exist for medicines that have left the warehouse including:

- type of medicines that have left the warehouse
- quantity of medicines that have left the warehouse
- the person who verified the amounts received
- the intended recipient of these medicines
- the time and date that the medicines arrived at the designated health facility
- documentation of any problems or irregularities with the supplies received (e.g. short or excess shipments, damage, incorrect shipment, etc.).

Interpretation guidelines: If there is no evidence of such system then the indicator will be rated with a 0. If the system exists, rate the indicator as a *method 2* question.

Indicator VIII.12:

Does the health facility have an appropriate procedure for requesting medicines?

Rationale: Requests made by health facilities should be made on real needs. To ensure that the right medicines in the right quantities are requested, there should be a standard format to be completed and checked by the responsible person. If there is no such form, there may be a risk of requesting unnecessary medicines or excess quantities leading to thefts, diversion and expiry of medicines.

Description: There should be a written standard form for health facilities for requesting medicines. The request form should provide as a minimum:

- the medicine to be supplied (INN);
- dosage form;
- strength;
- quantity;
- the requisition should be checked by the responsible person, dated and signed.

Interpretation guidelines: If there is no evidence of a standard form then the indicator will be rated with a 0. If the form exists, rate the indicator as a *method 2* question.

Indicator VIII.13:

Are there appropriate written guidelines on transportation and delivery of the medicines from/to the warehouse?

Rationale: Spoilage, theft, diversion and swapping of medicines could occur during transportation from warehouses to health facilities, unless special precautions are taken for safeguard.

Description: There should be an appropriate guidelines on transportation covering at least the following:

- problems of adverse transportation conditions such as exposure to excessive heat, moisture, sunlight
- problems of theft during transportation and methods for protection against this
- mechanism to prevent swapping of consignment during transportation
- requirement that the person responsible for transportation sign a receipt

Interpretation guidelines: If there is no evidence of a guideline then the indicator will be rated with a 0. If the guideline exists, rate the indicator as a *method 2* question.

Indicator VIII.14:

Is there a well-functioning communication system between the suppliers and the end-user for ordering, re-ordering and complaint?

Rationale: A good information system allows for coordination of the distribution system. Information dissemination, transparency and clear lines of communication can help reduce the risk of corruption. If the supplier and the recipient of the medicine supply have a reliable means of communication, information gaps are reduced and, with that, opportunities for abuse of the system are minimized. Transparency and accountability can be strengthened by publishing these reports, by external audit of these reports and by sending these reports to a Minister of Finance or similar agency with oversight responsibility

Description: A communication system between the warehouse and the distribution points can be a basic one (e.g. fax, and manual information sharing/exchange of documents) or a more advanced one that is based on a computer programme. It should include at least one of these options:

- a manual/document exchange system between distribution points at all levels
- telephone contact between all levels of the distribution points
- fax contact between all levels of the distribution points
- a secure computerized system.

There should be evidence that these elements are used appropriately and that documentation is maintained.

Interpretation guidelines: If there is no evidence of communication system or it exist but is not used then the indicator will be rated with a 0. If the system exists, rate the indicator with one.

Indicator VIII.15:

Does a programme exist for monitoring and evaluating the performance of the medicine distribution system?

Rationale: Monitoring and evaluation of the distribution system can help strengthen distribution system performance. If well designed it can help to identify vulnerabilities to corruption and allow corrective measures to be taken. Transparency and accountability can be strengthened by publishing reports and by sending them to relevant government institution with oversight responsibility for review and action.

Description: The distribution system should be subject to a regular programme of monitoring and periodic evaluation, including:

- monitoring conducted by an independent authority (e.g. MOH, external auditors, etc.)
- regular, systematic, documented monitoring
- evaluation carried out at least every 3-5 years
- reports identifying weaknesses and making recommendations available
- evidence that weaknesses are addressed exists
- posting reports publicly (e.g. on a government website).

Interpretation guidelines: If there is no evidence of monitoring system then the indicator will be rated with a 0. If the monitoring system exists, rate the indicator as a *method 2* question.

Indicator VIII.16:

Are sanctions imposed on individuals or agencies/companies for theft or other corrupt practices associated with distribution?

Rationale: This indicator assesses whether or not a government implements legislation and/or policy that addresses corruption in the pharmaceutical distribution system. Also the sanctions imposed on an individual or company for corrupt behaviour should be severe enough to act as a deterrent to others.

Description: Policies and/or procedures foreseeing the application of sanctions for corrupt behaviour should exist and be disseminated to staff, including the type of sanctions to be applied, depending on the nature and gravity of the act of corruption. There should also be evidence that individuals or agencies are sanctioned for corrupt behaviour. Types of corrupt behaviour include theft and diversion, deliberate destruction.

Interpretation guidelines: If there is no evidence of policy/procedure then the indicator will be rated with a 0. If the policy/procedure exists, rate the indicator as a *method 2* question.

Indicator VIII.17:

Does the medical store/health facility have appropriate procedures for disposal of expired and/or spoiled medicines?

Rationale: At the medical stores and health facilities store level sometimes medicines could expire or get spoiled. If there is no appropriate monitoring system, such medicines could be relabeled, repacked and sold on the market. Also, good quality medicines could be diverted, after being reported as spoiled or expired.

Description: There should be a written standard procedure for disposal of unwanted medicines including as minimum:

- mechanism to notify MRA about expired or spoiled medicines
- committee responsible for the supervision of disposal of medicines
- minutes taken about the disposal and signed by the committee members
- list of disposed medicines

Interpretation guidelines: If there is no evidence of a guideline then the indicator will be rated with a 0. If the guideline exists, rate the indicator as a *method 2* question.

Indicator VIII.18:

To what extent do you agree with the following statement: "there are very rarely leakages in the medicine distribution system in your country".

Rationale: Good policies and procedures may be in place for reception and inspection of goods, for inventory control, storage and transport throughout the distribution chain, but culturally some countries retain a permissive attitude towards abuses in the system. KIs may have access to documentation to check on the actual implementation of procedures.

Interpretation guidelines: *method 3*.

Indicator VIII.19:

If you were in a position of highest authority, what would be the first action that you would take to improve the systems and processes of public sector medicine distribution in your country?

Interpretation guidelines: *method 4*.

Questionnaire forms

Objective:

to assess the level of transparency in the pharmaceutical sector with a focus on eight areas:

- Registration
- Licensing
- Inspection
- Promotion
- Clinical trials
- Selection
- Procurement
- Distribution

Unedited draft

Unedited draft

SECTION I: QUESTIONNAIRE ON REGISTRATION OF MEDICINES

PRELIMINARY INFORMATION

Date: _____

Key informant number: _____

The key informant works in:

- Government (public sector)
- Private sector
- Nongovernmental organization
- International governmental organization
- Media
- Other (please specify): _____

Unedited draft

I.1 Is there an up-to-date list of all registered pharmaceutical products available in the country?

No	Yes	D.K.
0	1	

I.2 If such a list exists, does it provide a minimum level of information?

	No	Yes	D.K.
1. Product description: name of product	0	1	
2. Primary packaging any identifying mark	0	1	
3. Name of manufacturer	0	1	
4. Country of manufacture	0	1	
5. Site of manufacture	0	1	
6. Date of registration	0	1	
7. Validity of registration	0	1	
8. Conditions for registration (e.g. prescription only or over-the-counter)	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

I.3 Are there written procedures for applicants on how to submit an application for registration of medicinal products? If so:

	No	Yes	D.K.
1. Written procedures	0	1	
2. Publicly accessible	0	1	
3. Describe the process to follow in submitting an application	0	1	
4. Mention timeframe for processing	0	1	
5. Mention fees	0	1	
6. Mention data to be submitted	0	1	
7. Mention criteria for registration	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

I.4 Are there written procedures for assessors on how to assess applications submitted for registration of medicinal products? If so:

	No	Yes	D.K.
1. Written procedures	0	1	
2. Publicly accessible	0	1	
3. Describe the process to follow in assessing submissions	0	1	
4. Mention timeframe for processing	0	1	
5. Specify issues to be considered in assessing submissions	0	1	
6. Provide guidance on report writing	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

I.5 Is there a standard application form publicly available for submission of applications for registration of medicinal products? If so:

	No	Yes	D.K.
1. Publicly accessible	0	1	
2. Readily available at government office	0	1	
3. Requires description of the product: name of product (brand name & INN), composition per unit dose	0	1	
4. Brief summary of method of manufacture	0	1	
5. Specification of pharmaceutical ingredients and excipients	0	1	
6. Summary Product Characteristics (SPC): pharmacological action, therapeutic classification, indications, contraindications, etc.	0	1	
7. Packaging material and inserts	0	1	
8. Labelling	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

I.6 Are there written guidelines setting limits on how and where medicines registration officers meet with applicants?

No	Yes	D.K.
0	1	

I.7 Is there a functioning formal committee responsible for assessing applications for registration of pharmaceutical products?

No	Yes	D.K.
0	1	

I.8 Are there clear written criteria for selecting the members of the committee? If so:

	No	Yes	D.K.
1. Written criteria	0	1	
2. Criteria publicly available	0	1	
3. Specify professional qualification required	0	1	
4. Specify the technical skills and work experience related to the area	0	1	
5. Require declaration of conflict of interest (e.g. investment in pharmaceutical business)	0	1	
6. Give a timeframe to serve as a committee member	0	1	
Total			

Total yes
 Total valid answers
 Scoring
 (total yes/total valid answers)

I.9 Is there a written document that describes the composition and terms of reference of the committee? If so:

	No	Yes	D.K.
1. Up-to-date document	0	1	
2. Publicly accessible	0	1	
3. Includes names of the members	0	1	
4. Includes duties, responsibilities and obligations of the members	0	1	
5. Includes the accountability of the members	0	1	
6. Includes quorum requirement	0	1	
7. Includes membership terms/rotation requirements	0	1	
8. Includes the financial benefits given to members, if any	0	1	
Total			

Total yes
 Total valid answers
 Scoring
 (total yes/total valid answers)

I.10 Are there written guidelines on conflict of interest (COI) with regard to registration activities? If so:

	No	Yes	D.K.
1. Guidelines on COI exist in writing	0	1	
2. Guidelines are publicly available	0	1	
3. Form for declaration of COI for members of registration committee exists	0	1	
4. Includes rules on the acceptance of gifts	0	1	
5. Includes rules on reporting COI	0	1	
6. Includes a mechanism protecting informers of COI	0	1	
7. Includes actions to be taken in case of failure to comply with guidelines	0	1	
8. Evidence of enforcement of these guidelines	0	1	
Total			

Total yes
 Total valid answers

Scoring
(total yes/total valid answers)

- I.11 To what extent do you agree with the following statement: "The members of the registration committee are systematically and objectively selected based on the written criteria in force in your country"? (see question I.8)**

Strongly disagree	Disagree	Undecided	Agree	Strongly agree	N.A.	D.K.

- I.12 Are there clear and comprehensive guidelines for the committee's decision-making process? If so:**

	No	Yes	D.K.
1. Available in writing	0	1	
2. Publicly available	0	1	
3. Describe clearly the mandate of the committee	0	1	
4. Describe the number of meetings it should convene	0	1	
5. Describe procedures for decision-making	0	1	
6. Include clear time limits for the committee's decision-making process	0	1	
7. Describe the reporting structure	0	1	
8. Decisions of meetings made publicly available	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

- I.13 Is there a formal appeals system for applicants who have their registration applications rejected?**

No	Yes
0	1

- I.14 To what extent do you agree with the following statement: "Gifts and other benefits given to the officials in charge of medicines registration have no influence at all on the final decisions"?**

Strongly disagree	Disagree	Undecided	Agree	Strongly agree	N.A.	D.K.

- I.15 To what extent do you agree with the following statement: "The registration committee meets on a regular basis and keeps minutes of its meetings"?**

Strongly disagree	Disagree	Undecided	Agree	Strongly agree	N.A.	D.K.

I.16 In your opinion, what types of unethical behaviour are common in the registration system in your country?

I.17 If you were in a position of highest authority, what would be the first action that you would take to improve the registration process in your country?

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SECTION II: QUESTIONNAIRE ON LICENSING OF PHARMACEUTICAL ESTABLISHMENTS

PRELIMINARY INFORMATION

Date: _____

Key informant number: _____

The key informant works in:

- | | |
|---|--------------------------|
| Government (public sector) | <input type="checkbox"/> |
| Private sector | <input type="checkbox"/> |
| Nongovernmental organization | <input type="checkbox"/> |
| International governmental organization | <input type="checkbox"/> |
| Media | <input type="checkbox"/> |
| Other (please specify): _____ | <input type="checkbox"/> |

Unedited draft

II.1 Is it a legal requirement to have a licence in order to operate a pharmaceutical establishment?

No	Yes	D.K.
0	1	

II.2 Does the MRA have a unit responsible for issuing pharmaceutical establishment licences?

No	Yes	D.K.
0	1	

II.3 Are there written procedures for submission of applications for licensing? If so:

	No	Yes	D.K.
1. Publicly available	0	1	
2. Cover administrative criteria to be met by applicants	0	1	
3. Describe the processes to be followed in submitting an application	0	1	
4. Describe the requirements to be met in terms of premises, facilities, personnel, etc.	0	1	
5. Include the timeframe for processing application	0	1	
6. Include the fees.	0	1	
Total			

<i>Total yes</i>	
<i>Total valid answers</i>	
<i>Scoring (total yes/total valid answers)</i>	

II.4 Are there written guidelines for assessing applications for a licence?

No	Yes	D.K.
0	1	

II.5 Is the submission of pre-licensing inspection report one of the requirements for making decisions on whether to issue a license or not?

No	Yes	D.K.
0	1	

II.6 Is there a functioning formal committee that assesses applications for licensing of a pharmaceutical establishment?

No	Yes	D.K.
0	1	

II.7 Are there clear written criteria for selecting the members of the committee? If so:

	No	Yes	D.K.
1. Publicly available	0	1	
2. Require that committee be composed of heads of departments of the MRA	0	1	
3. Require that members sign conflict of interest form	0	1	
4. Refer to specific code of conduct.	0	1	
Total			

Total yes	
Total valid answers	
Scoring (total yes/total valid answers)	

II.8 Is there a written document that describes the composition and terms of reference of the committee? If so:

	No	Yes	D.K.
1. Publicly available	0	1	
2. List committee members by name and expertise	0	1	
3. Include the role and responsibilities of its members	0	1	
4. Accountability of its members and final benefits if any	0	1	
Total			

Total yes	
Total valid answers	
Scoring (total yes/total valid answers)	

II.9 Does the MRA carry out regular (at least every two years) post-licensing inspection of all licensed pharmaceutical establishments?

No	Yes	D.K.
0	1	

II.10 Is there an up-to-date list of all licensed pharmaceutical establishments available in the country? If so, does it include the following:

	No	Yes	D.K.
1. Name and address of premises,	0	1	
2. Validity date of licence,	0	1	
3. Name of qualified person/contact person,	0	1	
4. Last inspection date,	0	1	
5. Type of establishment.	0	1	
Total			

Total yes	
Total valid answers	
Scoring (total yes/total valid answers)	

II.11: To what extent do you agree with the following statement: "The licensing of pharmaceutical establishments is systematically carried out according to policies and procedures"?

Strongly disagree	Disagree	Undecided	Agree	Strongly agree	N.A.	D.K.

II.12 Is there an independent appeals system for applicants who have their applications for licensing rejected?

No	Yes	D.K.
0	1	

II.13: To what extent do you agree with the following statement: "The formal committee that assesses applications for licensing of pharmaceutical establishments is fully operational and meets on a regular basis"?

Strongly disagree	Disagree	Undecided	Agree	Strongly agree	N.A.	D.K.

II.14 In your opinion, what types of unethical practices commonly occur in the process of licensing pharmaceutical establishments in your country, if any?

II.15 If you were in a position of highest authority, what would be the first action that you would take to improve the licensing process for pharmaceutical establishments in your country?

Unedited draft

SECTION III: QUESTIONNAIRE ON INSPECTION AND MARKET CONTROL

PRELIMINARY INFORMATION

Date: _____

Key informant number: _____

The key informant works in:

- | | |
|---|--------------------------|
| Government (public sector) | <input type="checkbox"/> |
| Private sector | <input type="checkbox"/> |
| Nongovernmental organization | <input type="checkbox"/> |
| International governmental organization | <input type="checkbox"/> |
| Media | <input type="checkbox"/> |
| Other (please specify): _____ | <input type="checkbox"/> |

Unedited draft

III.1 Is there a provision in the medicines legislation/regulation covering inspection of pharmaceutical establishments?

No	Yes	D.K.
0	1	

III.2 Is the provision on inspection comprehensive enough? If so, as minimum, does it:

	No	Yes	D.K.
1. Provide power to MRA to inspect			
2. Provide power to inspectors to enter, at any reasonable time, any place where medicinal products are produced, packaged, stored, distributed or tested	0	1	
3. Define the inspector's duties and responsibilities	0	1	
4. Provide special identification document to the inspectors	0	1	
5. Provision is available to companies being inspected	0	1	
Total			

Total yes
 Total valid answers
 Scoring
 (total yes/total valid answers)

III.3 Are there written guidelines classifying non-compliance with Good Manufacturing Practices (GMP) that describe the types of deficiencies and the corresponding measures to be taken by the MRA? If so:

	No	Yes	D.K.
1. Guidelines available in writing	0	1	
2. Guidelines provide classification of GMP deficiencies	0	1	
3. Define corresponding measures to be taken in case of non-compliance	0	1	
4. Guidelines easily accessible to all stakeholders	0	1	
5. Provide appeals mechanism for companies	0	1	
6. Appeals system independent of the body making the original decision	0	1	
Total			

Total yes
 Total valid answers
 Scoring
 (total yes/total valid answers)

III.4 Are there written guidelines classifying non-compliance with Good Distribution Practices (GDP) that describe the types of deficiencies and the corresponding measures to be taken by the MRA? If so:

	No	Yes	D.K.
1. Guidelines available in writing	0	1	
2. Guidelines provide classification of GDP deficiencies	0	1	
3. Define corresponding measures to be taken in case of non-compliance	0	1	
4. Guidelines easily accessible to all stakeholders	0	1	
5. Provide appeals mechanism for companies	0	1	
6. Appeals system independent of the body making the original decision	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

III.5 Are there written procedures/mechanisms to prevent regulatory capture between inspectors and the manufacturers or distributors that he/she inspects? If so:

	No	Yes	D.K.
1. Procedures available in writing	0	1	
2. Require rotation of inspectors based on a scheduling system	0	1	
3. Require inspectors to visit sites in teams with a team leader	0	1	
4. Require inspectors to inspect under the observation of another inspector who will report on what he/she has observed (peer review)	0	1	
5. Rotation mechanism requires inspectors from one geographical area to inspect companies in other areas	0	1	
6. Require independent audit of the inspections (from another country)	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

III.6 Are there written guidelines on conflict of interest (COI) with regard to inspection activities? If so:

	No	Yes	D.K.
1. Guidelines on COI exist in writing	0	1	
2. Guidelines are publicly available	0	1	
3. Form for declaration of COI for inspectors exists	0	1	
4. Include rules on the acceptance of gifts	0	1	
5. Include rules on reporting COI	0	1	
6. Include a mechanism protecting informers of COI	0	1	
7. Include actions to be taken in case of failure to comply with guidelines	0	1	
8. Evidence of enforcement of these guidelines	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

III.7 Are inspection findings and conclusions subject to an internal review?

No	Yes	D.K.
0	1	

III.8 Are there written standard operating procedures (SOPs) for inspectors on how to conduct inspections? If so:

	No	Yes	D.K.
1. Include an inspection checklist/aide-memoire	0	1	
2. Procedures detailing requirements for pre-inspection activities	0	1	
3. Procedures detailing requirements for post-inspection activities	0	1	
4. Scheduling system identifying companies due for inspections within a set timeframe	0	1	
5. Format and content of inspection reports	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

III.9 Are there written criteria for the selection and recruitment of inspectors? If yes do they include the following:

	No	Yes	D.K.
1. Available in writing and publicly	0	1	
2. Qualification required (pharmacist, chemist, etc.)	0	1	
3. Minimum years of work experience in the area	0	1	
4. Recommendation from (past work place, association)	0	1	
5. Successful completion of specific training in inspection	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

III.10 To what extent do you agree with the following statement: "The integrity of inspectors is in no way influenced by personal gain, such as bribes, gifts, material or any other benefits, etc."?

Strongly disagree	Disagree	Undecided	Agree	Strongly agree	N.A.	D.K.

III.11 To what extent do you agree with the following statement: "Inspection activities are systematically carried out in accordance with the guidelines and procedures to prevent bias (e.g. peer review or rotation)"?

Strongly disagree	Disagree	Undecided	Agree	Strongly agree	N.A.	D.K.

III.12 In your opinion, what types of unethical behaviour are common in the inspection area in your country?

III.13 If you were in a position of highest authority, what would be the first action that you would take to improve the inspection process in your country?

Unedited draft

Unedited draft

SECTION IV: QUESTIONNAIRE ON MEDICINE PROMOTION CONTROL

PRELIMINARY INFORMATION

Date: _____

Key informant number: _____

The key informant works in:

- | | |
|---|--------------------------|
| Government (public sector) | <input type="checkbox"/> |
| Private sector | <input type="checkbox"/> |
| Nongovernmental organization | <input type="checkbox"/> |
| International governmental organization | <input type="checkbox"/> |
| Media | <input type="checkbox"/> |
| Other (please specify): _____ | <input type="checkbox"/> |

Unedited draft

IV.1 Is there a provision in the medicines legislation/regulations covering medicine promotion?

No	Yes	D.K.
0	1	

IV.2 Do the provisions on medicine promotion include explicit mention of the following forms of promotion?

	No	Yes	D.K.
1. Advertisement to professionals	0	1	
2. Advertisement to the public	0	1	
3. Qualification and training of medical representatives	0	1	
4. Restrictions on and monitoring of free samples	0	1	
5. Symposia and scientific meetings	0	1	
6. Post-marketing scientific studies	0	1	
7. Speakers' fees and consultancies	0	1	
8. Packaging, labelling and package inserts	0	1	
9. Promotion of exported medicines	0	1	
10. Restrictions and limits on gifts and gimmicks	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

IV.3 Is pre-approval of promotional materials officially required? If so, does the information submitted contain as a minimum:

	No	Yes	D.K.
1. Name of active ingredient (INN or generic name)	0	1	
2. Brand name	0	1	
3. Company name	0	1	
4. Major indication(s) for use	0	1	
5. Adverse effects	0	1	
6. Contraindications	0	1	
7. Medicine interactions	0	1	
8. Cost	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

IV.4 Do the provisions foresee an enforcement mechanism on promotion of medicines, stating the sanctions in cases of violation?

No	Yes	D.K.
0	1	

IV.5 Is there a formal complaints procedure to report unethical promotional practices? If so:

	No	Yes	D.K.
1. Written procedures for making complaints	0	1	
2. Procedures publicly available	0	1	
3. Evidence that complaints procedure is used	0	1	
4. Results of complaints are published	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

IV.6 Is there a service or committee responsible for monitoring and enforcing the provisions on medicine promotion?

No	Yes	D.K.
0	1	

IV.7 Are there clear criteria for selecting the members of the service/committee? If so, as a minimum, do they specify:

	No	Yes	D.K.
1. Are they available in writing	0	1	
2. Publicly available	0	1	
3. Professional qualifications	0	1	
4. Technical skills and work experience	0	1	
5. Require to declare real or perceived conflict of interest	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

IV.8 Is there a written document that describes the composition and terms of reference of the service/committee? If so, it should list:

	No	Yes	D.K.
1. Members by name and expertise	0	1	
2. Roles and responsibilities of its members	0	1	
3. Accountability of members and financial benefit if any	0	1	
4. The frequency of meetings	0	1	
5. Decisions of meetings publicly available	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

IV.9 Are there written and publicly available Standard Operating Procedures (SOPs) guiding the services responsible for pre-approving or monitoring medicine promotion and advertising? If so:

	No	Yes	D.K.
1. SOPs are written and publicly available	0	1	
2. A standard form or checklist (for pre-approval or monitoring) exists	0	1	
3. Standard form checks that information complies with information approved for medicine registration	0	1	
Total			

*Total yes
Total valid answers
Scoring
(total yes/total valid answers)*

IV.10 Are there written guidelines on conflicts of interest (COI) with regard to control of medicine promotion activities? If so:

	No	Yes	D.K.
1. Guidelines on COI exist in writing	0	1	
2. Guidelines are publicly available	0	1	
3. Form for declaration of COI for members of committee exists	0	1	
4. Include rules on the acceptance of gifts	0	1	
5. Include rules on reporting COI	0	1	
6. Include a mechanism protecting informers of COI	0	1	
7. Include actions to be taken in case of failure to comply with guidelines	0	1	
8. Evidence of enforcement of these guidelines	0	1	
Total			

*Total yes
Total valid answers
Scoring
(total yes/total valid answers)*

IV.11 To what extent do you agree with the following statement: "The legal provisions on medicine promotion have been developed in broad consultation with all interested parties"?

Strongly disagree	Disagree	Undecided	Agree	Strongly agree	N.A.	D.K.

IV.12 To what extent do you agree with the following statement: "Pre-approval of promotional and advertising materials are systematically obtained before they are made public"?

Strongly disagree	Disagree	Undecided	Agree	Strongly agree	N.A.	D.K.

IV.13 To what extent do you agree with the following statement: "Civil society/nongovernmental organizations have a great influence on improving the control of medicine promotion in your country"?

Strongly disagree	Disagree	Undecided	Agree	Strongly agree	N.A.	D.K.

IV.14 To what extent do you agree with the following statement: "Sanctions foreseen in the provisions on medicine promotion are systematically applied when there is a breach"?

Strongly disagree	Disagree	Undecided	Agree	Strongly agree	N.A.	D.K.

IV.15 In your opinion, what types of unethical behaviour are common in the medicine promotion area in your country?

Involving health professionals and health institutions in general

Involving regulatory office staff and committee members responsible for controlling medicine promotion

IV.16 If you were in a position of highest authority, what would be the first action that you would take to improve the medicine promotion process in your country?

Unedited draft

SECTION V: QUESTIONNAIRE ON CONTROL OF CLINICAL TRIALS

PRELIMINARY INFORMATION

Date: _____

Key informant number: _____

The key informant works in:

- | | |
|---|--------------------------|
| Government (public sector) | <input type="checkbox"/> |
| Private sector | <input type="checkbox"/> |
| Nongovernmental organization | <input type="checkbox"/> |
| International governmental organization | <input type="checkbox"/> |
| Media | <input type="checkbox"/> |
| Other (please specify): _____ | <input type="checkbox"/> |

Unedited draft

V.1 Is there a legal provision requiring the regulation of clinical trials (CT)?

No	Yes	D.K.
0	1	

V.2 Are there written national guidelines on principles of Good Clinical Practice (GCP)?

No	Yes	D.K.
0	1	

V.3 Is there written and publicly available guideline on submission of applications to MRA to conduct CT? If so, does it include the following:

	No	Yes	D.K.
1. Trials' objective and purpose	0	1	
2. Trial design	0	1	
3. Criteria for inclusion and exclusion of trial subjects	0	1	
4. Means of obtaining informed consent	0	1	
5. Timeframe for assessing applications	0	1	
Total			

Total yes	
Total valid answers	
Scoring (total yes/total valid answers)	

V.4 Is there a documented policy or procedure for submission of CT applications to an Independent Ethics Committee (IEC)? If so, does it include the following:

	No	Yes	D.K.
1. Acceptability of the investigator for the proposed trial	0	1	
2. Suitability of the protocol	0	1	
3. Means by which trial subjects will be recruited	0	1	
4. Adequacy and completeness of the information	0	1	
5. Provision for compensation or treatment in case of death or other loss or injury of a subject	0	1	
6. Form of payment of remuneration from the sponsor	0	1	
Total			

Total yes	
Total valid answers	
Scoring (total yes/total valid answers)	

V.5 Are there requirements for the manufacture, importation, exportation and use of investigational products?

No	Yes	D.K.
0	1	

V.6 Is there a formal review committee in the MRA responsible for reviewing applications and CT results?

No	Yes	D.K.
0	1	

V.7 Are there mechanisms in place to ensure that those involved in the review of applications and CT results have sufficient and current expertise in all required areas? If so, do they cover the following:

	No	Yes	D.K.
1. Their technical qualification	0	1	
2. Their experience in research and clinical investigation	0	1	
3. Declaration of conflict of interest	0	1	
4. Timeframe for serving as committee member	0	1	
Total			

<i>Total yes</i>	
<i>Total valid answers</i>	
<i>Scoring (total yes/total valid answers)</i>	

V.8 Is there a CT inspection system established and operational?

No	Yes	D.K.
0	1	

V.9: Do the national guidelines require the establishment of an Independent Ethics Committee (IEC)? If so, do they require the following:

	No	Yes	D.K.
1. IEC officially established	0	1	
2. Consists of members that have the necessary qualifications and experience	0	1	
3. Functions according to written operating procedures	0	1	
4. Complies with GCP guidelines and with the applicable regulatory requirements.	0	1	
Total			

<i>Total yes</i>	
<i>Total valid answers</i>	
<i>Scoring (total yes/total valid answers)</i>	

V.10 Does the review committee have a timeframe for assessing CT?

No	Yes	D.K.
0	1	

V.11 Are there written guidelines on conflicts of interest (COI) with regard to CT activities? If so, do they include the following:

	No	Yes	D.K.
1. Definition of what constitutes a COI	0	1	
2. Rules on the acceptance of gifts	0	1	
3. Rules on reporting COI	0	1	
4. Mechanism protecting informers of COI	0	1	
5. Actions to be taken in case of failure to comply with guidelines	0	1	
6. Evidence of enforcement of these regulations	0	1	
Total			

Total yes	
Total valid answers	
Scoring (total yes/total valid answers)	

V.12 Is there a list/database of all approved and rejected CT applications and is the list published? If so:

	No	Yes	D.K.
1. Is it publicly available	0	1	
2. Does it indicate all CT approved	0	1	
3. Does it indicate all CT amended	0	1	
4. Does it indicate all CT rejected.	0	1	
Total			

Total yes	
Total valid answers	
Scoring (total yes/total valid answers)	

V.13 To what extent do you agree with the following statement: "The IEC members are systematically selected based on the written selection criteria "?

Strongly disagree	Disagree	Undecided	Agree	Strongly agree	N.A.	D.K.

V.14 To what extent do you agree with the following statement: "The MRA review committee members are selected systematically based on the written selection criteria"?

Strongly disagree	Disagree	Undecided	Agree	Strongly agree	N.A.	D.K.

V.15 To what extent do you agree with the following statement: "The MRA is ensuring that CTs conducted in the country are done in accordance with the regulation and GCP principles"?

Strongly disagree	Disagree	Undecided	Agree	Strongly agree	N.A.	D.K.

V.16 In your opinion, what types of unethical behaviour are common in the clinical trials area in your country?

V.17 If you were in a position of highest authority, what would be the first actions that you would take to improve the way clinical trials are carried out in your country?

Unedited draft

Unedited draft

SECTION VI: QUESTIONNAIRE ON SELECTION OF MEDICINE

PRELIMINARY INFORMATION

Date: _____

Key informant number: _____

The key informant works in:

- Government (public sector)
- Private sector
- Nongovernmental organization
- International governmental organization
- Media
- Other: (please specify)_____

Unedited draft

VI.1 Does the government have an officially adopted national essential medicines list (EML) publicly available?

No	Yes	D.K.
0	1	

VI.2 To what extent do you agree with the following statement: "The national essential medicines list has been developed in consultation with all interested parties and using an evidence-based approach"?

Strongly disagree	Disagree	Undecided	Agree	Strongly agree	N.A.	D.K.

VI.3 Are there clearly written and publicly available guidelines for the selection process for including or deleting medicines from the national EML? If so:

	No	Yes	D.K.
1. Available in written format in the public domain	0	1	
2. Define criteria for inclusion of new medicines	0	1	
3. Define criteria for rejection of new medicines	0	1	
4. Define criteria for deleting medicines from existing EML	0	1	
5. Include only medicines with sound and adequate evidence of efficacy and safety	0	1	
6. Based on priority health needs of the country	0	1	
7. Based on cost-effectiveness	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

VI.4 Is the EML in line with WHO procedures? If so:

	No	Yes	D.K.
1. Published and easily accessible	0	1	
2. Disseminated widely to relevant health professionals	0	1	
3. By generic names	0	1	
4. By level of health care	0	1	
5. Linked to national standard treatment guidelines	0	1	
6. Revised within past 5 years	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

VI.5 Is there a committee responsible for the selection of the national EML?

No	Yes	D.K.
0	1	

VI.6 To what extent do you agree with the following statement: "The committee responsible for the selection of the national EML is operating free from external influence"?

Strongly disagree	Disagree	Undecided	Agree	Strongly agree	N.A.	D.K.

VI.7 Are there clear criteria for the selection of members of the selection committee? If so:

	No	Yes	D.K.
1. Criteria publicly available	0	1	
2. Criteria clearly written	0	1	
3. Criteria easily accessible	0	1	
4. Define the professional requirements			
5. Membership includes experts from different fields	0	1	
6. Require declaration on COI	0	1	
7. Requires membership on a rotation basis or limited in time	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

VI.8 Are there written guidelines on conflicts of interest (COI) with regard to selection of essential medicines? If so:

	No	Yes	D.K.
1. Guidelines on COI exist in writing	0	1	
2. Guidelines are publicly available	0	1	
3. Form for declaration of COI for members of selection committee exists	0	1	
4. Include rules on the acceptance of gifts	0	1	
5. Include rules on reporting COI	0	1	
6. Include a mechanism protecting informers of COI	0	1	
7. Include actions to be taken in case of failure to comply with policy	0	1	
8. Evidence of enforcement of these guidelines	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

VI.9 Are there clear terms of reference (TORs) that describe the role and responsibilities of the selection committee? If so:

	No	Yes	D.K.
1. Are they available in writing	0	1	
2. Are they publicly available	0	1	
3. Do they describe the rules for decision-making process	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

VI.10 Are there written SOPs for the committee's decision-making process? If so:

	No	Yes	D.K.
1. Decisions made by all members in a democratic manner	0	1	
2. Minutes of meeting produced and approved by members	0	1	
3. Require consultation with interested parties	0	1	
4. Final decision for selecting medicines made independently	0	1	
5. Decisions on selection process publicly available	0	1	
6. Decisions disseminated widely	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

VI.11 In your opinion, what types of unethical behaviour are common in the selection process in your country?

VI.12 If you were in a position of highest authority, what would be the first action that you would take to improve medicine selection in your country?

SECTION VII: QUESTIONNAIRE ON PROCUREMENT OF PHARMACEUTICALS

PRELIMINARY INFORMATION

Date: _____

Key informant number: _____

The key informant works in:

- | | |
|---|--------------------------|
| Government (public sector) | <input type="checkbox"/> |
| Private sector | <input type="checkbox"/> |
| Nongovernmental organization | <input type="checkbox"/> |
| International governmental organization | <input type="checkbox"/> |
| Media | <input type="checkbox"/> |
| Other: (please specify) _____ | <input type="checkbox"/> |

Unedited draft

VII.1 Does the government use transparent and explicit procedures for procurement of pharmaceutical products? If so:

	No	Yes	D.K.
1. Written procedures publicly available	0	1	
2. Describe the internal process to be followed by staff to process the bids	0	1	
3. Require the use of generic names	0	1	
4. Require procurement to be based on the national essential medicines list	0	1	
5. Require advertisement of tenders	0	1	
6. Require that contract specifications be publicly available	0	1	
7. Require that criteria for adjudication of tender be included as part of the tender package	0	1	
8. Require that contract awards be made by the tender committee	0	1	
9. Require that information on tender process and results are made public (to the extent permitted by law)	0	1	
Total			

*Total yes
Total valid answers
Scoring
(total yes/total valid answers)*

VII.2 Is there written guidance for procurement office staff on the type of procurement method to be used for different types of products?

No	Yes	D.K.
0	1	

VII.3 Is procurement done with an objective quantification method to determine the quantity of pharmaceuticals to be purchased?

No	Yes	D.K.
0	1	

VII.4 Is there a formal appeals process for applicants who have their bids rejected?

No	Yes	D.K.
0	1	

VII.5 Is there a tender committee (TC)? If so are the key functions of the procurement office and those of the tender committee clearly separated?

	No	Yes	D.K.
1. There is a TC formally established	0	1	
2. TC responsible for suppliers' selection for restricted tenders	0	1	
3. TC responsible for contract decisions	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

VII.6 To what extent to you agree with the following statement: "Decisions of the tender committee are always taken into account in the procurement process"?

Strongly disagree	Disagree	Undecided	Agree	Strongly agree	N.A.	D.K.

VII. 7 Are there specific criteria for tender committee membership? If so:

	No	Yes	D.K.
1. Criteria publicly available	0	1	
2. Criteria clearly written	0	1	
3. Require professionals with specific functions or skills	0	1	
4. Require representation from senior government officials	0	1	
5. Require representation from end-user facilities	0	1	
6. Require that membership changes periodically	0	1	
7. Require that members declare COI	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

VII.8 Are there written guidelines on conflicts of interest (COI) with regard to the procurement process? If so:

	No	Yes	D.K.
1. Guidelines on COI exist in writing	0	1	
2. Guidelines are publicly available	0	1	
3. Form for declaration of COI for procurement office staff exists	0	1	
4. Form for declaration of COI for members of tender committee exists	0	1	
5. Include rules on the acceptance of gifts	0	1	
6. Include rules on reporting conflict of interest	0	1	
7. Includes a mechanism protecting informers of COI	0	1	
8. Include actions to be taken in case of failure to comply with policy	0	1	
9. Require to be signed by both procurement office staff and tender committee members.	0	1	
10. Evidence of enforcement of these regulations	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

VII.9 To what extent do you agree with the following statement: "The members of the tender committee are systematically selected based on specific criteria (see question VII.7)"?

Strongly disagree	Disagree	Undecided	Agree	Strongly agree	N.A.	D.K.

VII.10 Is there a computerized management information system used to report product problems in procurement? If so:

	No	Yes	D.K.
1. Management information system exists	0	1	
2. Includes product records	0	1	
3. Monitors suppliers performance	0	1	
4. Monitors facilities (clients) performance	0	1	
5. Records quality assurance information	0	1	
6. Tracks status for each order	0	1	
7. Tracks quantities purchased compared with estimates	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

VII.11 Are there Standard Operating Procedures (SOPs) for routine inspection of consignments? If so:

	No	Yes	D.K.
1. Each shipment physically checked	0	1	
2. Samples taken and sent to quality control laboratories randomly for all consignments	0	1	
3. Samples taken and sent to quality control laboratories systematically for new suppliers	0	1	
4. Inspections reported in documents and archived in the procurement office	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

VII.12 Is there an efficient post-tender system in place to monitor and report on suppliers' performance to the tender committee? If so:

	No	Yes	D.K.
1. Supplier's performance monitored at least annually	0	1	
2. Monitoring system tracks suppliers lead-time	0	1	
3. Monitoring system tracks the shelf-life	0	1	
4. Monitoring system tracks the packaging of products	0	1	
5. Procurement agency has a list of previous suppliers	0	1	
6. Suppliers with poor performance are identified and blacklisted	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

VII.13 Does the procurement office undergo regular audits? If so:

	No	Yes	D.K.
1. Audit compulsory by law	0	1	
2. Done on an annual basis	0	1	
3. Results publicly available	0	1	
4. Audit conducted by an independent unit (internal or external)	0	1	
5. Reports operating costs of procurement office	0	1	
6. Reports pharmaceutical products tendered	0	1	
7. Reports quantities of the products	0	1	
8. Reports the beneficiaries	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

VII.14 To what extent do you agree with the following statement: "The procurement system in your country is operating in a totally transparent manner"?

Strongly disagree	Disagree	Undecided	Agree	Strongly agree	N.A.	D.K.

VII.15 In your opinion, what types of unethical behaviour are common in the procurement system in your country?

VII.16 If you were in a position of highest authority, what would be the first action that you would take to improve the systems and processes of procurement?

Unedited draft

SECTION VIII: QUESTIONNAIRE ON DISTRIBUTION OF PHARMACEUTICALS

PRELIMINARY INFORMATION

Date: _____

Key informant number: _____

The key informant works in:

- Government (public sector)
- Private sector
- Nongovernmental organization
- International governmental organization
- Media
- Other: (please specify)_____

Unedited draft

VIII.1 Is there system in place that can expedite port clearing?

No	Yes	D.K.
0	1	

VIII.2 To what extent do you agree with the following statement: "Port clearing is done smoothly and there is no need for bribery or gift-giving to expedite the process."

Strongly disagree	Disagree	Undecided	Agree	Strongly agree	N.A.	D.K.

VIII.3 Is there an inspection system to verify that the medicines delivered from the port or directly from a supplier match those that were shipped from the supplier? If so:

	No	Yes	D.K.
1. A separate space for checking the goods on arrival	0	1	
2. Designated person(s) responsible for checking receipts against packing list	0	1	
3. Documentation-based invoice	0	1	
4. Oversight system	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

VIII.4 Is there a coding system used to identify government medicines?

No	Yes	D.K.
0	1	

VIII.5 Is there systematic and orderly shelving of products in warehouses or store rooms? If so does it require:

	No	Yes	D.K.
1. Classification by alphabetical or therapeutic order	0	1	
2. Existence of a master map showing location of medicines	0	1	
3. Product placed taking into account the expiry date	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

VIII.6 Is there a security management system in place to oversee storage and distribution, if so including, as a minimum, the following elements?

	No	Yes	D.K.
1. Monitoring of entry and exit to warehouses	0	1	
2. Controlled substances (such as narcotics) separated and secured	0	1	
3. Locks with controlled key distribution	0	1	
4. Limited access to unauthorized persons	0	1	
5. Alarm system for security breaches	0	1	
6. Searches by security personnel of those leaving the warehouse	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

VIII.7 Are there SOPs for stock management at each level of the distribution system?

No	Yes	D.K.
0	1	

VIII.8 Is there an inventory management system at each level of the distribution system and which provides information, as a minimum, on the following elements?

	No	Yes	D.K.
1. The average working stock for each product	0	1	
2. The amount of safety stock for each product	0	1	
3. The frequency of reordering	0	1	
4. The quantity of reordering for each product	0	1	
5. The average inventory for each product	0	1	
6. The lead time	0	1	
7. The expiry date	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

VIII.9 Are stock records reconciled with physical counts at least every 3 months by internal staff?

No	Yes	D.K.
0	1	

VIII.10 Are there independent audits of warehouses by external inspectors or auditors? If so:

	No	Yes	D.K.
1. Evidence/report of warehouse audit	0	1	
2. Audit takes place at least once a year	0	1	
3. Audit carried out by an independent party	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

VIII.11 Is there a system (computerized or manual, historical or current) in place to track the movement of pharmaceuticals from a warehouse to a health facility, and which provides the following information for medicines that have left the warehouse?

	No	Yes	D.K.
1. Type of medicines that have left the warehouse	0	1	
2. Quantity of medicines that have left the warehouse	0	1	
3. The person who verified the amounts	0	1	
4. The intended recipient of these medicines	0	1	
5. The time and date that the medicines arrived at the appropriate health facility	0	1	
6. Documentation of any problems or irregularities with the supplies received	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

VIII.12 Does the health facility have an appropriate procedure for requesting medicines? If so, does it include the following:

	No	Yes	D.K.
1. The medicine to be supplied (INN)	0	1	
2. Dosage form	0	1	
3. Strength	0	1	
4. Quantity	0	1	
5. The requisition should be checked by the responsible person, dated and signed	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

VIII.13 Are there appropriate written guidelines on transportation and delivery of the medicines from/to the warehouse? If so, do they include the following:

	No	Yes	D.K.
1. Problems of adverse transportation conditions (exposure to excessive heat, moisture, sunlight)	0	1	
2. Problems of theft during transportation and methods for protection against this	0	1	
3. Mechanism to prevent swapping of consignment during transportation	0	1	
4. Requirement that the person responsible for transportation sign a receipt	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

VIII.14 Is there a well-functioning communication system between the suppliers and the end-users for ordering, re-ordering and complaint?

No	Yes	D.K.
0	1	

VIII.15 Does a programme exist for monitoring and evaluating the performance of the medicine distribution system? If so:

	No	Yes	D.K.
1. Monitoring and evaluation programme exists	0	1	
2. Done by an independent authority (e.g. MOH, external auditors, etc.)	0	1	
3. Monitoring is regular, systematic and documented	0	1	
4. Evaluation is carried out at least every two years	0	1	
5. Reports identifying weaknesses and making recommendations publicly available	0	1	
6. Evidence that weaknesses are addressed exists	0	1	
7. Reports are posted publicly	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

VIII.16 Are sanctions imposed on individuals or agencies/companies for theft or corrupt practices associated with distribution? If so:

	No	Yes	D.K.
1. Policies and/or procedures foreseeing the application of sanctions for corrupt behaviour exist	0	1	
2. They include the type of sanctions to be applied depending on the nature and gravity of the act of corruption	0	1	
3. There is evidence that individuals are sanctioned for corrupt behaviour	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

VIII.17 Does the medical store/health facility have appropriate procedures for disposal of expired and/or spoiled medicines? If so, do they include the following:

	No	Yes	D.K.
1. Mechanism to notify MRA about expired or spoiled medicines	0	1	
2. Committee responsible for the supervision of disposal of medicines	0	1	
3. Minutes taken about the disposal and signed by the committee members	0	1	
4. List of disposed medicines	0	1	
Total			

Total yes
Total valid answers
Scoring
(total yes/total valid answers)

VIII.18 To what extent do you agree with the following statement: "There are very rarely leakages in the medicine distribution system in your country".

Strongly disagree	Disagree	Undecided	Agree	Strongly agree	N.A.	D.K.

VIII.19 If you were in a position of highest authority, what would be the first action that you would take to improve the systems and processes of public sector medicine distribution in your country?

Glossary

Accountability

Accountability is the constraints placed on the behaviour of politicians and public officials by state institutions, organizations and constituencies having the power to apply sanctions. Accountability is the responsibility of a public institution, official or politician to carry out a given mandate and to justify his decisions and actions according to applicable rules and regulations. (*)

Auditing

Official examination of an organization or institution's accounts, to make sure money has been spent correctly, i.e. according to rules, regulations and norms. Audit institutions... make a vital contribution to good governance by detecting poor management and inappropriate use of public money. Auditing institutions can be seen as the taxpayers' independent and professional watchdogs. (*)

Bribery

Bribery is the act of offering someone money or other valuables, in order to persuade him to do something for you. Bribery is corruption by definition. Bribes are also called kickbacks, payola, hush money, sweetener, protection money, boodle, gratuity etc. Bribery is practiced at all levels from private familiar situations to international politics. Bribing of foreign officials is banned through several conventions, including the OECD Convention on Combating Bribery of Foreign Public Officials. (*)

Collusion

Secret agreement or understanding for purposes of trickery or fraud; underhand scheming or working with another; deceit, fraud, trickery. (Oxford English Dictionary).

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. See also annex 3 (WHO official conflict of interest form).

Corruption

Various definitions can be found in the literature:

- The World Bank defines corruption as "...behaviour on the part of officials in the public and private sectors, in which they improperly and unlawfully enrich themselves and/or those close to them, or induce others to do so, by misusing the position in which they are placed"; and

- Transparency International's definition is "the abuse of entrusted power for private gain".

Cronyism

Cronyism is favourable treatment of old friends and 'buddies'; it is favouritism, confidentiality and preferential treatment based on long-standing friendship; camaraderie. (*)

Easily accessible document

A document which is obtainable effortlessly when needed, without delays or any bureaucratic obstacle.

Essential medicines or Essential medicines list

Essential medicines are those that satisfy the priority health-care 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.¹

Favouritism

Favouritism is normal human proclivity to favour friends, family and anybody close and trusted. It is biased and favourable treatment based on closeness and obligations, due to clientelism or to ethnic, clan, religious, family (see nepotism), friendship or any other affinity. Favouritism is also the penchant of state officials and politicians, who have access to state resources and the power to decide upon the distribution of these, to give preferential treatment to certain people when distributing resources. (*)

Fraud

Fraud is economic crime involving deceit, trickery or false pretences, by which someone gains unlawfully. An actual fraud is motivated by the desire to cause harm by deceiving someone else, while a constructive fraud is a profit made from a relation of trust. Synonyms: swindling, deceit, double-dealing, cheat, and bluff. (*)

Generic medicine

A pharmaceutical product usually intended to be interchangeable with the innovator brand product, manufactured without a licence from the innovator manufacturer and marketed after the expiry of patent or other exclusivity rights.

Generic medicines are marketed either under a nonproprietary name (INN), for example diazepam or occasionally another approved name, rather than under a proprietary or brand name. However, they are also quite frequently marketed under brand names, often called

¹ Some countries will give a different name to what is in practical terms is their national essential medicines list, as defined by WHO. For example, some countries call their NEML a "national formulary" (e.g. Malaysia). For consistency NEML will be used in this manual, and the concept needs to be clear in the national assessors' mind.

"branded generics". In Kenya, for instance, there are six different generic products with brand names for diazepam.

The manual *Marketing Authorization of Pharmaceutical Products with Special Reference to Multi-source (Generic) Products* (WHO/DMP/RGS/98.5) defines and uses the term "multi-source pharmaceutical products" for generic products. This includes even an innovator brand for which the patent has expired. This definition of a generic is used in some countries, but this manual distinguishes between the innovator brand, regardless of its patent status, and generic equivalents.

Governance

The World Bank defines governance as the traditions and institutions by which authority in a country is exercised for the common good. This includes (i) the process by which those in authority are selected, monitored and replaced, (ii) the capacity of the government to effectively manage its resources and implement sound policies, and (iii) the respect of citizens and the state for the institutions that govern economic and social interactions among them.¹

In WHO's Good Governance for Medicines programme, Good Governance refers to the formulation and implementation of appropriate policies and procedures that ensure the effective, efficient and ethical management of pharmaceutical systems, in particular medicine regulatory systems and medicine supply systems, in a manner that is transparent, accountable, follows the rule of law and minimizes corruption.

Inspection

Inspection is an important area of the medicines regulatory system whereby staff of the regulatory authority enter premises where medicines are manufactured, stored and distributed to ensure that processes are carried out in accordance with norms and standards, as well as the national legislation/regulation.

International Nonproprietary Name (INN)

An International Nonproprietary Name (INN) 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.

The system was introduced by WHO in 1950 by World Health Assembly resolution WHA.3.11 and began operating in 1953 when the first list of INN was published. A comprehensive list of names for radicals and groups updated as per 2004 can be found in the document *International Nonproprietary Names (INN) for Pharmaceutical Substances* (WHO/EDM/QSM/2004.6) or at the following link <http://www.who.int/medicines/library/qsm/RadicalBook2004.pdf>

¹ <http://www.worldbank.org/wbi/governance/about.html>

Kickback

A kickback is a bribe, the 'return' of an undue favour or service rendered, an illegal secret payment made as a return for a favour. The word describes a bribe as seen from the angle of the bribed. For example, A gives B a favour and B gives A a kickback, a 'little something', in return. The term is used to describe in an 'innocent' way the returns of a corrupt or illegal transaction or the gains from rendering a special service. Also called a percentage, share, cut, commission, payoff, etc. (*)

Lead time

The time interval needed to complete the procurement cycle. It begins at the time the need for new stock is recognized and ends when that stock is received and available for issue.

Licensing

It is the process of authorization by an official body to an individual, an institution or a company to carry out a certain activity or business operation (e.g. run a retail pharmacy, a manufacturing plant, etc.).

Marketing authorization

An official document issued by the competent medicine regulatory authority for the purpose of the marketing or free distribution of a product after evaluation for safety, efficacy and quality. It must set out, *inter alia*, the name of the product, the pharmaceutical dosage form, the quantitative formula (including excipients) per unit dose (using International Nonproprietary Names or national generic names, where they exist), the shelf-life and storage conditions, and packaging characteristics. It also contains all the information approved for health professionals and the public (except promotional information), the sales category, the name and address of the license holder, and the period of validity of the license.

Medicine

Any dosage form containing a substance approved for the prevention and treatment of disease. The term "medicine" is increasingly used to distinguish it from a medicine as a substance that is misused.

Medicine Regulatory Authority (MRA)

An MRA is a national agency which is established by legislation to administer the full spectrum of medicine regulatory functions. Its main purpose is to ensure that the manufacture, trade and use of medicines are carried out in accordance with national legislation and regulations, standards and guidelines and that medicines are safe effective and of good quality and that information on medicines is true and correct. Its goal is to protect the public from harmful medicines and promote public health. The principal medicines regulatory functions include:

- licensing of the manufacture, import, export, distribution, promotion and advertising of medicines;
- assessing the safety, efficacy and quality of medicines, and issuing marketing authorization;
- inspecting and surveillance of manufacturers, importers, wholesalers and dispensers of medicines;

- controlling and monitoring the quality of medicines on the market;
- controlling promotion and advertising of medicines;
- monitoring adverse reactions to medicines;
- providing independent information on medicines to professionals and the public.

Formulary manual & national formulary

A formulary is a manual containing clinically oriented summaries of pharmacological information about a selected number of medicines. The manual may also include administrative and regulatory information pertaining to the prescribing and dispensing of medicines.

A national formulary generally concentrates on available and affordable medicines that are relevant to the treatment of diseases in a particular country. Formularies are also frequently created for different levels of health care, different sectors and for individual hospitals.

Nepotism

Nepotism is favouritism based on family ties; it is when someone who has power or authority uses this to get jobs or other favours for members of his own family or other relatives. Nepotism can take place at all levels of the state, from a post office manned largely by one extended family to the state elite. (*)

Pilfering

Plundering, robbery; stealing in small quantities, petty theft; an instance of this. (Oxford English Dictionary).

Promotion

All informational and persuasive activities by manufacturers and distributors, the effect of which is to induce the prescription, supply, purchase and/or use of medicinal medicines. In the definition used in this manual, promotion includes advertisements.

Publicly available document

A document which is found openly, widely and with no restrictions and to be found usually in more than one media (i.e. soft copy; website; hard copies; at a governmental office, documentation centre or in a national gazette).

Registration (see also marketing authorization and licence)

Any statutory system of approval required at national level as a precondition for introducing a pharmaceutical product on the market.

State capture

State capture is the phenomenon in which outside interests (often the private sector, mafia networks, etc.) are able to bend state laws, policies and regulations to their (mainly financial) benefit through corrupt transactions with public officers and politicians. The notion of state capture deviates from traditional concepts of corruption, in which a bureaucrat might extort bribes from powerless individuals or companies or politicians themselves steal state assets. State capture is recognized as a most destructive and intractable corruption problem, above

all in transition economies with incomplete or distorted processes of democratic consolidation and insecure property rights. (*)

Transparency

Transparency means clearness, honesty and openness. Transparency is the principle that those affected by administrative decisions should be informed, and the duty of civil servants, managers and trustees to act visibly, predictably and understandably. Transparency thus encompasses access, relevance, quality and reliability, and describes the increased flow of timely and reliable economic, social, and political information... Transparency enables institutions and the public to make informed political decisions, it improves the accountability of governments, and reduces the scope for corruption. Transparency is also essential to the economy: it improves resource allocation, enhances efficiency and increases growth prospects. (*)

(*) definitions found on U4 - Utstein Anti-Corruption Resource Centre website at the following link <http://www.u4.no/document/faqs5.cfm>

Unedited draft

Annexes

Annex 1: Terms of reference for national assessors

Desk work

1. Study well WHO's transparency assessment instrument
2. Study government website and other relevant sources of information to check availability of various guidelines, procedures and other documents examined in this study.
3. Preliminary visit to various relevant pharmaceutical services to brief key officials on the assessment and collect the relevant documents.
4. Contact some individuals you may know who can give you insight and access to the evidence.
5. Ensure to gather up-to-date information on all areas of the pharmaceutical sector, particularly in the areas of registration, licensing, inspection, promotion, clinical trials, selection, procurement and distribution. Check for NGO reports, government documents, private sector documents, etc.
6. Review and study all the questions in order to be ready to explain them during the interviews with the KIs.

Interviews

7. Determine whom you want to interview for the questionnaires (at least 10-15 people should be interviewed for each functions). The greater the number, the better.
8. Remember you should have a cross-section of upper-, middle- and junior-level persons from government, industry, NGOs, and the media.
9. Ensure that you send out a letter of request for an interview (see annex 2 for a model) to the requisite persons. Ideally, a letter should also be sent out to high level persons so they can either be interviewed or provide you with the name of a person who is appropriate (attach a copy of the clearance letter from MOH).
10. Follow up in contacting the requisite persons by telephone if you don't hear from them and be persistent in your follow up.
11. Set up meetings.
12. When you interview a key informant, remember to ensure that you write down and/or record all answers according to the indicators but also provide yourself with room to add additional information that may be relevant.

Analysis and report writing

13. Compile your responses based on your notes.
14. Score each indicator and each function as described in this WHO tool.
15. Cross-check qualitative and quantitative findings by triangulation for comprehensive interpretation of the findings
16. Write final report (see Annex 4 for a model outline) and submit it to WHO.

Annex 2: Model letter to send to key informants requesting interview

Dear _____,

Given your experience in the pharmaceutical sector and knowledge of the issues facing (name of country) today, I am writing to request your participation in a study conducted for the Ministry of Health (see attached letter).

As part of its Medicines Strategy, WHO is committed to supporting Member States to improve the transparency of the pharmaceutical public sector. This is part of its global efforts to improve access to medicines for all. Accordingly, WHO is supporting multi-country studies in various regions of the world.

I am collaborating in this study with WHO. Specifically, we want to determine what works well and where improvements can be made in eight core areas of the pharmaceutical sector: registration, licensing, inspection, promotion, clinical trials, selection and procurement. This study includes a uniform series of questions that we will be asking key stakeholders in various country settings. We would welcome your knowledge on the subject but will, of course, ensure that all of your answers remain confidential and will be anonymous in the final report.

If you are agreeable, I would like to arrange a meeting with you in the next week, ideally for an hour and a half. If you are unable to participate, I should be grateful if you could give me the name and contact details of a colleague you feel would be appropriate as an alternative.

Please feel free to contact me at (email address and telephone number) should you require any further information.

Yours sincerely,

Your Name

Your Position

Annex 3: 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.

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

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

Annex 4: Example of annotated content list for the final report

[The following list aims to assist National Assessors (NAs) in writing their reports by suggesting brief guidelines, based on the experience of other participating countries. The comments aim to help researchers produce sound reports suitable for publication while remaining reader-friendly to enhance accessibility. Making the report easy to understand and attractive to stakeholders, including policy makers, will enhance its usefulness in future efforts to mobilize in-country support for improving transparency and enhancing the governance systems for medicines.

NAs are encouraged to frequently consult the *interpretation guidelines* in the transparency assessment tool for useful tips on how to integrate results of indicators among each other. Please also refer back to the description of each indicator for ideas on wording of the descriptive sections in your report.

The suggested length of sections is based on the style: Font Times New Roman, Size 12, Lines single space.]

Executive summary

[- captures all main points in the report – can be used as a standalone document to communicate with stakeholders - (2 pages)]

Introduction

- Objectives

[-WHO objectives stated in the instrument - country objectives from participating in the assessment – (0.5-1 pages)]

- Methodology

[- summary of assessment instrument methodology tailored to the *actual* steps undertaken in the assessment – include information on the national assessors, number and distribution of the interviews, process of selection of KIs, difficulties encountered, etc. – (1-2 pages)]

Overview of the pharmaceutical sector in the country

[- brief history - information on structure of public pharmaceutical sector (regulatory authority, national medicines policy, legislation, quality assurance, medicines supply system, financing of medicines, production and trade, and other important structural features in the sector) – pharmaceutical research - political context - relevant cultural features – expenditure on pharmaceuticals - etc. – (2-3 pages)]

Data presentation (findings of assessment)

[- summary tables¹ and brief description of total results – under each section: each indicator stated as in the transparency assessment instrument, followed by a summary of the KIs' response to the question (1-3 paragraphs) – graphs or tables can be used to augment the description – if opinions differ between different KI groups (e.g. private versus government KIs) this should be highlighted - discrepancies/comparison between answers from KIs and evidence - a brief description for each function is useful before going into the details of KI answers – quantitative analysis may be inserted in annexes - (3-5 pages for each function)]

- Registration of medicines
- Licensing of pharmaceutical business
- Inspection of establishments

¹ Examples of summary tables to use are included in Annex 6.

- Control of medicine promotion
- Control of clinical trials
- Selection of essential medicines
- Procurement of medicines
- Distribution of medicines

Data analysis and interpretation

[- for method 3 questions it is important to contrast the existence of legal provisions, or administrative structures and procedures, with their perceived application – refer to the indicator comparative Table 1, page 16 – if there are inconsistencies in the KIs' responses then clarify – for each section, should offer an understanding of the findings – highlight positive aspects and strengths in the current system followed by weaknesses – you can refer to evidence gathered or other activities (e.g. focus group discussions) to verify the findings and enrich the analysis - (0.5-1 page for each function)].

General recommendations

[-capture recommendations which are crosscutting across all section – recommendations which are specific to the pharmaceutical sector as a whole – these should capture the way forward to developing medicines governance in the country – (1-2 pages)]

Specific Recommendations

[- utilize data collected and knowledge of the sector to formulate recommendations – contrasting views on recommendations maybe discussed briefly – use researchers' notes - (0.5-1 page for each function)]

Conclusions

[- summary of main findings of the study - pertinent points found diagnostic of the situation – general perception of the situation by KIs – highlight any issues important to the reader - (2-5 pages)]

References

Annexes:

- List of evidence obtained
- [- use consistent referencing style – sort documents for easy reference – include names of documents in English and in original language (where applicable)]
- Score sheets
 - Organizational charts of assessed institutions (Ministry of Health, MRA, procurement and distribution agencies).

Annex 5: Templates of tables for scoring assessment results

Country name:	Period assessment carried out:	Registration															Average per question**
***	***	KI 1	KI 2	KI 3	KI 4	KI 5	KI 6	KI 7	KI 8	KI 9	KI 10	KI 11	KI 12	KI 13	KI 14	KI 15	Total
Method	***																
Profession*	***																
Indicator I.1	M1																0
Indicator I.2	M2																0
Indicator I.3	M2																0
Indicator I.4	M2																0
Indicator I.5	M2																0
Indicator I.6	M1																0
Indicator I.7	M1																0
Indicator I.8	M2																0
Indicator I.9	M2																0
Indicator I.10	M2																0
Indicator I.11	M3																0
Indicator I.12	M2																0
Indicator I.13	M1																0
Indicator I.14	M3																0
Indicator I.15	M3																0
Indicator I.16	M4																0
Indicator I.17	M4																0
see text in narrative report																	
see text in narrative report																	
																	Total
																	***Final score Registration

G = Government or public official
P = Private sector (national or international)
N = Non-governmental organization (national or international)
IO = International governmental organization
M = Media
O = Other

* Profession:

** The average for each question is calculated only on valid responses and all D.K. and N.A. answers are discarded

*** score = total average/number of indicators x 10

SD = Strongly disagree
DI = Disagree
UD = Undecided
AG = Agree
SA = Strongly agree
DK = Does not know
NA = Not applicable

Method 3

Note:

Method 3 and Method 4 questions (M3, M4) are not part of the quantitative aspect of the assessment because they are not expressed with numbers/quantities. They are the base for the qualitative part of the assessment. For this reason M3 and M4 questions are not calculated in the totals and/or averages present in this consolidation table.

Country name: Licensing

Period assessment carried out: ---

Method ---

	Method	KI 1	KI 2	KI 3	KI 4	KI 5	KI 6	KI 7	KI 8	KI 9	KI 10	KI 11	KI 12	KI 13	KI 14	KI 15	Total	Average per question**	
Professor *	---																		
Indicator II.1	M1																	0	
Indicator II.2	M1																	0	
Indicator II.3	M2																	0	
Indicator II.4	M1																	0	
Indicator II.5	M2																	0	
Indicator II.6	M2																	0	
Indicator II.7	M2																	0	
Indicator II.8	M2																	0	
Indicator II.9	M1																	0	
Indicator II.10	M2																	0	
Indicator II.11	M3																	0	
Indicator II.12	M1																	0	
Indicator II.13	M3																	0	
Indicator II.14	M4							see text in narrative report											
Indicator II.15	M4							see text in narrative report											
Total																			
***Final score Licensing																			

Promotion

Country name: ****

Period assessment carried out: ****

	Method	KI 1	KI 2	KI 3	KI 4	KI 5	KI 6	KI 7	KI 8	KI 9	KI 10	KI 11	KI 12	KI 13	KI 14	KI 15	Total	Average per question**
<i>Profession*</i>	---																	
Indicator IV.1	M1																	0
Indicator IV.2	M2																	0
Indicator IV.3	M2																	0
Indicator IV.4	M1																	0
Indicator IV.5	M2																	0
Indicator IV.6	M1																	0
Indicator IV.7	M2																	0
Indicator IV.8	M2																	0
Indicator IV.9	M2																	0
Indicator IV.10	M2																	0
Indicator IV.11	M3																	0
Indicator IV.12	M3																	0
Indicator IV.13	M3																	0
Indicator IV.14	M3																	0
Indicator IV.15	M4																	0
Indicator IV.16	M4																	0
see text in narrative report																		
see text in narrative report																		
																	Total	
																	***Final score Promotion	

Country name:		Period assessment carried out:																	Clinical trials				
	Method	KI 1	KI 2	KI 3	KI 4	KI 5	KI 6	KI 7	KI 8	KI 9	KI 10	KI 11	KI 12	KI 13	KI 14	KI 15	Total	Average per question**					
Professor*	***																						
Indicator V.1	M1																	0					
Indicator V.2	M1																	0					
Indicator V.3	M2																	0					
Indicator V.4	M2																	0					
Indicator V.5	M2																	0					
Indicator V.6	M1																	0					
Indicator V.7	M2																	0					
Indicator V.8	M1																	0					
Indicator V.9	M2																	0					
Indicator V.10	M1																	0					
Indicator V.11	M2																	0					
Indicator V.12	M2																	0					
Indicator V.13	M3																	0					
Indicator V.14	M3																	0					
Indicator V.15	M3																	0					
Indicator V.16	M4																	0					
Indicator V.17	M4																	0					
		see text in narrative report																					
		see text in narrative report																					
																		Total					
																		***Final score Clinical trials					

Selection

Country name: ****

Period assessment carried out: ****

Method: ****

	Method	KI 1	KI 2	KI 3	KI 4	KI 5	KI 6	KI 7	KI 8	KI 9	KI 10	KI 11	KI 12	KI 13	KI 14	KI 15	Total	Average per question**	
<i>Professor*</i>	****																		
Indicator V1.1	M1																	0	
Indicator V1.2	M3																	0	
Indicator V1.3	M2																	0	
Indicator V1.4	M2																	0	
Indicator V1.5	M1																	0	
Indicator V1.6	M3																	0	
Indicator V1.7	M2																	0	
Indicator V1.8	M2																	0	
Indicator V1.9	M2																	0	
Indicator V1.10	M2																	0	
Indicator V1.11	M4	see text in narrative report																	
Indicator V1.12	M4	see text in narrative report																	
Total																			
***Final score Selection																			

Procurement

Country name:

Period assessment carried out:

Method	KI 1	KI 2	KI 3	KI 4	KI 5	KI 6	KI 7	KI 8	KI 9	KI 10	KI 11	KI 12	KI 13	KI 14	KI 15	Total	Average per question**
<i>Profession*</i>																	
Indicator VII.1																	0
Indicator VII.2																	0
Indicator VII.3																	0
Indicator VII.4																	0
Indicator VII.5																	0
Indicator VII.6																	0
Indicator VII.7																	0
Indicator VII.8																	0
Indicator VII.9																	0
Indicator VII.10																	0
Indicator VII.11																	0
Indicator VII.12																	0
Indicator VII.13																	0
Indicator VII.14																	0
Indicator VII.15																	0
Indicator VII.16																	0
	see text in narrative report																
	see text in narrative report																
	***Final score Procurement																
	Total																

Country name:		Period assessment carried out:															Distribution	
		KI 1	KI 2	KI 3	KI 4	KI 5	KI 6	KI 7	KI 8	KI 9	KI 10	KI 11	KI 12	KI 13	KI 14	KI 15	Total	Average per question**
Profession*		Method																
Indicator VIII.1	M1																	0
Indicator VIII.2	M3																	0
Indicator VIII.3	M2																	0
Indicator VIII.4	M1																	0
Indicator VIII.5	M2																	0
Indicator VIII.6	M2																	0
Indicator VIII.7	M1																	0
Indicator VIII.8	M2																	0
Indicator VIII.9	M1																	0
Indicator VIII.10	M2																	0
Indicator VIII.11	M2																	0
Indicator VIII.12	M2																	0
Indicator VIII.13	M2																	0
Indicator VIII.14	M1																	0
Indicator VIII.15	M2																	0
Indicator VIII.16	M2																	0
Indicator VIII.17	M2																	0
Indicator VIII.18	M3																	0
Indicator VIII.19	M4																	0
see text in narrative report																		
***Final score Distribution																		
Total																		

Annex 6: Examples of summary tables for data presentation chapter in assessment report

Example 1: Vulnerability scale scores in the different sections of the assessments

	Registration	Licensing	Inspection	Promotion	Clinical trials	Selection	Procurement	Distribution
Indicator 1*								
Indicator 2*								
Indicator 3*								
Indicator 4*								
Indicator 5*								
Indicator 6*								
Indicator 7*								
Indicator 8*								
Indicator 9*								
Indicator10*								
Indicator11*								
Indicator12*								
Indicator13*								
Total								
Final Score**								
Degree of Vulnerability								

* The numbers represent the Average per question; calculated only on valid responses

* All D.K & N.A answers are discarded.

** Final score = total average/number of indicators x 10

Example 2: Type of KIs Interviewed

	Government Official	Private Sector	NGO	International Organization	Academia	Media	Other	Total KI/Section
Registration								
Licensing								
Inspection								
Promotion								
Clinical trials								
Selection								
Procurement								
Distribution								
Total KI/type								

- Number of key informants for each function.
- The table is useful in showing the distribution of KIs.
- Further analysis may be offered if distribution of KIs is does not cover all types

Example 3: Perceptions of KIs on the transparency level of each function

Section	Question	Perception of KIs
Registration	The Members of the registration committee are systematically & objectively selected based on the written criteria in force	% Strongly Agree or % Agree % Disagree % Strongly Disagree
	Gifts & other benefits given to the officials in charge of medicines registration have no influence at all on the final decision	
Licensing	The licensing of pharmaceutical establishments is systematically carried according to policies and procedures	
	The formal committee that assesses applications for licensing of pharmaceutical establishments is fully operational and meets on a regular basis	
Inspection	The integrity of the inspectors is not at all influenced by personal gains, such as bribes, gifts, etc	
	Inspection activities are systematically carried out in accordance with the guidelines and procedures to prevent biases	
Promotion	The legal provisions on drug promotion have been developed in broad consultation with all interested parties	
	Pre-approval of promotional and advertising materials are systematically obtained before they are made public	
	Civil society/NGOs have a great influence on improving the control of medicine promotion	
	Sanctions foreseen in the provision on medicines promotion are systematically applied when there is a breach	
Clinical trials	The IEC members are systematically selected based on the written selection criteria	
	The MRA review committee members are selected systematically based on the written selection criteria	
	The MRA is ensuring that CTs conducted in the country are done in accordance with the regulation and GCP principles	
Selection	The national EML has been developed in consultation with all interested parties and using evidence-base approach	
	The committee responsible for the selection of the national EML is operating free from external influence	
Procurement	The member of the tender committee are systematically selected based on specific criteria	
	The procurement system in your country is operating in a totally transparent manner	
Distribution	The port clearing is done smoothly and there is no need for bribery or gift giving to expedite the process	
	There are very rarely leakages in the medicine distribution system	

Unedited draft

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