QUALITY ASSURANCE

CONTENT

1. Quality Assurance Process Outline and QA ideas for LMD
The following gives an overview of commonly accepted international pharmaceutical practices with regard to quality assurance of pharmaceutical products throughout the procurement and supply chain (PSC) and how these may be applied by LMD. At the time of manual preparation LMD does not have a complete quality assurance process.

This paper also tries to give a brief overview of currently used standards and practices in Nepal in comparison with the international standards and practices.

LMD acknowledges the contribution of Hera to this paper.

1 QUALITY ASSURANCE APPROACH

Quality assurance covers all steps in the provision of pharmaceuticals at all the different levels. Pre- and post-inspection including laboratory quality testing are certainly part of it. However, quality assurance is much more than quality control through laboratory testing at certain points in the procurement and supply chain. It also includes elements as prequalification of suppliers, the reception and storage conditions, the distribution, the documentation, the standard operating procedures used and others.

Quality assurance is a risk management process. It is doubtful that anyone or any system can assure 100% quality all the time at every level of the PSC. That is why it is necessary that any

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**Quality assurance**

Quality assurance is a wide-ranging concept covering all matters that individually or collectively influence the quality of a product. It is the totality of the arrangements made with the object of ensuring that pharmaceutical products are of the quality required for their intended use.

**Quality control**

Quality control is concerned with sampling, specifications and testing, and with the procurement agency's documentation and acceptance/rejection procedures which ensure that the necessary and relevant tests are actually carried out and that starting materials, intermediates and finished products are not accepted for use, sale or supply until their quality has been judged to be satisfactory.

Source: WHO Model Quality Assurance System for procurement agencies
system is aimed at reducing the risks through adopting a risk management approach.
The coverage of a quality assurance system is illustrated below. *Note that “traceability” of the pharmaceutical product through the PSC, from manufacturer up to the use by the patient is essential.*

Without traceability there can be no quality assurance. Traceability is ensured by using the combination of product description, manufacturer’s details (name and address) with an unique batch number on every PSC document that describes a movement (reception or supply document) or a location (during storage) of a pharmaceutical product.

The illustration below shows a generic coverage of a quality assurance system at country level. Please note that the illustration does not include the manufacturing process as this does not fall under a country’s responsibility.

**Illustration 1: Coverage of a quality assurance policy**

- **Objective**: Ensure procurement of quality and affordable medical products to ensure adequate answer to essential public needs
- **Means**: Compliant with Essential Medicines National List and national therapeutic guidelines

- **Objective**: Guarantee continuous procurement of quality pharmaceutical products
- **Means**: Compliance with national pharmaceutical law and international standard (WHO/USA FDA/HR countries/internal procedures)

- **Objective**: Ensure fair competitiveness while guaranteeing procurement of medical products compliant with PA quality criteria
- **Means**: Compliance with national public procurement code, WHO MOAS and internal SOPs

- **Objective**: Guarantee quality of the product all along the process (e.g.: coherence between selected, procured and received goods; storage condition does not affect the quality of the product, ...), and on time delivery of the requested items in right quantity to the customers
- **Means**: Compliance with WHO MOAS, GDP, GSP, internal SOPs

- **Objective**: Ensure continuous quality
- **Means**: Sources follow up (regular re-assessment of suppliers, variations management, QC testing)

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1 Both illustrations in this document have been copied from a QUAMED presentation (www.quamed.org)
The following illustration shows an example of what kind of documents are needed at SCM different levels. The underlying principle is that these documents relate to each other.

First, the Procurement Agency (PA) needs a **Quality Assurance policy**.

The PA quality assurance policy is based on the national medicines policy and the existing legislation and regulations that define the objectives, standards, norms and means that have to be applied in the pharmaceutical sector. The national quality policy, on its turn, is based on the internationally accepted standards and guidelines (see Annex 1) of which the most relevant for procurement agencies like LMD are the Model Quality Assurance System (MQAS) for procurement agencies and Good Distribution Practices (GDP). PA quality assurance policy can be developed by the procurement agent in collaboration with the pharmaceutical regulatory authority for example. In the case of Nepal, LMD, in cooperation with DDA Nepal, should develop, apply and manage its quality assurance policy with reference to the MQAS and existing national policies, legislation and regulations.

Subsequently, at every operational level, one needs **standard operating procedures (SOP)** that comply with the standards and norms defined in the quality assurance policy.

The SOP should cover the operational activities related to procurement, storage and distribution as well as the controls in place. They should be available at every level in the procurement and supply chain so that the actual activities can be easily monitored and audited against the SOP.

The staff has to be trained in how to use these SOP through **operating instructions**.

The operating instructions are often part of the SOP. The idea behind the operating instructions is to ensure that the SOP are not just a theoretical description of how the system is supposed to work. The operating instructions (as part of the SOP or as a separate document) ensure that staff knows what are the SOP and how to apply them at the work floor. In special cases operating instructions are displayed near the site where the activities take place, for example where dangerous products are being stored.
Finally, all steps taken have to be captured in **records**.

What kind of records and how they are to be filled in and kept is described in the SOP. In any case the records are archived and will remain accessible for a certain minimum period of time. The records also facilitate the monitoring and auditing. They are indispensable in the case of recalls of pharmaceutical products.

Illustration 2: Quality assurance “document kit”

As indicated above, quality assurance starts at the point of identification of the compounds to produce the active ingredients up to the moment that product is taken by the patient.

For all of the abovementioned steps standard operating procedures should exist describing what should be done at each moment.

A number of selected elements that are part of a quality assurance approach in procurement agencies are described in the following paragraphs.
Procurement

The SOP should describe, among other, selection of products, sourcing of suppliers and market information, tendering and shopping, contracting and contract monitoring, monitoring of suppliers’ performance and the record keeping.

Reception and storage

In the case of storage, the WHO MQAS recommends that at a minimum the following elements are covered by SOP:

- Receiving of products
- Storage of products
- Access control to areas (warehouse security)
- Handling of damaged containers
- Pre-shipment sampling and testing
- Post-shipment sampling and testing
- Handling of rejected products
- Handling of returned products
- Procedure for gowning
- Fire control
- Environmental monitoring
- Cleaning of storage areas
- FEFO
- Rodent and pest control
- Packaging of freeze sensitive materials
- Temperature mapping studies
- Handling of toxic and flammable goods
- Handling of spillages
- Stock reconciliation
- Control of obsolete materials and products
- Handling of waste materials

Distribution

For distribution, the following is another list with suggested SOP:
- Packaging of products in containers
- Maintaining appropriate storage conditions during transport
- Maintaining the cold chain
- Calibration of temperature sensors and devices
- Verification of authorized recipients
- Labeling of outer containers
- Maintaining dispatch records

**Quality assurance**

The PA should have a Quality Assurance Unit that can take decisions regarding quality independent from operational functions. The QA Unit should be in charge of the prequalification of products and/or suppliers, quality control testing (be it during pre- or post-shipment inspection) and release of received products for distribution as well as post marketing surveillance (Pharmaco-vigilance, post marketing inspection).

The head of the QA Unit is normally a registered pharmacist acknowledged by the national regulatory authority. Most importantly, the QA Unit is responsible for regular self-inspections (at least twice per year) to check if SOP are adhered to and if they still comply with the requirements of the international and national agreed standards and guidelines.

How all these elements are defined, applied and managed depends on the particular situation of each country. The functional and working relationship between the procurement agent and the regulatory authority is an important factor that determines who is responsible for what.

Whether the procurement agent is a government agency or a private sector actor also plays a role. Usually, the regulatory authority inspection branch pays inspection visits to the procurement agencies, at least once every 2 years.

Although the principles in a quality assurance system are generic, the application, management and details have to be adapted to each country’s specific circumstances to arrive at an optimal cost-effective and cost-efficient quality assurance system.
2 Nepal: current situation

There are a number of explicit references to quality assurance in different policies and at different levels.

In respect to quality assurance the 2007 draft of the National Drug Policy has formulated the following objectives: ²

“To strengthen the system of quality assurance to make quality as an essential attribute in national production and importation”

“All the medicines procured for the government health institutions shall be monitored for quality”.

“Medicines related activities such as procurement, distribution, storage and dispensing at government as well as non-government institutions will be carried out by qualified pharmacy personnel.”

According to the Nepal Pharmacy Council, there is a written requirement for retail pharmacies. It indicates that:

“The pharmacy should have a quality manual, which should describe quality policy and quality goals and should state, in detail, the necessary steps to be carried out for fulfilment of the desired quality goals. The manual should also enlist the details of the activities, routines, roles and responsibilities, work procedures and instructions that are necessary for achieving the quality goals in day-to-day operations in the pharmacy.”

Specific requirements for wholesalers or public sector warehousing do not yet exist. The Department of Drug Administration (DDA) however, has recently finalized a draft on “Good Distribution Practices” for pharmaceutical warehousing.

The DDA regulates medicine production, import, export, storage, supply, sales, distribution, quality assessment, regulatory control, rational use of drugs and information flow.

The LMD does have draft standard operating procedures for procurement with some sections still to be completed. These have been developed with the support of Crown Agents.

² 2007 NDP draft version
For the warehousing at central and regional level, standard storage guidelines have been developed under a USAID funded project and are presented in Annex 3. They have been disseminated to the central, regional and district stores as well as to the peripheral health facilities. They address a number of essential issues. They do not, however, constitute the complete standard operating procedures as required for the management of a pharmaceutical warehouse/storage.

Of the following listing, the first 10 points are under the direct responsibility of the DoHS/LMD.

**Selection and prequalification.**

1. **Selection**: the selection of products is made on the basis of the national list of essential medicines. It is made by the concerned divisions (FHD, CHD etc.). However, the absence of a pharmacist or experienced procurement experts with extensive pharmaceutical knowledge at the central level in LMD, makes that there is no check on the selection in pharmaceutical terms. Although the divisions are best placed to choose the medicines they need, the strength, exact composition, primary pack size, form and other pharmaceutical elements should be verified by a pharmacist to avoid procurement of inappropriate products.

2. **Technical specifications**: the LMD maintains a technical specifications bank that is regularly updated. **Compliance with national pharmaceutical standards**: formally all the imported pharmaceutical products have to be registered at the DDA for market authorization. Products procured with donor funds have to be prequalified by WHO, SRA or other authority. In practice the former requirement does not always apply as an existing loophole described below is often used by the importers.

Import of unregistered product: Rule 4B(4) mentions circumstances when the DDA can issue an import recommendation letter for unregistered products such as:

- A life saving drug, on the basis of recommendation from a doctor;
- A drug donation received by a governmental, NGO or other organization; and
- When a governmental body wishes to import a drug through an International Competitive Bidding (ICB).
Procurement

3. **Procurement**: The procurement unit at the LMD works with prequalification of manufacturers and the products where possible. The procurement done by the districts is currently not subject to a specific quality assurance policy. All medicines the districts purchase are DDA registered.

4. **Pre-shipment inspection**: Pre-shipment inspection on all medicines before it leaves the manufacturers premises was done on a regular basis. Inspection included review of the manufacturer’s internal quality control documents, random sample taking and the appropriate laboratory tests to ensure compliance with the requirements of the specifications. This was done through an international independent third party inspection agency and the quality testing was done in an ISO 17025 accredited laboratory.

Reception and storage

5. **Post-shipment inspection**: Post-shipment inspection is conducted on all shipments when it is delivered to the first receiving warehouse/store. This inspection is part and parcel of the receipt procedure. This is done by the warehouse personnel. In the past this was limited to the quantity checks and physical verification of the products and did not include randomized quality testing. At present LMD has started to draw samples from all batches as reference samples. There is one ISO 17025 qualified laboratory in the country.

There have been systematic pre- and post-shipment inspections in the past but not currently because of the difficulties in the appointment of an international inspection agency. The inspection task has been divided between several local firms with limited experience. The LMD has recently launched a tender to select a firm for pre- and post-shipment inspections. There is however, no quality control testing plan. It is not necessary to do quality control testing for all products. One approach can be to limit it to those products that are not WHO pre-qualified or that have no registration with a stringent regulatory authority. This is something to be developed by LMD.

6. **Reference Sample library**: This is non-existent until now. Some of the reference samples which are drawn upon receipt at the stores are kept at the normal storage conditions.

7. **Reception and storage management and conditions**: No traceability of batch numbers, no reception and storage standard operating procedures, little monitoring or supervision from one level to the other, no DDA involvement in the inspection of the government managed pharmaceutical warehouses. Storage conditions are not always optimal. Good distribution practices are not always adhered to. There is no batch documentation archive, no batch sample library. None
of the batch numbers are recorded once the products are delivered to the central or regional medical stores by the suppliers. Recall of a batch is not possible in the current system. In any case, no recall policy exists.

8. **Distribution:** LMD is responsible for the distribution of medicines from its central and regional stores to the district stores. While the stores are responsible for preparing the packages for distribution, a private transporter is employed to deliver it to the district stores on a regular basis. The transportation of medicines to the peripheral health facilities is done by the respective DHO/DPHO. There are no SOP on transport conditions.

**Monitoring**

9. **Recall procedure:** there is no recall procedure

10. **Post marketing surveillance:** There is no post marketing surveillance.

11. **Parmaco-vigilance system**

The latter two elements are not necessarily a DoHS responsibility but rather the responsibility of the Department of Drug Administration functions.

### 3  **CONCLUSION**

The conclusion of this technical brief is that the 2007 draft NDP does cover quality assurance policy sufficiently. However, the LMD as the DoHS procurement agency needs to have an explicit quality assurance policy for pharmaceutical products (including reproductive health products). This policy should comply with the 2007 draft NDP and the MQAS/GDP.

The existing LMD standard operating procedures do not cover all steps in the procurement and supply process. There is also no product traceability. **As a result, the risks of substandard medicines being brought into the market are unacceptable high.**

A number of general and detailed recommendations will be made in the LMD assessment report.
The overall recommendation is that the LMD should develop a quality assurance policy for the procurement and supply chain for which it bears the responsibility as the procurement agent. This quality assurance policy should include all elements that are referred to in the previous paragraphs as well as a quality control testing approach.