MEDICINES CONTROL COUNCIL

GOOD WHOLESALING PRACTICE FOR WHOLESALERS, DISTRIBUTORS and BONDED WAREHOUSES

This document has been prepared to serve as a recommendation to applicants wishing to conduct business as medicine wholesalers, distributors and those who wish to operate bonded warehouses. I t represents the Medicines Control Council's current thinking on the safety, quality and efficacy of medicines. It is not intended as an exclusive approach.

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REGISTRAR OF MEDICINES

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TABLE OF CONTENTS

TABLE OF CONTENTS

1 Introduction

Wholesaler distribution forms part of the supply chain of pharmaceutical products manufactured. Wholesalers/ Distributors are responsible for the effective, efficient and safe handling, storage and distribution of such products ensuring the quality and identity of these during all aspects of the wholesaling and distribution process. This Guideline sets out appropriate steps for meeting this responsibility. Further does this code also apply to the storage of medicine in a Bonded Warehouse.

Pharmaceutical products that contain scheduled substances and are not registered with the Medicines Control Council; and are transmitted through the Republic shall, while in the Republic, be stored in a bonded warehouse which is registered with the relevant Authorities.

Except for a brief mention under "storage", the Guideline does not deal with either common or statute law requirements such as the obligations of contractors, Occupational Health and Safety, Customs and Excise, Narcotics, Dangerous Goods, or the many legal requirements surrounding building construction. These must be understood by and met by the wholesaler / distributor.

2 Scope of the Document

This document lays down guidelines for the distribution of pharmaceutical products and applies equally to products for human and for veterinary use. In this Guideline, the word "should" indicates requirements that are expected to apply unless shown to be inapplicable or replaced by an alternative demonstrated to provide at least an equivalent level of quality assurance.

3 Definitions

The definitions provided below apply to words and phrases used in these guidelines. Applicants should also consider the definitions as prescribed by the Medicines and Related Substances Act, 1965 as amended, the Foodstuffs, Cosmetics and Disinfectants Act, 1972 (Act 54 of 1972) and the Pharmacy Act, 1974 (Act 53 of 1974).

“auditing”	means an independent and objective activity designed to add value and improve an organization’s operations by helping an organization to accomplish its objectives by using a systematic, disciplined approach to evaluate and improve the effectiveness of risk management, control and governance processes; and **“audit”** and **“inspection”** have corresponding meanings;
“calibration”	means the set of operations which establish, under specified conditions, the relationship between values indicated by an instrument or system for measuring, recording, and controlling, or the values represented by a material measure, and the corresponding known values of a reference standard. Limits for acceptance of the results of measuring should be established. Including the maximum permissible error or uncertainty of measurement;
“change control”	means a formal system by which qualified representatives of appropriate disciplines review proposed or actual changes that might affect a validated status. The intent is to determine the need for action that would ensure that the system is maintained in a validated state; and that all affected players and processes are prepared to accommodate the change;

"cold chain"	means all of the materials, equipment, processes and procedures used to maintain all products (which require cold chain conditions) within the required temperature range of 2 °C to 8 °C from the time of manufacture until the products are administered to individuals;
"cold chain incident"	means the exposure of a products (which require cold chain conditions) to a temperature outside the required temperature range of 2 °C to 8 °C for any period of time and the potency of the product is potentially compromised. The product temperature excursion tolerance and permissible time excursion is determined by each product manufacturer for each such product;
"cold-chain product"	means all products which require constant storage between 2 °C and not exceeding 8 °C. This also includes vaccines and other products that require storage at product specific temperatures. "thermolabile products" has a corresponding meaning;
"computerised system"	means a system including the input of data, electronic processing and the output of information to be used either for reporting or automatic control;
"computer validation"	means documented evidence which provides a high degree of assurance that a computerized system records data correctly and that data processing complies with predetermined specifications;
"consignment"	means the quantity of pharmaceutical products supplied at one time in response to a particular request or order. A consignment may comprise one or more packages or containers and may include pharmaceutical products belonging to more than one batch;
"container"	means the material employed in the packaging of a pharmaceutical product. Containers include primary, secondary and transportation containers. Containers are referred to as primary if they are intended to be in direct contact with the product. Secondary containers are not intended to be in direct contact with the product; (containers could also be referred to as packaging)
"contamination"	means the undesired introduction of impurities of a chemical or microbiological nature, or of foreign matter, into or onto starting material or onto, products, medical devices or IVDs during handling, production, sampling, packaging or repackaging, storage or transportation;
"contract"	means business agreement for the supply of goods or performance of work for a specified or agreed time at a specified or agreed price;
"**contractor**"	means a company or person under contract**:** a company or person with a formal contract to do a specific job, supplying labour and materials and providing and overseeing staff if needed;
"corrective action"	means any action taken when the results of monitoring at the critical control point indicates a loss of control; and the action taken in response to audit findings;

"courier company"	means a company employed to deliver messages, small packages and mail**;**
"critical control point"	means a step at which control can be applied and is essential to prevent or eliminate a pharmaceutical quality hazard or reduce it to an acceptable level;
"cross contamination"	means the contamination of a starting material, intermediate product or finished product with another starting material or product during production, storage and transportation;
"cycle counting"	means an inventory accuracy audit technique whereby inventory is counted on a cyclic schedule rather than once a year. A cycle inventory count is usually taken on a regular, defined basis (often more frequently for high-value or fast moving items). Most effective cycle counting systems require the counting of a certain number of items every workday with each item counted at a prescribed frequency. The key purpose of cycle counting is to identify items in error, thus triggering research, identification and elimination of the cause of the errors;
"destruction certificate"	means documentary proof of product destruction provided by a certified / approved waste destruction company;
"direct personal supervision"	means guidance and support by a Pharmacist whilst physically present in a pharmacy ;
"deviation"	means the failure to fulfil a specified requirement in terms of processes, standards and regulations as prescribed by the Pharmacy Act and the Medicines Act ;
"distribution"	means the procuring, purchasing, holding, storing, selling, supplying, importing, exporting, or movement of pharmaceutical products, with the exception of the dispensing or providing pharmaceutical products directly to a patient or his or her agent;
"finished product"	means products which has undergone all stages of production, including packaging in its final container;
"first expiry/first out (FEFO)"	means a distribution procedure that ensures that the stock with the earliest expiry date is distributed and/or used before an identical stock item with a later expiry date is distributed and/or used;
"first in/ first out (FIFO)"	means a distribution procedure to ensure that the oldest stock is distributed and/or used before a newer and identical stock item is distributed and/ or used;
"first in/ last out (FILO)"	means a distribution procedure whereby products are stored systematically on a first-in/last-out (FILO) basis;
"freight forwarder"	means an organization that collects shipments from a number of businesses and consolidates them into larger shipments for economies of scale. A freight forwarder may also deals with route selection, price negotiation, and documentation of distribution, and can act as an agent for a business. [By consolidating loads, a freight forwarder can negotiate cheaper rates of transportation than the individual businesses and can pre-book space to ensure a more rapid delivery schedule];

"fridge box/ cold box" means a lagged container, validated to maintain the cold chain for a specific time period, when packed in a specified manner with a specific number of ice packs or gel pack configurations (*see lagged container*);

"fridge item" see cold-chain product

"hazard" means any circumstance in the production, control and distribution of a pharmaceutical product which can cause an adverse health effect;

"ice packs/ soft gel packs" means specialized packs that can be frozen or conditioned;

"lagged container" means an insulated container that has been tested and internally validated to meet the requirements of storing and transporting pharmaceutical products at the required temperatures for the necessary duration of time;

***"*logistics service provider"** means pharmaceutical wholesalers and distributors;

"material safety data sheet (MSDS)" provides information regarding *inter alia* the safety, chemical properties, storage, handling, and disposal of the product. It may also describe the hazardous components of a product, how to treat leaks, spills and fires, and how to treat improper human contact with the product;

"Medicines Act" means the Medicines and Related Substances Act, 1965 (Act 101 of 1965);

"non-conformance/non-conformity" means the failure to fulfil a specified requirement;

"pedigree" means a complete record that traces the ownership of and transactions relating to a pharmaceutical product as it is distributed through the supply chain.

"Pharmacy Act" means the Pharmacy Act, 1974 (Act 53 of 1974);

"preventive action" means an action to eliminate the cause of a potential non-conformity or other undesirable potential situation;

"qualification" means an action of proving that any premises, systems and items of equipment work correctly and actually lead to the expected results. The meaning of the word "validation" is sometimes extended to incorporate the concept of qualification.

"**quality"** means the degree to which a set of inherent properties of a product, system or process fulfils requirements;

"quality assurance" means the activity of or group responsibility for ensuring that the facility (wholesaler or distributor) and its systems meet Good Wholesaling and Distribution Practice requirements;

"quality management" means all management activities and functions involved in determination of quality policy and its implementation through means such as quality planning and quality assurance;

"quality management system"	means the collective policies, plans, practices, and the supporting infrastructure by which an organization aims to reduce and eventually eliminate non-conformance to specifications, standards, and customer expectations in the most cost effective and efficient manner;
"quality manual"	means a detailed document that sets forth practices and sequence of activities aimed at translating an organization's quality policy into operational results, or conformance to standards (such as a ISO 9000 series);
"quality policies"	means principles, rules and guidelines formulated or adopted by an organization to reach its long-term goals;
"quality records"	means documents recording specific information relating to a procedure or work instruction. Quality records are proof that an organization is complying with its procedures and policies;
"quality risk management"	means a systematic process for the assessment, control, communication and review of risks to the quality of a pharmaceutical product across the product lifecycle;
"quarantine"	means the status of starting or packaging materials, intermediate, bulk or finished products isolated physically or by other effective means whilst awaiting a decision on their release or refusal;
"recall"	means the removal of specific batch/batches of a pharmaceutical product from the market for reasons relating to deficiencies in quality, safety or efficacy;
"re-validation"	means the repeat of the initial process validation to provide assurance that changes in the process and/ or in the process environment, whether intentional or unintentional, do not adversely affect process characteristics and product quality;
"return"	means sending back to the manufacturer, wholesaler or distributor a pharmaceutical product, which may or may not present a quality defect;
"risk"	means the combination of the probability of occurrence of harm and the severity of that harm;
"sampling"	means operations designed to obtain a representative portion of a pharmaceutical product., based on an appropriate statistical procedure, for a defined purpose, e.g. acceptance of consignments or batch release;
"Scheduled substance"	means any medicine or other substance prescribed by the Minister of Health under Section 22A of the Medicines Act;
"Service Level Agreement (SLA)"	means a negotiated agreement designed to create a common understanding about services, priorities and responsibilities;

"shelf-life" means the recommendation of time that products can be stored, during which the defined quality of a specified proportion of the goods remains acceptable under expected (or specified) conditions of distribution, storage and display;

"Site Master File" means a document prepared by the wholesaler or distributor containing specific and factual Good Warehousing and Distribution Practices (GWDP) about the control of wholesaler and distribution operations of pharmaceutical products carried out at the named site;

"Standard Operating Procedure (SOP)" an authorized, written procedure giving instructions for performing operations not necessarily specific to a given product but of a more general nature (e.g. equipment operation, maintenance and cleaning, validation, cleaning of premises and environmental control, sampling and inspection); and

"storage" means the storing of products up to the point of use;

"supplier" means a person or entity engaged in the activity of providing or making available products or services along the supply chain;

"**supply chain"** means a system of organizations, people, technology, activities, information and resources involved in moving a product or service from supplier to customer;

"temperature mapping" means a process that verifies that a storage facility or storage equipment does indeed create and maintain the temperatures for which it was designed;

"temperature recording device" means an electronic device capable of monitoring the exact temperature reached during the different stages of storage and movement of a shipment of a pharmaceutical product. in storage or transit, and provides a detailed reading either through a recorder chart or downloading of the information recorded through a software package;

"thermolabile products" means all products which require constant storage between 2 °C and not exceeding 8 °C. This also includes vaccines and other products that require storage at product specific temperatures below room temperature. "**Cold-chain products"** has a corresponding meaning;

"transit" means the period during which pharmaceutical products are in the process of being carried, conveyed, or transported across, over or through a passage or route to reach the destination;

"validation" means action of proving, in accordance with Good Wholesaling and Distribution Practices, that any procedure, process, equipment, material, activity or system actually leads to the expected results (see also qualification);

"validation master plan"	means a document that summarises the firm's overall philosophy, intentions and approach to be used for establishing performance adequacy. The Validation Master Plan (VMP) presents an overview of the entire validation operation, its organisational structure, its content and planning. The core of the VMP being the list/ inventory of the items to be validated and the planning schedule;
"validation protocol"	means a written plan stating how validation will be conducted, including test parameters, product characteristics, production equipment and decision points on what constitutes acceptable test results;
"validation report"	means a written report on the validation activities, the validation data and the conclusion drawn;
"vehicle"	means trucks, vans, buses, minibuses, cars, trailers, aircraft, railway carriages, boats and other means which are used to convey products;
"vendor"	means anyone who provides goods or services to a company; and "supplier" has a corresponding meaning;
"vendor / contractor audit"	means an evaluation of the ability of the manufacturer, applicant or contractor to deliver a quality service, pharmaceutical product.;
"verification"	means the act of reviewing, inspecting, testing, checking, auditing or otherwise establishing and documenting whether items, processes, services or documents conform to specified requirements;
"withdrawal"	means the total withdrawal of a pharmaceutical product from the market.

4 Guiding Principles

4.1 The Wholesaler may only sell into the retail sector within South African territory.

4.2 All parties involved in the supply chain of pharmaceutical products are responsible for the effective, efficient and safe handling, storage and distribution of such products in a manner that does not risk exposure to temperatures outside of their recommended storage conditions. This would prevent any excursions from the recommended storage conditions that could potentially impact on the quality, safety and effectiveness of the products.

4.3 The principles of Good Warehousing and Distribution Practices are equally applicable to pharmaceutical products moving through the supply chain from the manufacturer to the end user, as well as pharmaceutical products which are moving backwards in the chain as a result of the return or recall thereof.

4.4 All parties involved in the wholesaling and distribution process should apply due diligence with adherence to the principles of Good Wholesaling and Distribution Practices, for example, procedures relating to traceability, recognition of security risks, purchasing suspect products, poor storage or failure to establish the *bona fides* of purchasers.

5 Relevant Legislation

This guideline supports legislative requirements as outlined in the various Acts. This guideline does not replace or supersede any aspect as described in any one of the Acts or the Regulations within the Acts.

5.1 In terms of the provisions of Regulation 2 of the Pharmacy Act relating to the "Ownership and Licensing of Pharmacies", the State or any person may, subject to the provisions of Regulation 7(a) of the said Regulations, own or have a beneficial interest in a wholesale or distributor pharmacy.

5.2 In terms of the provisions of Regulation 7 of the Pharmacy Act relating to the "Conditions for the ownership of wholesale pharmacies", a person who may own a wholesale or distribution pharmacy in terms of Section 22A of the Pharmacy Act and who applies for a licence in terms of Section 22 of the said Act shall provide the Director-General, Department of Health with:

a) Proof that such a person is able to comply with the standards of Good Pharmacy Practice as determined by the Pharmacy Council, and where applicable, Good Distribution Practice as determined by the Medicines Control Council; and

b) An undertaking that such person shall comply with the standards referred to in paragraph (a).

5.3 In terms of the provisions of Section 22C(1)(b) of the Medicines Act, the Council may, on application in the prescribed manner and on payment of the prescribed fee, issue to a wholesaler or distributor of a pharmaceutical product a licence to act as a wholesaler, upon such conditions as to the application of such acceptable quality assurance principles and Good Wholesaling and Distribution practices as the Council may determine.

5.4 In terms of the provisions of Section 22D read together with Regulations 20 of the Medicines Act, a licence is valid for a period of 5 years upon which the licence must be renewed on application to the Medicines Control Council. An application for the renewal of a licence to act as a Wholesaler or Distributor of pharmaceutical products shall be made to the Council at least ninety days before the expiry of the existing licence.

5.5 In terms of the provisions of Regulation 19 of the Medicines Act, the licensee must pay an annual license fee to the Medicines Control Council for continued registration. In accordance with the Council's Guidelines "Fees Payable to the Registrar", the annual retention fee in respect of a licence issued in terms of Section 22C(1)(b) of the Medicines Act is payable on or before the last working day of June each year, failing which registration may be cancelled.

5.6 In terms of the provisions of Regulation 19 of the Medicines Act, the licensee must notify the Registrar of Medicines of any changes to any particulars that was furnished in the application or appearing on the license i.e. change in business address, change in Responsible Pharmacist etc.

5.7 A wholesaler may only buy medicine from a Manufacturer issued by the Medicines Control Council with a Manufacturing licence.

5.8 A wholesaler may not import any medicine.

5.9 A wholesaler may only sell into the retail sector within the territory of South Africa.

5.10 In terms of the provisions of Section 22(1) of the Pharmacy Act, the wholesale or distributor pharmacy of products, medical devices or IVDs shall apply to the Director-General of the Department of Health for a licence for the premises wherein or from which such business shall be carried on.

5.11 A wholesale or distributor pharmacy issued with a licence in terms of Section 22(1) of the Pharmacy Act, shall notify the Pharmacy Council thereof in writing and on production of the said licence the Pharmacy Council shall record the name, business address, date of licence, licence number and any other particulars as prescribed.

5 Relevant Legislation - continued

5.12 In terms of the provisions of Section 22(4) of the Pharmacy Act, a wholesale or distributor pharmacy shall, subject to such conditions as may be prescribed, be conducted under the continuous personal supervision of a Pharmacist, in accordance with good pharmacy practice as determined in the rules made by the Pharmacy Council. A deputy Pharmacist must be appointed for the Pharmacist in charge.

5.13 In terms of the provisions of Section 22(5) of the Pharmacy Act, the Pharmacist shall be responsible for any act performed by or on behalf of the wholesaler or distributor of medicines, including any omission to perform an act required to be performed by or on behalf of the wholesaler or distributor in medicines, which may involve disciplinary actions by the Pharmacy Council, unless he satisfies the Pharmacy Council that the responsibility for such act rests upon a Pharmacist other than himself or herself employed by the said wholesaler or distributor of medicines.

5.14 In terms of the provisions of Section 22H(a) of the Medicines Act, no wholesaler shall purchase products, medical devices or IVDs from any source other than from the original manufacturer or from the primary importer/ applicant for registration of the finished product.

5.15 In terms of Section 22A of the Medicines Act, a wholesale of products, medical devices or IVDs may sell Schedule 1 to Schedule 6 products, medical devices or IVDs to any person who may lawfully possess such products;

5.16 The Responsible Pharmacist shall be responsible to control the access to Scheduled products, medical devices or IVDs and shall ensure that the wholesaler or distributor does not sell any Schedule 1 to Schedule 6 pharmaceutical product. to any unlicensed / unregistered entity or permit holder.

5.17 The Responsible Pharmacist shall be responsible to survey on a regular basis if the licence/ permit holder continues to perform his or her approved activities at a specific physical address. The licence/ permit holder shall periodically provide the wholesaler or distributor of products, medical devices or IVDs with:

(a) A copy of annual renewal of registration with his/ her professional Council;

(b) An annual statement from his/ her municipal service provider regarding the licensed premises from which he conducts her or his approved activities;

(c) A copy of the current licence or permit issued by the Medicines Control Council, the Pharmacy Council or the Department of Health, indicating the physical address from which the approved activities will be conducted.

5.18 Furthermore, except as provided for in the Medicines Act, the following services pertaining to the scope of practice of a Pharmacist, may be provided in a wholesale pharmacy in accordance with the provisions of Regulation 17 of the Pharmacy Act:

(a) The wholesale distribution of any pharmaceutical product. through the purchasing, acquiring, keeping, possessing, using, supplying or selling thereof;

5 Relevant Legislation - continued

(b) The furnishing of information and advice to any person with regard to any products, medical devices or IVDs distributed by him, her or it;

(c) The application for the registration of products, medical devices or IVDs;

(d) The initiation and conducting of pharmaceutical research of products, medical devices or IVDs; and

(e) Any other health service as may be approved by the Pharmacy Council from time to time.

5.19 In terms of the provisions of Regulation 45 of the Medicines Act, the following requirements shall apply to any advertisement of a medicine:

(a) Products, medical devices or IVDs which do not contain a scheduled substance and those products, medical devices or IVDs which contain a substance appearing in Schedule 0 or Schedule 1 may be advertised to the public;

(b) Products, medical devices which contain a substance appearing in Schedule 2, Schedule 3, Schedule 4, Schedule 5 or Schedule 6 may be advertised only for the information of medical practitioners, dentists, veterinarians, pharmacists and other persons authorised to prescribe or in a publication which is normally or only made available to persons referred to therein;

(c) In terms of Regulation 45 it shall not be so construed as to prohibit informing the public of the prices, names, pack sizes and strengths of products, medical devices or IVDs which contain a substance appearing in Schedule 2, Schedule 3, Schedule 4, Schedule 5 or Schedule 6; and

(d) The Responsible Pharmacist is responsible to approve and sign off all advertising material and to ensure that the materials comply with the provisions of Regulation 45 of the Medicines Act.

6 Contractual Activities, Service Level Agreements and Technical Agreements

6.1 Authorized procurement and release procedures for all administrative and technical operations performed should be in place to ensure that appropriate pharmaceutical products are sourced only from approved suppliers and distributed by approved entities. The approval should come from the competent authority of the individual country where the legal entity is registered.

6.2 The Responsible Pharmacist is responsible to ensure that contracts exist between the wholesaler/distributor (contract giver) and 3rd party contractors (contract acceptor) stipulating where all the responsibilities in terms of GWDP lie.

6.3 Any activity relating to the supply chain of pharmaceutical products which is delegated to another party or entity should be agreed upon in a contract.

6.4 Apart from any commercial agreement in place between the parties, a technical contract or formal agreement must be put in place addressing all quality matters relating to the wholesaling/distribution of the pharmaceutical products. It should define in detail the responsibilities and accountabilities of the contract giver and contract acceptor at the start and end of the contract to ensure product quality compliance. The Responsible Pharmacist must co-sign the technical document when the matter relates to the quality of products.

6.5 Recommended Service Level Agreements (SLA's) should include as a minimum and when applicable:

a) Rodent and pest control;

b) Cleaning services;

6 Contractual Activities, Service Level Agreements and Technical Agreements - continued

c) Couriers and freight forwarding (including any third party services);

d) Calibration services;

e) Fire extinguishers;

f) Waste disposal;

g) Preventive maintenance of critical equipment;

h) Security; and

i) IT.

6.6 The SLAs must ensure that the service provider is compliant with Good Warehousing and Distribution Practices and will be held responsible for any deviation from the agreement.

6.7 The contract should permit the contract giver to visit the facilities of the contract acceptor for a vendor approval inspection.

6.8 In accordance with Good Wholesaling and Distribution Practices, the contract giver is obliged to perform an annual vendor inspection at the premises of the contract acceptor.

6.9 All contract acceptors must comply with the relevant requirements stated in these guidelines.

6.10 Subcontracting of services by the contract acceptor may be permissible under certain conditions subject to a written approval by the contract giver.

6.11 Inspection, auditing and certification of compliance with a quality system (such as the applicable International Standardization Organization (ISO) series, or national or international guidelines) by external bodies are recommended. Such certification should not, however, be seen as a substitute for compliance with these GDP guidelines and the applicable principles of GMP relating to pharmaceutical products.

7 Customer Verification

7.1 In terms of Act 101 of 1965 as amended wholesalers and distributors may supply scheduled products, medical devices or IVDs to registered and licensed entities only as per the provisions of Section 22A of the Medicines Act however Schedule 0 products are available for open sale (i.e. in both pharmacy and non pharmacy retail stores)

7.2 The wholesaler of distributor must have a process in place that verifies the following:

a) The name of the entity ordering;

b) The Pharmacy, Dispensing or Department of Health licence/authorisation number;

c) All accompanying documentation;

d) That the delivery address on the account and invoice matches the physical delivery address displayed on the licence;

e) The expiry date of the licence in the case of e.g. dispensing doctors;

f) That the order correlates to the name on the licence; and

g) Any change of ownership or delivery address;

7.3 Only the Responsible Pharmacist has the authority to override or change the authorization of the supply of scheduled products, medical devices or IVDs.

7 Customer Verification - continued

7.4 A retail pharmacy within a hospital building must have a separate licence to that of the hospital pharmacy.

7.5 An individual pharmacy within a commercial grouping such as pharmacy chain stores must each have its own separate licence, which is separate to that of the head office and reflects the physical address from which the business of a pharmacy will be carried out from.

7.6 If a change of ownership or a change of premises occurs a new licence must be obtained.

7.7 A process must be put in place, where the current registration/licensing status can be verified on an annual basis to ensure that the wholesaler/distributor only supplies an entity that is still in good standing with the relevant regulatory bodies.

7.8 If there is more than one doctor in a practise that is dispensing pharmaceutical products each doctor is required to have his or her own dispensing licence. (The licence is issued to a doctor and not to a practice).

8 Vendor Verification

All wholesalers and distributors must ensure that the vendors from which they procure any pharmaceutical products, medical devices or IVDs must have the necessary licences in place; and that the pharmaceutical products, medical devices or IVDs are legitimate, from a legitimate source and registered with the Medicines Control Council.

9 Organization and Management

9.1 The wholesaler or distributor must be an entity that is appropriately authorized to perform the intended function in terms of the applicable legislation, and which can be held accountable for its activities.

9.2 There should be an adequate organizational structure defined with the aid of an organizational chart. The responsibility, authority and interrelationships of all personnel should be clearly indicated. This must be duly dated, be current, valid and authorised.

9.3 A designated qualified person should be appointed at each branch that has the defined authority and responsibility for ensuring that a quality management system is implemented and maintained.

9.4 Senior Management must be represented at all feedback of findings of audits.

9.5 Each facility is required to have its own Responsible Pharmacist.

9.6 Managerial and technical personnel must have the authority and resources needed to carry out their duties and to set up and maintain a quality management system, as well as to identify and correct deviations from the established quality management system.

9.7 The responsibilities placed on any one individual should not be so extensive as to present any risks to the pharmaceutical products quality or process.

9.8 There should be arrangements in place to ensure that management and personnel are not subject to commercial, political, financial and other pressures or conflicts of interest that may have an adverse effect on the quality of service provided.

9 Organization and Management - continued

9.9 Individual responsibilities should be clearly defined and understood by the individuals concerned and recorded as written job descriptions. Certain activities may require special attention such as the supervision of performance of activities, in accordance with legislation.

9.10 Duties may be delegated or contracted out to suitably designated persons or entities as necessary. There should, however, be no gaps or unexplained overlaps with regard to the application of Good Wholesaling and Distribution Practices. These activities should be documented in quality agreements or contracts. There should be periodic audit of such activities with regards to application of Good Wholesaling and Distribution Practices.

9.11 Safety procedures relating to all relevant aspects including the safety of personnel and property, environmental protection and pharmaceutical product. Integrity, should be in place.

10 Personnel

10.1 General

10.1.1 All personnel involved in wholesaling or distribution activities should have the education, training, experience or combination of these elements that will allow then to effectively discharge this responsibility and be capable of meeting these requirements. This training should be documented.

10.1.2 Procedures and conditions of work for employees and other persons having access to the products must be designed and administered to minimise the possibility of pharmaceutical products coming into unauthorised possession.

10.1.3 Key personnel involved in the wholesaling or distribution of a pharmaceutical product should have the ability appropriate to their responsibility for ensuring that pharmaceutical products are handled, stored and distributed in accordance with minimum standards.

10.1.4 There must be an adequate number of competent personnel involved in all stages of the distribution of pharmaceutical products in order to ensure that the quality of these products is maintained.

10.1.5 Regulations by the relevant authorities with regard to qualification and training of personnel should be complied with.

10.1.6 Personnel involved in the wholesaling or distribution of pharmaceutical products should be supplied with appropriate personal protective equipment suitable for the activities that they perform.

10.1.7 Personnel dealing with hazardous pharmaceutical products, including products containing materials that are highly active, toxic, infectious or sensitizing, should be provided with specialised protective garments as necessary.

10.1.8 Material safety data sheets must be accessible to any staff member that requires the information. A Spillage Handling SOP must be available.

10.1.9 Appropriate procedures relating to personnel personal hygiene and sanitation relevant to the activities to be carried out, should be established and observed. Such procedures should cover health, hygiene and clothing of personnel.

10.1.10 Codes of practice and disciplinary procedures should be in place to prevent and address situations where persons involved in the wholesaling or distribution of pharmaceutical products are suspected of, or found to be implicated in, the misappropriation and/or theft thereof.

10.2 Responsible Pharmacist

10.2.1 In accordance with Regulation 22 of the Pharmacy Act "Regulations Relating to the Practice of Pharmacy", every wholesale and distributor pharmacy shall be conducted under the direct personal supervision of a Responsible Pharmacist whose name must be displayed conspicuously over the main entrance of such pharmacy;

10.2.2 In accordance with Regulation 28 of the "Regulations Relating to the Practice of Pharmacy", the Responsible Pharmacist must:

a) Ensure that he or she in fact continuously supervises the wholesale or distributor pharmacy in which he or she has been appointed;

b) Have appropriate qualifications and experience in the services being rendered by a wholesale or distributor pharmacy;

c) Ensure that persons employed in such wholesale or distributor pharmacy and who provide services forming part of the scope of practice of a Pharmacist are appropriately registered with the Pharmacy Council;

d) Notify the Pharmacy Council and the Medicines Control Council immediately upon receiving knowledge that his/her services as Responsible Pharmacist have been or will be terminated;

e) Take corrective measures in respect of deficiencies with regard to inspection reports of the Pharmacy Council or in terms of the Medicines Control Council; and

f) In addition to the general responsibilities also:

(i) Ensure that unauthorised persons do not obtain access to pharmaceutical products or the wholesale or distributor pharmacy premises outside of normal trading hours;

(ii) Establish policies and procedures for the employees of the wholesale and distributor pharmacy with regard to the acts performed and services provided in the wholesale pharmacy;

(iii) Ensure the safe and effective storage and keeping of pharmaceutical products in the wholesale and distributor pharmacy under his/her direct personal supervision;

(iv) Ensure correct and effective record keeping of the purchase, sale, possession, storage, safekeeping and return of pharmaceutical products.

(v) Ensure that the following registrations, recordings and licences are current and in place:

aa. The registration of the Responsible Pharmacist with the Pharmacy Council in accordance with the provisions of Section 14 of the Pharmacy Act;

bb. The premises licence of the wholesale or distributor pharmacy issued by the Director-General, Department of Health, in accordance with the provisions of Section 22(1) of the Pharmacy Act;

cc. The recording of the premises licence of the wholesale or distributor pharmacy at the Pharmacy Council in accordance with Section 22(2) of the Pharmacy Act, read together with Regulation 8(5) of the "Regulations relating to Ownership and Licensing of Pharmacies"; and

dd. The wholesale licence issued by the Medicines Control Council in accordance with Section 22C (1) (b) of the Medicines Act.

10.2 Responsible Pharmacist - continued

10.2.3 In accordance with Regulation 3.2 of the Pharmacy Act "Recommended standards regarding staff selection, appraisal and training", the Responsible Pharmacist should-

a) Ensure that written job descriptions are prepared for all staff and that all staff are acquainted with their job descriptions and responsibilities;

b) Set performance objectives at least annually in consultation with each staff member. Performance must be monitored and evaluated against the job descriptions and established objectives. Results should be discussed with the staff member and clearly documented on their personal record;

c) Assess the educational needs of all pharmaceutical staff. Training should relate to the work to be undertaken by the individual.

10.2.4 In accordance with Regulation 3.7 of the Pharmacy Act "Minimum Standards for the Management of Human Resources in Wholesale and Manufacturing Pharmacies" the Responsible Pharmacist must:

a) Have expert knowledge with regard to the wholesale and distribution of pharmaceutical products;

b) Safe-guard product users against potential hazards arising from poor wholesale and distribution practices as a result of e.g. purchasing suspect products, poor storage or failure to establish the *bona fides* of purchasers;

c) Ensure that the conditions of the wholesale or distributor pharmacy's licence are met and that there is compliance with the standards and guidelines on pharmacy practice;

d) In addition, the Responsible Pharmacist of a wholesale or distributor must:

(i) Have a direct line of communication with and be part of management;

(ii) Have access to all areas, sites, stores and records which relate to the activities being performed;

(iii) Regularly review and monitor all such areas, sites, etc. or have delegated arrangements whereby he/she receives written reports that such actions have been carried out on his/her behalf;

(iv) Keep appropriate records relating to the discharge of his/her responsibility;

(v) Ensure the physical security of the stock or have written assurance from the manager responsible for security that administrative and physical security systems are in place and are adhered to by all personnel.

10.2.5 In accordance with Regulation 4 of the Pharmacy Act "Minimum Standards for Management of the Wholesale and Distribution Pharmacies" the Responsible Pharmacist must:

a) Ensure that there are sufficient pharmacists and pharmacy support personnel to undertake the pharmaceutical services provided by the wholesale or distributor pharmacy concerned;

b) Demonstrate a high standard of professionalism and commitment to quality development;

c) Ensure that all regulations covering the operations of the wholesale or distributor pharmacy are complied with;

d) Review his or her level of professional knowledge and expertise continually and document an appropriate self-development plan;

e) Participate regularly in continuing professional development (CPD) programmes;

10.2 Responsible Pharmacist - continued

f) Be responsible for the preparation of the mission statement and/or statement of purposes, the wholesale or distributor pharmacy strategic plan, contracts for the supply of services and the said pharmacy's client profile and client expectations;

g) Develop, document and approve the quality improvement plan for the wholesale or distributor pharmacy;

h) Ensure that standards for the operation of wholesale or distributor pharmacy services are established and that performance against these standards are monitored;

i) Participate with appropriate staff in regular professional audit activities to review the standard of services. From the review process strategies should be developed, documented and employed to improve performance; and

j) Be responsible for the existence of SOPs in a wholesale or distributor pharmacy and must be involved in the compilation of the said SOPs.

10.2.6 In addition, the Responsible Pharmacist of a wholesale or distributor pharmacy must:

a) Approve and sign off all advertising, promotions and promotional material in accordance with the provisions of Regulation 45 of the Medicines Act;

b) In the event that another pharmacist or *locum* is available in the wholesale or distributor pharmacy to provide pharmaceutical services in the absence of the Responsible Pharmacist, the Responsible Pharmacist may be absent only if suitable mechanisms or procedures or policies were in place;

c) Provide Pharmacy Council in writing the delegation duties and responsibilities for which he or she is accountable;

d) Ensure that all directors are *au fait* with the current ethical rules of the Pharmacy Act and agree to abide thereby;

e) Ensure that all reference sources required in accordance with Regulation 1.2 "Minimum Standards for Pharmacy Premises, Facilities and Equipment" of the Pharmacy Act are on hand; and

f) Ensure that every key, key card or other device, or the combination of any device, which allows access to a wholesale or distributor pharmacy when it is locked, is kept only on his/ her person or the person of another pharmacist at all times;

10.3 Pharmacy Support Personnel

10.3.1 As defined by the Pharmacy Council, a pharmacist's assistant (basic) registered in the category pharmacist's assistant (basic) may perform the following services or acts under the direct personal supervision of a pharmacist pertaining to the activities of a wholesale/distribution pharmacy:

(a) The sale of Schedule 1 medicines or Scheduled substances;

(b) The distribution and control of stock of Schedule 1 to Schedule 6 medicines or scheduled substances; and

(c) The provision of information to individuals in order to promote health.

10.3.2 Pharmacist's Assistant (learner basic) — A pharmacist's assistant registered in the category Pharmacist's Assistant (learner basic) may for the purposes of education and training, provide the services or perform the acts prescribed in Regulation 9 under the direct personal supervision of a pharmacist in a pharmacy.

10.3 Pharmacy Support Personnel - continued

10.3.3 Pharmacist's Assistant (post-basic) — A pharmacist's assistant registered in the category Pharmacist's Assistant (post-basic) may perform the following services or acts under the direct personal supervision of a pharmacist pertaining to the activities of a wholesale/distribution pharmacy:

(a) The sale of Schedule 1 and Schedule 2 medicines or scheduled substances;

(b) The distribution and control of stock of Schedule 1 to Schedule 6 medicines or scheduled substances;

(c) The ordering of medicine and scheduled substances up to and including Schedule 6 according to an instruction of a person authorised in terms of the Medicines Act to purchase or obtain such medicine or scheduled substance;

(d) The provision of instructions regarding the correct use of medicine supplied;

(e) The provision of information to individuals in order to promote health.

10.3.4 Pharmacy Student

(a) A pharmacy student may provide or perform all the services or acts pertaining to the scope of practice of a pharmacist's assistant registered in the category "Pharmacist's Assistant (basic)" under the direct personal supervision of a pharmacist in a wholesale pharmacy.

(b) A pharmacy student who has successfully completed his or her second year of study may provide or perform all the services or acts pertaining to the scope of practice of a Pharmacist's Assistant registered in the category "Pharmacist's Assistant (post-basic)" under the direct personal supervision of a Pharmacist in a wholesale pharmacy.

10.4 Pharmacist

10.4.1 The following services and/or acts are regarded to be acts specifically pertaining to a pharmacist in a wholesale and distributor pharmacy:

(a) The purchasing, acquiring, keeping, possessing, releasing, storage, supplying or selling of any pharmaceutical product. supplied or the supervision thereof;

(b) The scope of practice of a pharmacist in a wholesale and distributor pharmacy includes:

(i) The distribution of any pharmaceutical product;

(ii) The initiation and conducting of pharmaceutical research and development.

10.5 Training

10.5.1 A written procedure on the training of personnel must be available.

10.5.2 The Responsible Pharmacist for the wholesaler or distributor is responsible for:

(a) Ensuring that training takes place;

(b) Reviewing on a regular basis the effectiveness of the training programs;

(c) Evaluating the relevance of the course content e.g. training on Storage and Handling of pharmaceutical products etc;

(d) Identifying which staff will be entered into the training programs;

(e) Monitoring whether staff has participated as planned in the training programs;

10.5 Training - continued

(f) Ensuring that adequate training records are maintained;

(g) Personnel should receive initial (induction) and continuing training relevant to their tasks, and be assessed as applicable, in accordance with a written training program; and

(h) Personnel dealing with hazardous products (such as highly active and radioactive materials, narcotics, and other hazardous, sensitive and/or dangerous pharmaceutical products, as well as products presenting special risk or abuse, fire or explosion) should be given specific training.

11 Quality Management System

11.1 General

11.1.1 Senior management should provide evidence of its commitment to the development and implementation of the Quality Management System (QMS) and continual improvement of its effectiveness by:

a) Communicating to the organization the importance of adhering to customer requirements; and regulatory (Good Wholesaling and Distribution Practices) and legal requirements, including environmental, health and safety aspects;

b) Establishing a quality policy with quality objectives;

c) Ensuring regular reviews of quality management systems;

d) Applying risk assessments;

e) Maintaining appropriate conditions throughout the organization for processes and systems;

f) Ensuring the availability of resources, particularly enough manpower that is suitably trained.

11.1.2 The Quality Manual must be established, documented and maintained.

11.1.3 The Quality Manuel should include as a minimum:

a) The company's quality policy statement, organizational structures and resources, service provision and interaction between the processes, quality management system description and quality objectives;

b) Standard Operating Procedures (SOPs) and Technical Guidelines;

c) Work Instructions and Process Maps;

d) Forms and Records.

11.2 Self-Inspections

The System of Quality Assurance of the wholesale and distribution pharmacy should include self-inspections. These inspections should be in line with the principles of Good Wholesaling and Distribution Practices and if necessary, to trigger corrective and preventative measures.

11.2.1 The Responsible Pharmacist is responsible to ensure that self-inspections are performed and any deviation are followed up and concluded.

11.2.2 Written procedures for self- inspections should be established to provide minimum and uniform standards.

12.2 Self-inspections - continued

11.2.3 Self-inspections should be conducted in an independent and detailed way by a designated and competent person.

11.2.4 Self-inspections should cover all aspects of Good Wholesaling and Distribution Practices.

11.2.5 The frequency of self-inspections should be at least once a year.

11.2.6 Inspection reports should include results, evaluation, conclusions, and recommended measures. These reports should be summarized and periodically submitted to Senior Management as an integral part of the management review process.

11.2.7 There should be an effective follow-up programme, whereby company management must evaluate both the report and corrective measures. The follow-up activities should verify the effectiveness of the corrective action taken.

11.3 Corrective and Preventive Actions (CAPA)

11.3.1 Corrective Action

11.3.1.1 Corrective action is taken to eliminate the cause of an existing nonconformity or other undesirable situation.

11.3.1.2 Corrective action procedures must be implemented and the effectiveness of the results must be verified. It must be determined whether the nonconformity is an isolated or a repetitive problem, and any actions to be taken, if necessary.

11.3.1.3 Corrective action is taken to prevent recurrence of a situation or nonconformity.

11.3.2 Preventive Action

11.3.2.1 Preventive action is taken to prevent occurrence. Preventive action should be considered if there are opportunities to improve the quality management system.

11.3.2.2 Corrective action is taken after nonconformities are identified. Preventive action is taken when a potential nonconformity is identified as a result of the analysis of records and other relevant sources of information, such as:

(a) Statistical process control documents;

(b) Customer complaints;

(c) Review product, process and quality system information;

(d) Risk analysis and risk assessment of products and processes.

11.3.2.3 Records relating to the product performance should be analyzed regularly, to detect trends and to identify areas of risk that may lead to nonconformities.

11.3.2.4 The analysis should also determine how to prevent any identified potential problems.

11.3.2.5 Information on preventive action taken must be part of the management review to maintain and improve the quality system.

11.4 Validation

11.4.1 Wholesalers and distributors should have a Validation Master Plan. The Validation Master Plan provides a summary of the company's philosophy, policy, intentions and approach to validation.

11.4.2 The following should be validated as a minimum:

(a) Warehouse premises: ambient and cold-chain storage conditions including temperature mapping;

(b) Lagged containers;

(c) Cold-chain processes; and

(d) Computerised systems.

11.4.3 Validation should be conducted in accordance with a validation protocol. A written Validation Report should be available after completion of the validation.

11.5 Calibration

11.5.1 All measuring equipment must be calibrated in accordance with an approved schedule that details which equipment requires calibration, as well as the frequency of calibration. The frequency will depend on the type of equipment used, as well as the purpose for which it is used.

11.5.2 It is the Responsible Pharmacist's responsibility to approve the calibration schedule.

11.6 Electronic Records

11.6.1 Records of temperature monitoring data should be available for review. There should be defined intervals for checking temperature. The equipment used for monitoring should be checked at suitable predetermined intervals and the results of such checks should be recorded and retained. All monitoring records should be kept for at least the shelf-life of the stored pharmaceutical product plus one year, or as required by the relevant national legislation.

11.6.2 Temperature mapping should show uniformity of the temperature across the storage facility. It is recommended that temperature monitors be located in areas that are most likely to show fluctuations.

11.6.3 Data, especially, legal records, may be recorded by electronic data processing systems but detailed procedures relating to the system in use should be available and the accuracy of the records should be checked.

11.6.4 A written detailed description of the system should be produced (including diagrams as appropriate) and kept up to date. It should describe the principles, objectives, security measures and scope of the system and the main features of the way in which the computer is used and how it interacts with other systems and procedures.

11.6.5 Only authorised persons should be able to enter or modify data in the computer. Access should be restricted by passwords or other means. User should have a unique identifier (User ID) for their personal and sole use so that activities can subsequently be traced to the responsible individual.

11.6.6 Written procedures should be in place for the validation of computerized systems in order to demonstrate security of access and data integrity.

11.6 Electronic Records - continued

11.6.7 There should be a record of changes and deletions. Any alteration to an entry of critical data (which must be defined by each organisation) should be authorised and recorded with the reason for the change in accordance with the SOP for "Quality Assurance Change Control". Consideration should be given to the system creating a complete record of all entries and amendments (an "audit trail").

11.6.8 Records electronically stored should be protected by back-up transfer on magnetic tape, microfilm, paper or other means, at regular intervals. Back-up data should be stored as long as possible at a separate and secure off site location.

11.7 Risk Management

11.7.1 Risk can be defined as the measure of the probability and consequence of not achieving a specific goal. It therefore depends on both the likelihood (probability) of an event occurring and on the consequence (impact) of that event, should it occur.

11.7.2 Effective Risk Management allows the risks to be controlled to such an extent that the unwanted subset of a set of uncertain outcomes can be mitigated adequately.

11.7.3 Because planned actions can be subject to large costs and benefit risks, a thorough risk assessment and risk management plan is critical for the success of such actions.

11.7.4 Risk assessment plays a crucial role in not only security management, but also in ensuring delivery of consistent quality service in the healthcare supply chain. In this environment it equates to quality pharmaceutical products delivered to the correct customers, under the correct storage and transportation conditions.

11.7.5 Distributors should annually conduct risk assessments to assess potential risks to the quality and integrity of pharmaceutical products. The quality system should be developed and implemented to address any potential risks identified. The quality system should be reviewed and revised annually to address new risks identified during a risk assessment.

11.7.6 Preferable a Risk Matrix must be used by the wholesaler or distributor, to not only identify and assess areas of risk in critical business processes, but also to allow for the identification of solutions to address the risk adequately - to mitigate or avoid the risk factor.

11.7.7 It is paramount that the Risk Management system is practical, realistic, compliant with internal and external standards and cost-efficient.

11.7.8 Most risk management systems comprises of five distinct areas:

(a) Risk identification;

(b) Risk classification;

(c) Risk analysis;

(d) Risk attitude;

(e) Risk response, control, policy and reporting.

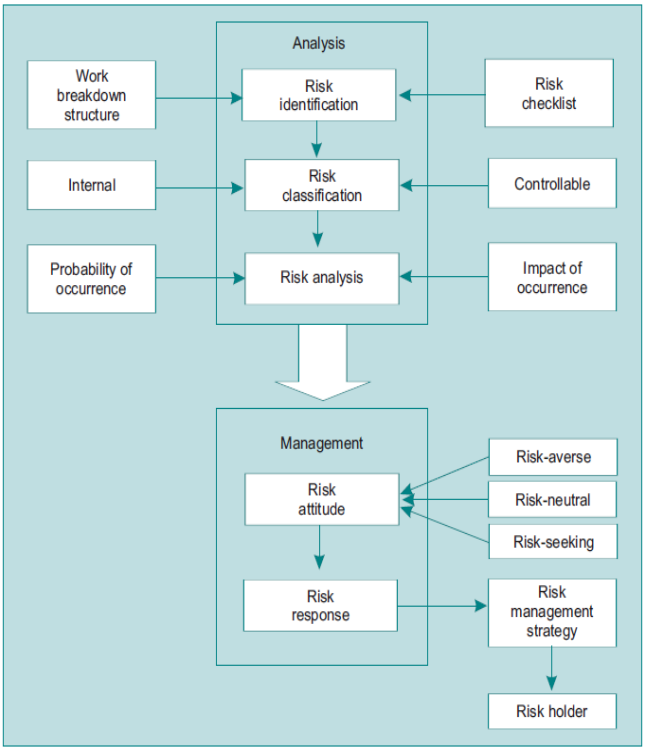

Figure 1: Risk Management System

As part of the Risk Analysis, the various risks can be mapped / profiled by plotting the Impact and the Probability on an axis and then developing an appropriate strategy to deal with or manage the risk factor. It is important to note that risk is not stagnant and as the variables change over time, so does the risk profile – this continuous monitoring and feedback is essential, as with any process that has a quality focus.

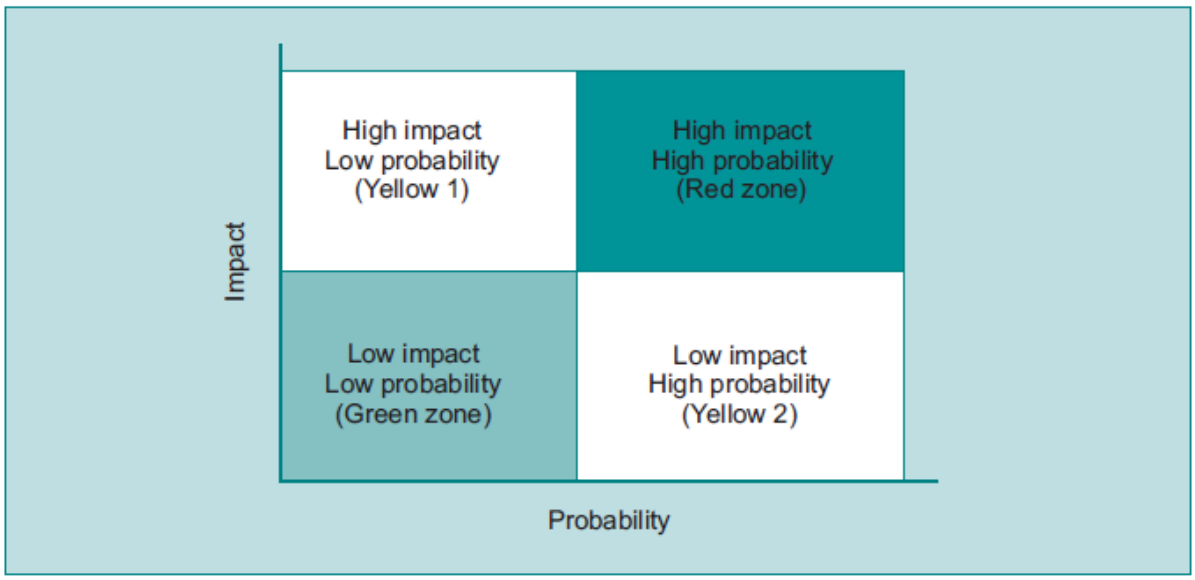

Figure 2: Risk Measuring

11.7 Risk Management - continued

11.7.9 The Risk Response options may include any of the following:

11.7.9.1 Risk retention;

11.7.9.2 Risk reduction;

11.7.9.3 Risk transfer;

11.7.9.4 Risk avoidance;

11.7.9.5 Seeking additional information about the risk element.

11.8 Change Control

11.8.1 Change Control within the Quality Management system is used to introduce changes on processes, products, structures or systems in a controlled and coordinated manner that allows for the assessment, evaluation and approval of the change prior to its implementation. By following a Change Control process the organisation avoids disruption to its current operations as unnecessary changes or disruptive changes will be identified and appropriate steps can be taken to manage the change to have the desired effect or reject the change altogether if it poses an unacceptable risk to the organisation.

11.8.2 To initiate change normally a formal request for a proposed change on a standardised Change Control Request form is prepared.

11.8.3 The reasons or justification for the change should be clearly documented and the Change Request then submitted to Management/Change Control Committee for review and analysis (which would include an element of Risk Assessment) – it is recommended that a multi-disciplinary group participates in the assessment and evaluation process as various aspects such as impact on Quality, Safety and Health, Operations, IT etc. should be given due consideration, as well as changes made by other individuals/groups that might be affected as a result of introducing this new change.

11.8.4 Once the Change Request has been approved, the initiator or responsible person should formulate the implementation plan, and manage the change as a project with objectives, milestones, timelines etc.

11.8.5 All documentation for the Change Request and subsequent Project Plan etc. must be retained in line with the organisations archiving procedure.

12 Documentation and Record Keeping

Good documentation constitutes an essential part of the Quality Assurance system and should include the relevant SOPs, legal records, documentation system and electronic records. Any computerized document or format should comply with the current legislative requirements and/or international practices for electronic documentation and computerized system. Records should be made available for inspection.

Written instructions and records which document all activities relating to the distribution of pharmaceutical products, including all applicable receipts and issues (invoices) should be available. Invoices or packaging slips should be issued for each delivery and accompany the goods. Clear and readily available records should be maintained showing the receipt and disposal of all products purchased and sold. Such records should be kept in an accessible form and place for at least five years, unless otherwise specified in national or regional regulations.

12.1 Standard Operating Procedures

12.1.1 The Responsible Pharmacist is responsible for the compilation, review, updating and authorization of Standard Operating Procedures (SOPs) in a wholesale or distributor pharmacy.

12.1.2 Copies of all SOPs must be present at the point of use.

12.1.3 The following SOPs should (as a minimum requirement) be in place in a wholesale pharmacy:

(1) How to create, review and update SOPs;

(2) Preparation of Site Master File;

(3) Contract/service level agreement activities;

(4) Responsibilities and job descriptions;

(5) Delivery and transportation;

(6) Advertising and promotions control;

(7) Handling of technical complaints

(8) Handling of Adverse drug reactions reporting;

(9) Handling of Temperature deviations;

(10) Handling of and requests for Change control;

(11) Procurement of pharmaceutical products;

(12) Good housekeeping/sanitation practices;

(13) Conditions of employment;

(14) Performing and closing out of Self-inspections;

(15) Receipt of stock;

(16) Storage of pharmaceutical products;

(17) Control of pharmaceutical products in quarantine;

(18) Products that require special storage/ handling instructions;

(19) Cold chain management;

(20) Control of counterfeit pharmaceutical products;

(21) Rodent and pest control;

(22) Training/keeping training records;

(23) Distribution control;

(24) Cleaning of spillages;

(25) Transportation and goods in transit;

(26) Vehicle cleaning;

(27) Vehicle maintenance;

(28) Delivery protocol;

(29) Delivery debrief;

12.1 SOPs - continued

(30) Loading of vehicles;

(31) Vehicle monitoring

(32) Vendor verification;

(33) Customer verification;

(34) Control of returned, damaged, rejected goods;

(35) Storage of "Specified" Schedule 5 and Schedule 6 medicines;

(36) Destruction of expired/ damaged/ contaminated stock;

(37) Destruction of "Specified" Schedule 5 and Schedule 6 medicines;

(38) Effective stock rotation of pharmaceutical products;

(39) Stock control;

(40) Recall/ withdrawal of pharmaceutical products;

(41) Warehouse and refrigerator temperature monitoring, recording and control;

(42) Calibration of measuring devices;

(43) Risk management;

(44) Access to warehouse in an emergency situation;

(45) Health and safety;

(46) Security of personnel, pharmaceutical products;

(47) Warehouse fire safety;

(48) Waste disposal;

(49) Personal hygiene.

12.2 Documentation System

12.2.1 Written procedures must be established and maintained for the development, control, distribution and review of all documents relating to the wholesaling and distribution process.

12.2.2 The title, nature and purpose of each document should be stated clearly. The contents of documents should be clear and unambiguous and should be current and valid.

12.2.3 All documents should be completed, approved, signed and dated by an appropriate authorized person(s) / key personnel and should not be changed without the necessary authorization.

12.2.4 Documents should be reviewed regularly and kept up to date. When a document has been revised, a system should exist to prevent inadvertent use of the superseded version.

12.2.5 All records must be readily retrievable, stored and retained.

12.3 Site Master File

12.3.1 It is mandatory for a wholesaler or distributor of pharmaceutical products to submit a Site Master File to the Medicines Control Council.

12.3.2 Written procedures should be in place for the preparation, review and update of the Site Master File.

12.3.3 The Responsible Pharmacist is to maintain and update the Site Master File. Updates should be submitted to the Medicines Control Council at least every 3 years or should any changes occur.

12.3.4 The Site Master File should be in compliance with the "Guidelines for Preparation of Site Master File" issued by the Medicines Control Council.

12.4 Legal Records

12.4.1 Sales Records

12.4.1.1 Regulations should foster a safe, transparent and secure distribution system which includes product traceability throughout the supply chain. This is a shared responsibility among the parties involved. There should be procedures in place to ensure document traceability of products received and distributed, to facilitate product recall.

12.4.1.2 Ideally there should be a procedure in place for the creation and maintenance of a pedigree for pharmaceutical products. Provision should be made for a visual and/or analytical identification of potential counterfeit products. The procedure to be followed when a suspected product is identified should include provisions for notification, as appropriate, of the holder of the certificate of registration, entity identified on the label (if different from the manufacturer), the appropriate national and/or international regulatory bodies, as well as other relevant competent authorities.

12.4.1.3 Sales records should be maintained for any wholesale sale of pharmaceutical products or distribution thereof.

12.4.1.4 A record of receipts and sales of the pharmaceutical products shall be kept, stating the name of the product, pack size, date of transaction, invoice/ delivery order number, name and address of purchaser/ supplier, batch number, expiry date, quantity received/ sold and stock balance.

12.4.1.5 In accordance with the provisions of Regulation 11(4) of the Medicines Act, the manufacturer or wholesaler shall keep a record of Schedule 2, 3, 4, 5 and 6 pharmaceutical products in the form of invoices that will reflect:

a) The date and transaction of every sale;

b) The name of the medicine;

c) The name and address of every purchaser;

d) The quantities sold;

e) The batch number; and

f) The price at which the medicine was sold.

12.4.2 Regulation 11(5) of the Medicines Act stipulates that a sales record shall be kept for a period of five years from the date of sale.

12.5 Specified Schedule 5 and Schedule 6 Products, Sales and Register

12.5.1 In terms of the provisions of Section 22A(5)(c) of the Medicines Act, any Specified Schedule 5 and Schedule 6 pharmaceutical product may not be sold to any person who may not lawfully possess such substance.

12.5.2 In terms of the provisions of Regulation 28(4) of the Medicines Act, every order for a Schedule 6 pharmaceutical product must be written in legible print, typewritten or computer generated and signed in person by an authorized person and must state at least the following:

a) The name, qualification, practice number and address of the authorized person placing the order;

b) The date of issue of the order;

c) The approved name or the proprietary name of the pharmaceutical product;

d) The dosage form;

e) The strength of the dosage form and the quantity of the pharmaceutical product to be supplied.

12.5.3 In the case of a faxed, e-mailed, telephone or electronic transmission by other means of an order, wholesale dealer in pharmaceutical products or distributor must verify the authenticity of the order in terms of the provisions of Regulation 28(4) of the Medicines Act.

12.5.4 The provisions of Section 22A(6)(j) of the Medicines Act stipulate that in an emergency in which the life of a patient is at stake, the pharmacist engaged in wholesale practice, may on receipt of a telephonic or telefaxed or other electronic request, supply a Schedule 6 pharmaceutical product without a written order provided that:

a) It shall be the responsibility of such pharmacist, medical practitioner, dentist, veterinarian, practitioner, nurse or other person to ensure that the pharmacist engaged in wholesale practice receives a written order within seven days;

b) The Schedule 6 pharmaceutical product shall be supplied in the smallest unit sales pack available (not multiples thereof).

12.5.5 In terms of the provisions of Section 22A (9) (a) (I) of the Medicines Act, a pharmacist engaged in wholesale practice, may on receipt of a written order as mentioned above, supply any Schedule 6 product to an analyst or researcher for the purpose of education, analysis or research who has been issued with a permit by the Director-General for such acquisition, use, possession for the purpose of education, analysis or research.

12.5.6 Any seller (pharmacist engaged in wholesale practice), of a Schedule 6 pharmaceutical product referred to in Section 22A(6) of the Medicines Act shall retain the order concerned for a period of not less than five years as from the date of such sale.

12.5.7 A register shall be maintained for the transactions of all “specified Schedule 5” and/or Schedule 6 pharmaceutical products. This is a legal requirement as stipulated under Section 22A (6) (p) and Regulation 30(1) of the Medicines Act.

12.5.8 The register referred to in Regulation 30(1) of the Medicines Act, must indicate the quantity of every such pharmaceutical product remaining in stock on the last day of March, June, September and December of each year and must also contain the following information:

12.5 Specified Schedule 5 and Schedule 6 Products Sales and Register - continued

a) The date on which the pharmaceutical product. was received or supplied;

b) The name, business address of the person from whom the pharmaceutical product was received or sent and in the case of imported pharmaceutical products, the import permit number;

c) The name and address of the person who purchased the pharmaceutical products;

d) The quantity, in words and figures, of such pharmaceutical products indicated per dosage unit, mass or volume;

e) Entries shall be made on the day of transaction; and

f) Balancing of the register shall be completed within the fourteen days following each of the said dates on the last day of March, June, September and December of each year.

12.6 Post-Importation Testing of "Specified Schedule 5" and/ or Schedule 6 Products, Medical Devices and IVD's

In the event that "Specified Schedule 5" and/or Schedule 6 samples need to be drawn for testing by a Quality Control Laboratory that has been licensed by the Medicines Control Council, these orders must be processed by the Holder of the Certificate of Registration of the "Specified Schedule 5" and/ or Schedule 6 pharmaceutical products.

13 Procurement for Wholesalers

13.1 Written procedures should be available for the procurement of pharmaceutical products.

13.2 In accordance with the licensing conditions as stipulated under Section 22C (1)(b) of the Medicines Act, a wholesaler or distributer may not perform any activities relating to the import or export of pharmaceutical products. A wholesaler or distributor however is permitted to facilitate the import and export of pharmaceutical products on behalf of the Manufacture or Holder of the Certificate of Registration.

13.3 There should be adherence to the Medicines Control Council's guidelines on "Medicine Donations to South Africa" in the case of pharmaceutical products which are donated.

14 Premises, Warehousing and Storage

Premises should provide protection for the goods from contamination and deterioration, including protection from excessive local heating or undue exposure to direct sunlight. The goods received or dispatched at receiving or dispatch bays, docks, platforms or areas should be protected from dust, dirt and rain. Premises should be kept free of rodents, vermin, birds, pets and pests.

Premises should have dedicated and demarcated areas available for the receipt of stock, general storage area, goods in quarantine, goods rejected, cold-chain storage, good returned, dispatch and storage of "Specified Schedule 5" and/or Schedule 6 pharmaceutical products.

"Specified Schedule 5" and/or Schedule 6 substances must be stored in a secure lockable area directly under the control of a pharmacist.

14.1 Receipt of Stock

14.1.1 Written procedures should be available for the receipt of stock. Particular attention should be paid to those pharmaceutical products that require special storage and handling instructions. A list of products that require special handling and storage requirements must be available at the receiving area.

14.1.2 The receiving personnel must do spot checks on the delivery vehicle and inspect the delivery vehicles for the following:

a) That the products were protected from light and rain, i.e. the delivery truck has a closed canopy;

b) The delivery truck does not have evidence of spillage inside that could lead to possible contamination or have been exposed to anything that can cause contamination to the products, e.g. any hazardous substances etc

c) The delivery truck is lockable to secure the products delivered;

d) The products are not mixed with other materials that will compromise the integrity of the products delivered.

14.1.3 Stock must be received in a separate and dedicated receiving area.

14.1.4 Receiving and dispatch bays should protect products from the weather.

14.1.5 Receiving and dispatch bays must be de-dusted on an ongoing basis and be kept free of contamination.

14.1.6 Upon receipt, each incoming delivery should be checked against the relevant documentation and physically verified by:

a) The identity of the stock;

b) The batch numbers of the stock;

c) The expiry date of the stock;

d) The pack size;

e) The condition of the stock;

f) The status as to whether released or quarantined;

g) The quantity of the stock received;

h) The suppliers details;

i) The signature of the person who received the stock.

14.1.7 All containers should be carefully inspected for tampering, contamination and damage and if necessary the suspected container of the entire delivery should be quarantined or set aside for further investigation.

14.1.8 Records should be retained for each delivery. They should include the description of the goods, quality, quantity, supplier, supplier's batch number, the date of receipt and assigned batch number.

14.1.9 If any discrepancies are identified, all these discrepancies must be documented. In addition, the supplier must be notified immediately and the goods must be clearly identified and segregated.

14.2 General Storage Areas

14.2.1 Precautions must be taken to prevent unauthorized persons from entering storage areas.

14.2.2 Storage areas should have sufficient capacity to allow the orderly storage of the various categories of pharmaceutical products namely finished products, products in quarantine, released, rejected, returned or recalled products.

14.2.3 Storage areas should be designed or adapted to ensure good storage conditions. In particular they should be clean and dry and maintained within specified temperature limits. Pharmaceutical products should be stored off the floor and suitably spaced to permit cleaning and inspection. Pallets should be kept in a good state of cleanliness and repair.

14.2.4 Products must be stored according to the particular goods legal requirements.

14.2.5 Secure measures should be taken to ensure that rejected products cannot be used and they should be stored separately from other products while awaiting destruction or return to the supplier. The measures adopted should possess adequate safeguards to prevent uncontrolled or unsatisfactory pharmaceutical products from being used or released.

14.2.6 Storage areas should be clean, and free from accumulated waste and vermin.

14.2.7 Written procedures and a sanitation program should be available, indicating the frequency of cleaning and the methods to be used to clean the premises and storage areas.

14.2.8 A cleaning log must be in place and completed and signed and checked by the appropriate designated person.

14.2.9 There should be a written procedure and a programme available for pest control. The pest-control agents used should be safe, and there should be no risk of contamination of pharmaceutical products. A on the site flow plan indicating where the bait stations are situated must be available.

14.2.10 There should be appropriate written procedures available for the cleanup of any spillage to ensure complete removal of any risk of contamination.

14.2.11 There should be appropriate written procedures available for the removal of spilled hazardous products and cytotoxic substances and products to ensure any risk of contamination or health hazard.

14.2.12 If sampling is performed in the storage area, it should be conducted in accordance with a written procedure and in such a way as to prevent contamination or cross-contamination.

14.2.13 Written procedures should be available for the isolation and control of goods. Goods should be moved to a controlled area in the event of:

a) Pharmaceutical products that await the release by the Holder of the Certificate of Registration;

b) Pharmaceutical products deemed to be of counterfeit origin;

c) Returned, damaged or expired pharmaceutical products for destruction;

d) Pharmaceutical products that have been recalled or withdrawn from the market;

e) Pharmaceutical products that are being investigated after a cold-chain failure;

f) On the instructions by the regulatory authority or the Holder of the Certificate of Registration.

14.2 General Storage Areas - continued

14.2.14 Where quarantine status is ensured by storage in separate areas, these areas must be clearly marked and their access restricted to authorized personnel. Any system replacing physical quarantine should provide equivalent security. For example, computerized systems can be used, provided that they are validated to demonstrate security of access.

14.2.15 Physical or other equivalent validated (e.g. electronic) segregation should be provided for the storage of rejected, expired, recalled or returned products. The products and areas concerned should be appropriately identified.

14.2.16 Radioactive materials, narcotics and other hazardous, sensitive and/ or dangerous pharmaceutical products, as well as products presenting special risks of abuse, fire or explosion (e.g. combustible liquids and solids and pressurized gases) should be stored in dedicated areas that are subject to appropriate additional safety and security measures.

14.2.17 Pharmaceutical products should be handled and stored in such a manner as to prevent contamination, mix-ups and cross-contamination.

14.2.18 Broken or damaged items should be withdrawn from usable stock and stored separately.

14.2.19 Storage areas should be provided with adequate lighting to enable all operations to be carried out accurately and safely.

14.2.20 Sufficient warehouse security should be maintained to prevent misappropriation of the goods

a) To prevent unauthorized possession of, or access to the product;

b) To allow for appropriate stock control.

14.2.21 Stock losses should be minimized by taking appropriate measures:

a) A single exit/ entry point to the warehouse being used;

b) Vehicles (other than delivery vehicles) not being allowed near the warehouse;

c) All goods leaving the store being carefully checked against the relevant documentation;

d) Security checks of all vehicles entering or leaving the warehouse area taking place;

e) High-risk goods being well protected, ideally in a separate area that is sealed off from the rest of the warehouse with access control;

f) Implementing good housekeeping;

g) Ensuring that workers are not able to leave the warehouse area during working hours without going through security;

h) Preventing theft by using appropriate security systems;

i) Avoiding fires in the warehouse by removing combustible waste materials several times a day. No-Smoking policies and notice boards should be in place.

j) Implementing and adhering to The Occupational Health and Safety Act, 1993 (Act 85 of 1993) in the warehouse to ensure a healthy and safe work environment. Details of the Act should be displayed in the work environment for all staff to see.

14.3 Ambient Storage Conditions for Pharmaceutical Products

14.3.1 Storage conditions for pharmaceutical products as described by the product storage requirements should be in compliance with the instructions on the label and package insert, which are based on the results of stability testing. When specified on the label, controls for temperature, humidity, light etc. should be in place.

14.3.2 The warehouse or storage facility should be maintained at a temperature not exceeding 25 °C at all times.

14.3.3 All warehouses should be temperature mapped over a period of at least one year to determine the temperature distribution under seasonal extremes.

14.3.4 Temperature mapping should be repeated every two to three years and after every significant modification to the premises, stock layout or ventilation system.

14.3.5 Temperature monitoring should be done at strategic locations (hot and cold spots) covering the stock containment areas and must be read and data recorded twice daily. Temperatures should be recorded at low and high levels.

14.3.6 Continuous temperature monitoring and recording of environmental conditions must take place.

14.3.7 Written procedures should be available describing the action to be taken in the event of temperature deviating outside of the set standards and conditions must be appropriately investigated. The fate of the goods outside of the set standards must be decided by the Responsible Pharmacist in consultation with the Holder of Certificate of Registration.

14.4 Monitoring of Storage Conditions

14.4.1 Temperatures should be controlled and monitored using calibrated monitoring devices.

14.4.2 Monitoring is conducted at points representing the extremes of the temperature range (hot spots or cold spots) based on temperature mapping.

14.4.3 Recorded temperature monitoring data should be available for review.

14.4.4 The equipment used for monitoring should be checked at suitable intervals and the results of such checks should be recorded.

14.4.5 Monitoring equipment should be calibrated once a year.

14.4.6 All monitoring records should be kept for at least the shelf-life of the stored pharmaceutical products plus one year.

14.5 Storage Conditions for Thermolabile Products

14.5.1 All Thermolabile products must be stored in a refrigerator or cold room, in a temperature regulated environment between 2 °C and 8 °C or as per the information on the product label; and the cold chain must be maintained at all times.

14.5.2 Thermolabile products that are required to be frozen must be maintained at -20 °C.

14.5.3 The refrigerator or cold room must be connected to an alarm system in the event of a power failure or if the refrigerator temperatures limits are exceeded.

14.5 Storage Conditions for Thermolabile Products - continued

14.5.4 The refrigerator or cold room must be connected to a standby generator or other emergency power system to ensure uninterrupted power supply in the event of a power failure.

14.5.5 There must be a written procedure in place in the event of a power failure.

14.5.6 Refrigerators, cold rooms and freezers used to store thermolabile pharmaceutical products should:

a) Be well maintained;

b) Be equipped;

c) Be free from frost build-up;

d) Allow for adequate air distribution and orderly storage within the chamber. Good storage practices and loading configurations should not lead to the obstruction of air distribution;

e) Have sensors for continuous temperature monitoring and alarms located at the points representing the temperature extremes.

14.5.7 The refrigerator or cold room must be mapped in terms of temperature.

14.5.8 Products should not be stored in areas shown by temperature mapping to present a risk (e.g. in the airflow from the refrigeration unit).

14.5.9 Sufficient space should be maintained to permit adequate air circulation especially between shelving. If the refrigerator is filled to capacity, the effect on temperature distribution should be investigated.

14.5.10 Ensure that no condensation from chillers collects or drips onto product or collects inside the facility.

14.5.11 On receipt of a shipment of thermolabile stock, all cold chain items should be moved to the refrigerator within the shortest possible time from offloading the truck.

14.5.12 When a lagged container used for transportation of the product is opened, all cold chain products must immediately be removed and exposed to the refrigerator's temperatures, in order to maintain the cold chain. Checks should be done to ensure that the cold chain has been maintained during transportation.

14.6 Inventory Management

14.6.1 Comprehensive records should be maintained showing all receipts and issues of pharmaceutical products according to batch number and expiry date.

14.6.2 Annual physical cyclical counts should involve counting all items and comparing the counts with the records.

14.6.3 The differences should be reconciled i.e. all significant stock discrepancies should be investigated to check that there have been no inadvertent mix-ups, incorrect issue and/or misappropriation of pharmaceutical products; and any stock discrepancy must be referred to the Responsible Pharmacist.

14.6.4 A written procedure should be in place to ensure effective stock rotation. Pharmaceutical products due to expire first must be sold and/or distributed in accordance with the first expiry, first out (FEFO) principles. Where no expiry dates exist for the pharmaceutical products, the first in, first out (FIFO) principle should be applied.

14.6.5 All stock must be checked regularly for obsolete and shorted dated stock items. All due precaution should be observed to prevent the issue of such short dated or expired stock.

14.6 Inventory Management - continued

14.6.6 Pharmaceutical products with broken seals, damaged packaging or suspected of possible tampering/ contamination must not be sold or supplied and must be segregated pending an investigation and decision.

14.6.7 Pharmaceutical products bearing an expiry date must not be received or supplied after their expiry date.

14.6.8 If a pharmaceutical product is so close to its expiry date and that the expiry date is likely to be reached before the pharmaceutical product is likely to be used by the consumer the product should not be received or supplied.

14.6.9 Recalls of pharmaceutical products must be carried out as per written procedure of the appropriate manufacturer or Holder of Certificate of Registration.

15 Shipment Containers and Container Labelling

15.1 All pharmaceutical products should be stored and distributed in shipment containers which do not have an adverse effect on the quality of the products, and which offer adequate protection from external influences, including contamination.

15.2 Shipment containers may not necessarily need to bear labels with full description of the identity of the container's content, but should provide sufficient information on the handling and storage conditions and precautions to ensure the pharmaceutical products are properly handled at all times.

15.3 The need for any special transport and/or storage conditions should be stated on the label.

15.4 Special care should be taken when using dry ice in containers. In addition to safety issues it must be ensured that the pharmaceutical products do not come into contact with the dry ice, as it may have an adverse effect on the quality of the product.

15.5 Written procedures should be available for the handling of damaged and/or broken shipment containers. Particular attention should be paid to those containing potentially toxic and hazardous products.

15.6 Validated Lagged Container

15.6.1 Vaccines are normally transported in lagged containers. During transport the vaccines must be protected by validated insulated packaging during distribution. The containers should be filled with sufficient ice packs configured to ensure product quality is maintained.

15.6.2 There should be a written procedure available for the validation of the lagged containers.

15.6.3 The lagged containers should be validated to maintain the cold chain items at a constant storage between 2°C and 8°C for a specific time period that is based on worst case conditions of environmental temperature.

15.7 Lagged Container Consumables

15.7.1 The fridge line supervisor is normally responsible for the replenishment of lagged container consumables.

16 Equipment

16.1 Equipment used to move, store or handle pharmaceutical products should be suitable for their use to prevent exposure of products to conditions that could affect their stability and packaging integrity, and prevent contamination of any kind.

16.2 The design and use of equipment must aim to minimize the risk of errors and permit effective cleaning and/or maintenance to avoid contamination, build-up of dust or dirt and/or any adverse effect on the quality of pharmaceutical products being distributed.

16.3 Where non-dedicated equipment is used, procedures must be in place to ensure that the quality of the pharmaceutical products will not be compromised in any way.

16.4 Appropriate cleaning should be performed and checked.

16.5 Defective equipment should not be used, and should either be labelled as such or removed from area.

16.6 There must be procedures in place for the operation and maintenance of all equipment involved in the distribution process, including cleaning, safety precautions and preventative maintenance requirements.

16.7 Normally only equipment with non combustible engines should be used.

16.8 All equipment storage must comply with Health and Safety requirements.

16.9 Equipment should be kept clean and dry and free from accumulated waste. A written cleaning programme should be available, indicating the frequency of cleaning and the methods to be used.

16.10 Equipment should be kept free from rodents, vermin, fungi, birds and other pests.

16.11 There should be a written programme for pest control and elimination. Cleaning and fumigation agents should not have an adverse effect on product quality or be a source of contamination.

16.12 Equipment used for monitoring conditions e.g. temperature and humidity, should be calibrated.

16.13 Measures should be in place to prevent unauthorized persons from entering and/or tampering equipment, as well as to prevent the theft or misappropriation thereof.

17 Vehicles

17.1 Vehicles used to move, store or handle pharmaceutical products should be suitable for their use to prevent exposure of products to conditions that could affect their stability and packaging integrity.

17.2 Vehicles should be loaded and packed correctly so to prevent movement and breakages and preferably on a First In, Last Out (FILO) basis.

17.3 The vehicles must:

a) Be clean and free from contamination of rats, vermin, birds, fungi etc;

b) Have solid sides;

c) Not transport non pharmaceutical products which could result in contamination.

17.4 Vehicles should be of sufficient capacity to allow orderly storage of the various categories of pharmaceutical products during transportation.

17.5 Where special storage conditions (e.g. temperature and or relative humidity) different from the expected environmental conditions are required during transit these should be provided, checked and monitored and recorded.

17 Vehicles - continued

17.6 Mechanisms should be available to allow for the segregation during transit of rejected, recalled and returned pharmaceutical products as well as those suspected being counterfeits. Such goods must be securely packaged, clearly labelled, and be accompanied by appropriate supporting documentation.

17.7 Pharmaceutical products should not be returned without the necessary and relevant documentation.

17.8 Pharmaceutical products should not be returned in non-protective packaging such as a plastic bag.

17.9 Measures should be in place to prevent unauthorized persons from entering and/or tampering with vehicles, as well as to prevent the theft or misappropriation thereof or of the pharmaceutical products.

17.10 Procedures should be in place to ensure that the integrity of the products is not compromised during transportation.

17.11 Where third-party carriers are used, wholesalers/distributors should develop written agreements with carriers to ensure that appropriate measures are taken to safeguard pharmaceutical products, including maintaining appropriate documentation and records.

18 Sale and Dispatch of Pharmaceutical products

18.1 Written procedures for the dispatch of pharmaceutical products should be established. Such procedures should take into account the nature of the product, as well as any special precautions to be observed.

18.2 All the prescribed particulars of every sale of a pharmaceutical product shall be recorded in the prescribed manner in a permanent record required to be kept for five years and must be easily retrievable.

18.3 Pharmaceutical products should only be sold and/or distributed to persons or entities that are entitled to acquire such products. Customer verification must be performed; written proof of such authority must be obtained prior to the dispatch of products to such persons or entities.

18.4 The Responsible Pharmacist shall be responsible to survey the purchasing patterns for Schedule 5, “Specified Schedule 5” and Schedule 6 medicines or substances. In the event of exceptional high volumes being purchased, the Responsible Pharmacist should inform the national regulatory authority accordingly.

18.5 In the event of an emergency a wholesaler or distributor may supply a Schedule 6 pharmaceutical product. to a pharmacist, medical practitioner, dentist, veterinarian, practitioner, nurse or other person registered under the Health Professions Act, 1974 without a written order provided that:

a) The pharmacist, medical practitioner, dentist, veterinarian, practitioner, nurse or other person ensures that such Pharmacist receives a written order within seven days; and

b) The Schedule 6 substance must be supplied in the smallest unit sales pack available.

18.6 There should be adequate provision for the security, storage condition and protection of the quality of pharmaceutical products during transportation to the customer. The transport process should not affect the integrity and quality of the products.

18.7 Pharmaceutical products should be transported in such a way that:

a) Identification is not lost;

b) They do not contaminate, and are not contaminated by, other products or materials;

18 Sale and Dispatch of Pharmaceutical products - continued

c) Adequate precautions are taken against spillage, breakage or theft;

d) They are secure and not subjected to unacceptable degrees of heat, cold, light, moisture or other adverse influence, or to attack by micro organisms or pests;

e) The products are secured so as to prevent unauthorised possession;

f) The point of delivery must be consistent with the delivery address on the waybill or delivery note or label;

18.8 For the deliveries of "Specified Schedule 5" and/or Schedule 6 pharmaceutical products, requirements stipulated in Section 22A of the Medicines Act should be followed.

18.9 An invoice of the dispatched pharmaceutical products should be prepared and should include at least the following information:

a) Date of dispatch;

b) Name and address of the customer;

c) A description of the products including, e.g. name, dosage form and strength (if applicable);

d) Quantity of the products, i.e. number of containers and quantity per container;

e) Clearly identifying products requiring specialised handling;

f) A unique number to allow identification of the delivery order.

18.10 Delivery documentation should contain enough information to enable traceability of the pharmaceutical product. Such records should facilitate the recall of a batch of a product if necessary. Each party involved in the supply chain has a responsibility to ensure traceability.

18.11 Thermolabile pharmaceutical products requiring controlled temperature storage should be transported by appropriate or specialized means.

19 Transportation and Products in Transit

The transportation process should not compromise the integrity and quality of pharmaceutical products.

19.1 Delivery of pharmaceutical products requiring controlled temperatures should be in accordance with the applicable storage and transport conditions.

19.2 Freight forwarders and courier companies are not licensed by the Medicines Control Council and therefore pharmaceutical products should not be stored in the local sorting or consolidation hubs for extended periods.

19.3 Delivery schedules should be established and routes planned, taking local needs and conditions into account. Such schedules and plans should be realistic and systematic. Security risks should be taken into account when planning the schedules and routes of the delivery. This should be covered in the service level agreement with the transport company being utilized.

19.4 Freight forwarders and courier companies should collect, sort and consolidate these products for onward distribution in accordance with the client's Service Level Agreement (SLA) as well as Good Wholesaling and Distribution Practices (GWDP). Any delays in the sorting and onward distribution should be reported to the client as soon as possible.

19 Transportation and Products in Transit - continued

19.5 The manufacturer should communicate all relevant conditions for storage and transportation to those responsible for the transportation of pharmaceutical products. Adherence to these requirements throughout transportation and at any intermediate storage stages is required.

19.6 Care should be taken to ensure that pharmaceutical products are delivered as soon as possible.

19.7 The required storage conditions for pharmaceutical products must be maintained within acceptable limits during transportation and should not be exposed to excessive environmental conditions.

19.8 Pharmaceutical products should be stored and transported in accordance with procedures such that:

a) The identity of the pharmaceutical product. is not lost;

b) The pharmaceutical products does not contaminate and is not contaminated by other pharmaceutical products;

c) Adequate precautions are taken against spillage, breakage, misappropriation and theft; and

d) Appropriate temperature and relative humidity conditions are maintained in the case of pharmaceutical products, e.g. using cold chain for thermolabile products.

19.9 Pharmaceutical products comprises of highly active and radioactive materials, other dangerous substances presenting special risks of abuse, fire or explosion e.g. flammable liquids, solids and pressurized gases should be transported in safe, dedicated and secure containers and vehicles.

19.10 Pharmaceutical products containing narcotics and other high risk items should be transported in safe and secure containers and vehicles.

19.11 Spillages should be cleaned as soon as possible to prevent possible contamination, cross-contamination and hazards. Written procedures should be in place for the handling of such occurrences. Spillages must be reported to the Responsible Pharmacist for immediate action.

19.12 Sufficient security should be provided to prevent theft and other misappropriation of pharmaceutical products. Steps should be taken to prevent unauthorized access to these products during transport.

19.13 Damage to containers and any other event or problem which occurs during transit must be recorded and reported to the Responsible Pharmacist.

19.14 Drivers of vehicles should identify themselves and present appropriate documentation to demonstrate that they are authorized to transport the load.

20 Repackaging and Relabeling

20.1 A wholesaler or distributer may not perform any activities relating to the repackaging and relabeling of pharmaceutical products.

20.2 All labels and containers should not be altered, tampered or changed. The legislation relating to labels and containers should be adhered to at all times.

21 Complaints

21.1 Complaints can be one of the following types:

a) General product complaints;

b) Technical or quality product complaints which relates to the product and its packaging;

c) Adverse Reaction or events;

d) Other distribution/logistic type complaints which are not product related and therefore not for the attention of the Responsible Pharmacist.

21.2 The Responsible Pharmacist is responsible to ensure that all product complaints are kept on file and are forwarded onto the applicant or Holder of the Certificate of Registration for attention and advise.

21.3 In the event of a complaint involving “adverse drug reactions”, it should be followed up without delay in accordance with the Medicine Control Council’s Guidelines on “Reporting Adverse Drug Reactions in South Africa”.

21.4 In addition it is to be noted that all drug adverse reactions must be reported to National Adverse Drug Event Monitoring Centre (NADEMC) in Cape Town.

21.5 In the event of a technical complaint, the manufacturer and/or primary importer of the product as well as the Medicines Control Council should be informed as soon as possible.

21.6 All complaints and other information concerning potentially defective and potentially counterfeit pharmaceutical products should be reviewed according to written procedures describing the action to be taken. The Responsible Pharmacist should advise the Applicant or Holder of the Certificate of Registration without delay.

21.7 If any counterfeit products are identified the Applicant, Medicines Control Council and the South African Police Service should be notified immediately and this must be handled in accordance with a written procedure (SOP).

21.8 If a defect relating to a pharmaceutical product is discovered or suspected, consideration should be given to whether other batches of the product should also be checked and should advise the applicant or holder of the certificate of registration as soon as possible.

21.9 Where necessary, appropriate follow-up action should be taken after investigation and evaluation of the complaint.

22 Recall or Withdrawal of Pharmaceutical products

22.1 The Responsible Pharmacist is responsible to handle a recall of pharmaceutical products and to assist the manufacturer/Applicant/Holder of Certificate of Registration of the said product with the product recall.

22.2 The Responsible Pharmacist is responsible to ensure that all batches of pharmaceutical products are batch traceable in the event of a recall or withdrawal of a specific product.

22.3 Product batch numbers must be recorded and kept on file and should be easily retrievable in the event of a recall.

22.4 There should be a system which includes a written procedure, to recall or withdraw promptly and effectively pharmaceutical products known or suspected to be defective, with a designated person(s) responsible for recalls.

22 Recall or Withdrawal of Pharmaceutical products - continued

22.5 The said procedures should be in compliance with the "Guidelines for Recall/ Withdrawal of Medicines" issued by the Medicines Control Council.

22.6 The Responsible Pharmacist should inform the Applicant or Holder of the Certificate of Registration as soon as possible of all information relating to the recall and must take responsibility for all actions required in a recall process relative to the area to which goods have been supplied.

22.7 The effectiveness of the arrangements for recalls or withdrawals should be evaluated at regular intervals by staging a "mock recall" (at least 1 per annum) to ensure the effectiveness thereof.

22.8 All pharmaceutical products that have been recalled or withdrawn should be stored in a secure, segregated area pending appropriate action.

22.9 Recalled or withdrawn pharmaceutical products should be segregated during transit and clearly labelled as "recalled products". Where segregation in transit is not possible, such goods must be securely packaged, clearly labelled, and be accompanied by appropriate documentation.

22.10 The storage conditions applicable to pharmaceutical products which are subject to a recall or a withdrawal should be maintained during storage and transit until such time as a decision has been made regarding the fate of the product(s) in question.

22.11 All records should be readily available to the designated person(s) responsible for recalls or withdrawals. These records should contain sufficient information on the pharmaceutical products supplied to customers. Reconciliation after the recall must be done as per the Medicines Control Council's Guidelines in the designated timeframe and this must be communicated to the applicant or holder of the certificate of registration as soon as possible for referral to the Council.

22.12 The progress of a recall or withdrawal process should be recorded and a final report issued, which includes reconciliation between delivered and recovered quantities of pharmaceutical products.

23 Returned and Rejected Products

23.1 The Responsible Pharmacist is responsible to ensure that goods returned/ due to be rejected are handled in a procedurally correct manner, reasons for returns determined and any further actions followed through and recorded.

23.2 All returned and rejected products must be clearly labelled, sealed and stored separately in a secure manner in a clearly marked designated area.

23.3 The Responsible Pharmacist is responsible for the final decision, after evaluation, to return the goods to stock or destroy any rejected goods.

23.4 Written procedures describing the handling of returned pharmaceutical products and the corresponding records of all returns should be kept.

23.5 When receiving rejected or returned goods the delivery vehicle should be inspected for the following:

a) That the products were protected from light and rain, i.e. the delivery truck has a closed canopy;

b) The delivery truck does not have evidence of spillage inside;

c) The delivery truck is lockable to secure the products delivered;

d) The products are not mixed with other materials that will compromise the integrity of the products delivered; and

e) The products have not been exposed to anything that can cause contamination to the products.

23 Returned and Rejected Products - continued

23.6 Any Schedule 0 to Schedule 6 pharmaceutical products that are returned from a customer in the retail sector; should be logged with the wholesaler or distributor within the shortest possible time after the stock has been delivered to the customer.

23.7 Goods which have left the care of the wholesaler or distributor should only be returned to saleable stock if:

a) Proof of purchase is supplied, they are in their original unopened containers, the original label is intact, there is no sign of spoilage or contamination, it is evident that they have not been subjected to adverse conditions and that the shelf life is still intact; and

b) They have been examined and assessed by a person authorised to do so. Such assessment should take into account the nature of the goods, and any special storage conditions they may require. If necessary, advice should be sought from the person responsible for the quality of the pharmaceutical product.

23.8 In the event of cold-chain items that are returned, a "No Returns" policy may be in place unless under exceptional circumstances:

a) Under these circumstances the Responsible Pharmacist must take full responsibility for the action taken;

b) If a product return is logged for a cold-chain item, the Responsible Pharmacist may perform a "Product Quality Evaluation" in order to assess if the cold chain has been maintained or whether it was compromised;

c) For the "Product Quality Evaluation", the Responsible Pharmacist must request a copy of the customer's "Fridge Log" as well as a letter from the customer's Responsible Pharmacist stating that the pharmaceutical products were handled and stored in the required manner whilst in their custody; and

d) The cold-chain products must be returned in an appropriate lagged container, packed with the required consumables, and delivered back to the wholesaler or distributor within twenty four hours after the stock has been delivered to the customer.

23.9 All returned pharmaceutical products should be kept apart from saleable stock to prevent redistribution until a decision has been reached regarding their disposal.

23.10 Returned pharmaceutical products from a recall should be handled in accordance with a written procedure, detailing the action to be taken in recalling the said products on behalf of the manufacturer or primary importer. The procedure should be consistent with the "Guidelines for Recall/ Withdrawal of Medicines" as issued by the Medicines Control Council.

23.11 These products must be separated, sealed and clearly labelled and placed in a designated locked area to which there is no free access.

23.12 The reconditioning or re-packaging/ relabeling of returned pharmaceutical products must not be carried out by the wholesalers or distributors. Such activity is not specifically exempted from the requirements to hold a manufacturers licence.

23.13 The storage conditions applicable to pharmaceutical products which is rejected or returned should be maintained during storage and transit until such time as a decision has been made regarding the product in question.

23 Returned and Rejected Products - continued

23.14 Written procedures should be available for the handling of rejected goods. Rejected pharmaceutical products should be identified and controlled under a quarantine system designed to prevent their use until a final decision is taken on their fate.

23.15 The status of rejected goods should be changed from "Quarantined" to "Reject". Goods should be moved to the "Reject Area" that is a clearly labelled and segregated area. A list of rejected goods should be kept.

23.16 Provision should also be made for the appropriate and safe transport of rejected and waste materials prior to their disposal.

24 Disposal of products

24.1 A written procedure on disposal of (expired, defective or rejected) pharmaceutical products must be available, and must be in accordance with guidelines issued by the Medicines Control Council.

24.2 No pharmaceutical products may be disposed of into municipal sewerage systems.

24.3 The destruction or disposal of pharmaceutical products containing scheduled substances must be conducted in such a manner as determined by the Medicines Control Council to ensure that they are not retrievable.

24.4 Records of all returned, rejected and/or destroyed pharmaceutical products must be kept. Destruction certificates issued by the contracted certified waste processing company must be kept on file.

24.5 The Responsible Pharmacist is responsible to ensure that the destruction of all Schedule 5 and Schedule 6 medicines are conducted according to the Medicines Control Council's "Guidelines for the destruction of Schedule 5 medicines and substances" and "Guidelines for the destruction of Schedule 6 medicines and substances".

24.6 In terms of Regulation 27 of the Medicines Act, pharmaceutical products may be destroyed as follows:

a) A pharmaceutical product containing a Schedule 5, 6, 7 or 8 substance may only be destroyed in the presence of an inspector, an officer of the South African Police Service or any other person authorised by the Director-General: Department of Health. Such inspector, person or officer, as the case may be, shall issue a certificate confirming the destruction of the medicine and in the case of an officer; the case number must be entered in the register;

b) Notwithstanding paragraph (a), the Council may authorise the destruction of a pharmaceutical product that contains Schedules 5 or 6 substances by a manufacturer of such substances in the absence of an inspector; and

c) In the case of a pharmaceutical product that contains a Schedule 1, 2, 3 and 4 substances, a pharmacist or an authorised person in charge of the area in which the products are kept may destroy the products. The pharmacist or authorised person must certify the destruction.

24.7 The Responsible Pharmacist will ensure that the appropriate waste disposal method and location is selected in accordance with the provisions of the Nuclear Energy Act, 1982 (Act 92 of 1982), the National Environmental Management Act, 1998 (Act 107 of 1998), the Waste Act, 2008 (Act 59 of 2008) and the Air Quality Act, 2004 (Act 39 of 2004); and other legislation in terms of local municipal Regulations.

24.8 In addition, the Responsible Pharmacist or appointed designate, should accompany the goods to the disposal site, witness the disposal and obtain a "Destruction Certificate".

25 Counterfeit Pharmaceutical products

25.1 There must be a written procedure detailing the action to be taken in handling of counterfeit pharmaceutical products.

25.2 Any counterfeit or suspected pharmaceutical product found in the pharmaceutical supply chain should be segregated, sealed and clearly labelled quarantined goods.

25.3 Suspected cases of counterfeit pharmaceutical products should be clearly documented and the Medicines Control Council and South African Police Force must be informed without delay.

25.4 The Responsible Pharmacist must do a preliminary investigation and record as much relevant information as possible e.g. the driver's names and ID, the vehicle registration and any other information deemed to be relevant to the investigation.

25.5 These products should be clearly labelled to prevent further distribution or sale.

25.6 Upon confirmation of the product being counterfeit, a formal decision should be taken on its disposal and the decision recorded.

26 Export

In accordance with the licensing conditions as stipulated under Section 22C (1) (b) of the Medicines Act, the said wholesaler or distributer may not perform any activities relating to the export of pharmaceutical products, unless the wholesaler is doing this on behalf of the manufacturer and is appointed in writing to do so by the Holder of the Certificate of Registration. Only the Holder of the Certificate of Registration may export medicines.

27 Importation

27.1 The only body permitted to import pharmaceutical products is the Holder of the Certificate of Registration (including products imported through Section 15C of the Medicines Act).

27.2 Importation may only take place through the approved ports of entry (Regulation 12 of the Medicines Act):

a) Cape Town Airport or harbour;

b) Port Elizabeth Airport or harbour;

c) Durban Airport (King Shaka) or harbour; and

d) Johannesburg International Airport (OR Tambo)

28 Contact details

The Registrar of Medicines
Private Bag X828
PRETORIA
0001

Tel: +27 (0)12 395 8003

29 References

29.1 The Medicines and Related Substances Act, 1965 (Act 101 of 1965) and its Regulations;

29.2 The Pharmacy Act, 1974 (Act 53 of 1974) and its Regulations;

29.3 The Occupational Health and Safety Act, 1993 (Act 85 of 1993) as amended by the Occupational Health and Safety Amendment Act, 1993 (Act 181 of 1993);

29.4 The Nuclear Energy Act, 1982 (Act 92 0f 1982);

29.5 The National Environmental Management Act, 1998 (Act 107 of 1998);

29.6 The Waste Act, 2008 (Act 59 of 2008);

29.7 The Air Quality Act, 2004 (Act 39 of 2004);

29.8 Guide to Good Manufacturing Practice for Medicines in South Africa, Version 3;

29.9 WHO Guide to Good Storage Practices for Pharmaceuticals. (WHO Technical Report Series No. 908, Annex 9);

29.10 Guidelines for the destruction of Schedule 5 medicines and substances, May 2003;

29.11 Guidelines for the destruction of Schedule 6 medicines and substances, May 2003;

29.12 Guidelines for Recall/ Withdrawal of Medicines, 31 March 2009;

29.13 Guidelines for Lodging a Complaint on a Medicine, September 2006;

29.14 Guidelines for Medicine Donations to South Africa, May 2003;

29.15 Guidelines for Preparation of Site Master File, June 2003;

29.16 Guidelines on Reporting Adverse Drug Reactions May 2003;

29.17 Supplementary Guidelines on Good Manufacturing Practices (GMP): Validation;

29.18 Quality Management System (QMS) for Active Pharmaceutical Ingredient (API) Manufacturers Integrating GMP (ICH Q7a into ISO (9001: 2000), September 2005;

29.19 CH Harmonized Tripartite Guideline: Quality Risk Management Q9, November 2005;

29.20 APICS Dictionary, 12th Edition; and

29.21 Quality Assurance of Pharmaceuticals, Volume 2, Second Updated Edition, World Health Organization, 2007.