



Guidelines

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Review of Quality Assurance (QA)  
Mechanisms for Medicines and Medical  
Supplies in Humanitarian Aid

EUROPEAN COMMISSION



Humanitarian Aid

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Humanitarian Aid

**GFE**

**CONSULTING WORLDWIDE**

Gesellschaft für Forschung und Entwicklungsprojektorierung GmbH

Grüner Weg 13, D-52070 Aachen, Germany

Tel.: 0049-(0)241-918300 Fax: 0049-(0)241-9183050

E-mail: INFO@gfe.de Internet: <http://www.gfe.de>

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## Review of Quality Assurance (QA) Mechanisms for Medicines and Medical Supplies in Humanitarian Aid

### Guidelines

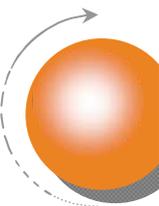
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Authors: Mrs. Véronique POMATTO (Team Leader)  
Dr. Claudio SCHUFTAN, MD (Medical Expert)

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Véronique POMATTO

Dr. Claudio SCHUFTAN, MD

## LIST OF ACRONYMS

ADR	Adverse Drug Reaction
API	Active Pharmaceutical Ingredient
ASRAMES	Association Régionale d'Approvisionnement en Médicaments Essentiels
BIOSOL	Biomédical - Solaire
EC	European Commission
CHMP	Centrale Humanitaire Médico-Pharmaceutique
CIF	Conseil Information et Formation
CRF	Case Report Forms
DRA	Drug Regulatory Authority
DG ECHO	European Commission's Directorate-General for Humanitarian Aid
EMA	European Medicines Agency
EML	Essential Medicines List
EOI	Expression of Interest
GCP	Good Clinical Practices
GFATM	Global Fund for Aids, Tuberculosis and malaria
GHTF	Global Harmonization Task Force
GTDP	Good Trade and Distributing Practices
GMP	Good manufacturing Practices
GSP	Good Storage Practices
HPC	Humanitarian Procurement Centre
ICH	International Conference on Harmonization
IDA	International Dispensary Association



INN	International Non-proprietary Name
ISO	International Organisation for Standardisation
NGO	Non-governmental Organisation
MOH	Ministry of Health
MOH-GOSS	Ministry of Health – Government of South Sudan
MoU	Memorandum of Understanding
MQAS	Model Quality Assurance System for Procurement Agencies
PHO	Provincial Health Office
PIC-S	Pharmaceutical Inspection Co-operation Scheme
PSFCI	Pharmaciens sans Frontières - Comité International
QA	Quality Assurance
SOP	Standard Operating Procedures
UMC	Uppsala Monitoring Centre
UNICEF	United Nations Children’s Fund
WHO	World Health Organization



## EXECUTIVE SUMMARY

1. As a part of DG ECHO's commitment to capacity building in the humanitarian sector, this review has been undertaken to promote the issue of quality assurance (QA) of medicines and medical supplies. This review is in particular intended to assist its Partner NGOs at HQ and in the field. In the financing of humanitarian operations DG ECHO is obliged to respect, and thus also its partners, the international rules on procurement that have been established under the General Agreement on Tariffs and Trade (GATT). International rules and standards for QA of medicines exist and the most important of them are listed in these Guidelines.

2. Under Annex V of DG ECHO's Framework Partnership Agreement, see section 4.4.1, specific requirements are set out relating to the procurement of pharmaceutical products and medical devices:

- a) *“Humanitarian Organisations shall abide by international norms for the procurement of pharmaceutical products and respect patents and national drug regulations in the individual countries.*
- b) *The purchase of medicines shall be based on the pre-qualification of pharmaceutical manufacturers who comply with the World Health Organisation Good Manufacturing Practice Guidelines.*
- c) *The award criteria shall give priority to suppliers of medical devices that comply with ISO certification 9001/EN46001 or ISO 9002/EN46002. In respect to Medical equipment, the award criteria shall give priority to suppliers that comply with essential requirements described in the Council Directive 93/42/EEC of 14 June 1993, concerning medical devices.*

*This enumeration of international standards is neither exhaustive, nor definitive. Humanitarian Organisations shall take as a reference any internationally recognised standard that may be set and the updates and revisions of the standards mentioned hereof.”*

3. In recognition of the fact that more guidance may be needed, DG ECHO undertook this technical review. DG ECHO's partners should regard this review as a point of reference to be consulted.

4. Minimum professional requirements for QA require that, a comprehensive QA Manual exists at the partner level and, also that Standard Operating Procedures (SOPs) are in force. Both of these tools should be regularly updated. The SOPs should cover each step of the drug management cycle; the responsible staff members should use these tools as a part of the control environment.

5. Definition of the four steps of the Drug Management Cycle:

- Selection: The selection of pharmaceutical products involves reviewing the prevalent



health problems, identifying treatments of choice, choosing individually needed medicines and dosage forms, quantifying the medicine requirements and deciding which medicines will be made available at each level of the health care system;

- **Procurement:** The procurement of these products includes, selecting procurement methods, managing tenders, establishing contractual terms with providers, assuring drug quality, obtaining the best possible price/quality ratios, and ensuring adherence to contractual terms;
- **Distribution:** The distribution includes clearing customs, the control of stocks, store management, and delivery to drug depots and health facilities; and
- **Rational Use:** The rational use includes diagnosing, prescribing, dispensing, and proper consumption of medicines by the patient. For the purpose of this document, the 'Waste Disposal of pharmaceutical products' is also included in this step.

6. The tables on the next pages summarises the main steps partners are expected to undertake in emergency situations in each of the steps of the cycle. Activities and results indicators are proposed to allow each partner to evaluate and monitor their own QA procedures.

7. It must be stressed that the tables, even more than the Guidelines as a whole, are a living document; they reflect the current situation and may change in the future. Hence, the recommended approaches will need to be updated as time goes by.

Recommendations	Activity Indicators	Result Indicators
<b>Acute Emergency</b>		
<p>Use kits or standard lists for 10,000 persons during 3 months, when no needs assessment can be made.</p> <p><u>Exceptions:</u></p> <p>A partner's team is in the field before the emergency and is able to send a specific list.</p>	<ul style="list-style-type: none"> <li>Standardised kits lists are available at partners' headquarters.</li> <li>Kits are available in stock for the partner to use.</li> </ul>	<ul style="list-style-type: none"> <li>No stock shortages occur.</li> <li>No excess stock exists.</li> <li>Most of the encountered pathologies can be treated.</li> </ul>
<b>Post-acute and Chronic Emergency</b>		
The quantity of needed medicines should be assessed by the patient morbidity standard treatment method or the adjusted consumption method.	<ul style="list-style-type: none"> <li>An assessment of the needed quantity is done by one of the recommended methods.</li> </ul>	<ul style="list-style-type: none"> <li>No stock shortages occur.</li> <li>No excess stock results.</li> <li>All the pathologies can be treated.</li> </ul>
The medicines procured should be compliant with the National Essential Medicines Lists or the WHO Essential Medicines Lists.	<ul style="list-style-type: none"> <li>The National Essential Medicines List is available at the decision-making point.</li> </ul>	<ul style="list-style-type: none"> <li>None of the pharmaceutical products received in the country are different from the National Essential Medicines List.</li> </ul>
Packaging for dangerous materials is foreseen and ordered in compliance with IATA or other pertinent regulations.	<ul style="list-style-type: none"> <li>Class of dangerous materials is identified.</li> <li>Weight and/or volume of each type is identified. Compliance with the foreseen transport regulations is checked.</li> </ul>	<ul style="list-style-type: none"> <li>The final destination is reached safely for all of the dangerous materials.</li> </ul>
The requirements for a cold chain are assessed from the selection phase of the products.	<ul style="list-style-type: none"> <li>The volumes of the goods to be stored at controlled temperature(s) are identified.</li> <li>The time for these items to be stored cold is calculated.</li> <li>The needed variety and quantity of temperature control materials is defined.</li> </ul>	<ul style="list-style-type: none"> <li>The cold chain package is compliant with the WHO standards.<sup>1</sup></li> <li>The cold chain is maintained until the final destination of the respective pharmaceutical products.</li> <li>The efficacy of the cold chain is monitored and temperatures registered until the final destination.</li> </ul>

**SELECTION**



<sup>1</sup> Product Information Sheets, 2000 edition. Equipment for: Expanded Programme on Immunization (EPI), Acute Respiratory Infections (ARI), Blood Safety (BLS), Emergency Campaigns (EC), Primary Health Care (PHC). WHO/V&B/00.13

Recommendations	Activity Indicators	Result Indicators
<p>To pre-qualify the suppliers (international or regional manufacturer, wholesaler, distributor) in compliance with the MQAS document.</p> <p><u>Exceptions:</u></p> <p>If DG ECHO partners buy from HPCs, the pre-qualification of each product/supplier pair has to be carried out by the HPC and is therefore the responsibility of the HPC.</p>	<ul style="list-style-type: none"> <li>• A specific SOP to pre-qualify a product/supplier pair is available.</li> <li>• Eols are sent for each pharmaceutical product to be procured, every year.</li> <li>• Controls of pharmaceutical QA are performed on the specific site of the product manufacture on a regular basis.</li> </ul>	<ul style="list-style-type: none"> <li>• The procedure is known by the person in charge of the procurement of medicines.</li> <li>• A list of pre-qualified suppliers per product exists, is used and is maintained.</li> </ul>
<p>The WHO pre-qualified list of pharmaceutical products/manufacturers should be used for the medicines being procured</p>	<ul style="list-style-type: none"> <li>• Compliance with lists of pre-qualified medicines is a routine on the part of ECHO partners in any tendering that they do.</li> </ul>	<ul style="list-style-type: none"> <li>• WHO pre-qualified pharmaceutical products (or local equivalent) are being procured and used for HIV (including diagnostic tests), TB, and malaria.</li> </ul>
<p>Re-qualification and monitoring of suppliers are regularly performed.</p>	<ul style="list-style-type: none"> <li>• Re-evaluation of product information is carried out every three years.</li> <li>• Re-inspection of manufacturers takes place at least once every year.</li> <li>• Random samples of batches are sent to QC laboratories.</li> </ul>	<ul style="list-style-type: none"> <li>• Updated reports on all of these actions are available.</li> </ul>
<p>Restricted tenders are called by direct invitation of all pre-qualified suppliers.</p> <p><u>Exceptions:</u></p> <p>When procuring from an HPC, the procurement can be done through a single-bid procedure.</p>	<ul style="list-style-type: none"> <li>• Restricted tenders consider at least three pre-qualified suppliers.</li> <li>• <u>Exception:</u></li> <li>• If less than three suppliers respond to the yearly Eol for a specific medicine. (DG ECHO must be notified)</li> </ul>	<ul style="list-style-type: none"> <li>• The best quality/price ratio is chosen and final price is within the 'international indicator price' range.</li> </ul>
<p>A contractual agreement or MoU could be signed between the supplier (manufacturer, wholesaler, distributor or HPC) and the partner.</p>	<ul style="list-style-type: none"> <li>• A model contractual agreement or MoU is established between HPCs and each partner., this is on a voluntary basis.</li> </ul>	<ul style="list-style-type: none"> <li>• Signed MoU or contractual agreement established.</li> </ul>

**PROCUREMENT**



Recommendations	Activity Indicators	Result Indicators
Warehouses to be managed at least in compliance with WHO guidelines (or equivalent) and premises to respect its basic prescriptions.	<ul style="list-style-type: none"> <li>The field warehouse staffs are properly trained.</li> </ul>	<ul style="list-style-type: none"> <li>Good Distributing Practices and Good Storage Practices are respected.</li> </ul>
Pharmaceutically competent staff is designated in the partner team.	<ul style="list-style-type: none"> <li>A job description exists including what to do in each phase of the distribution cycle.</li> </ul>	<ul style="list-style-type: none"> <li>Designated staff members are in charge of the distribution of the pharmaceutical products, as well as the management of waste from it (see next chapter).</li> </ul>
Each batch number is tracked from the receipt to the final point of delivery of each product.	<ul style="list-style-type: none"> <li>Records are regularly updated.</li> </ul>	<ul style="list-style-type: none"> <li>The health facility to whom each batch number was sent can be identified from records in less than 1 day</li> </ul>
An independent quality control laboratory should be identified either in the country or in a third country.	<ul style="list-style-type: none"> <li>Medicines are sent for analysis when and as needed.</li> </ul>	<ul style="list-style-type: none"> <li>While tests are ongoing, products are kept in quarantine and released when the analysis is favourable.</li> </ul>
For economies of scale, the transport to health facilities (especially if by air) should be coordinated with other partners so as to maximise bulk and minimise cost.	<ul style="list-style-type: none"> <li>Internet connections and/or phone contacts exist and are used by the different partners' logisticians.</li> </ul>	<ul style="list-style-type: none"> <li>Pharmaceutical products do not have to wait more than two days at the airport before being sent on.</li> </ul>
The cold chain is strictly respected and monitored all along the transport for temperature-sensitive products.	<ul style="list-style-type: none"> <li>An independent energy supply is available.</li> <li>Fridges or cold rooms are available in the warehouse.</li> <li>Temperature of this equipment is monitored.</li> <li>Cold boxes and freeze packs are used for transportation in accordance with WHO standards</li> </ul>	<ul style="list-style-type: none"> <li>The cold chain is not interrupted during the storage and transport.</li> </ul>
Packaging of dangerous materials should be compliant with the relevant international standards or standards as required by transporters.	<ul style="list-style-type: none"> <li>Dangerous materials are properly identified and labelled.</li> <li>Specific packaging is ordered in the field or comes from the supplier for all the products that need it.</li> </ul>	<ul style="list-style-type: none"> <li>All dangerous pharmaceutical materials reach their destination safely and on time.</li> </ul>

**DISTRIBUTION**



Humanitarian Aid

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Recommendations	Activity Indicators	Result Indicators	<b>RATIONAL USE</b>
Partners are encouraged to take some Quality Control measures in their clinical settings, i.e. regular medicines stock verification and performance monitoring as it relates to good prescription practices, rational use of drugs and good dispensing practices.	<ul style="list-style-type: none"> <li>• Controls of rational use, the good prescription and dispensing practices are performed and reports are discussed with the team.</li> <li>• Corrective measures are implemented and results indicators are identified and used.</li> </ul>	<ul style="list-style-type: none"> <li>• Identified result indicators show improvement.</li> <li>• Corrective measures are less and less numerous.</li> </ul>	
DG ECHO partners are strongly advised to report detected adverse effects of medicines, prescribed by their own or associated staff, to national authorities and to the WHO Collaborating Centre for International Drug Monitoring (the Uppsala Monitoring Centre).	<ul style="list-style-type: none"> <li>• If national forms do not exist, adverse effect report forms are introduced at the health facilities level.</li> <li>• Advocacy to national health authorities is undertaken with the aim of strengthening this crucial step regarding the safety of medicines.</li> </ul>	<ul style="list-style-type: none"> <li>• Reports are filled and collected by the humanitarian organisation.</li> <li>• Reports are sent to the national authority, if any.</li> <li>• Reports are sent to the relevant WHO department.</li> </ul>	
Partners should follow the WHO Adverse Reactions Terminology.	<ul style="list-style-type: none"> <li>• The reference document is available at the field level.</li> <li>• The terminology is included in the training of health workers,</li> </ul>	<ul style="list-style-type: none"> <li>• The right terminology is used and known by the local partner.</li> </ul>	
Donations should be checked for compliance with the WHO's Guidelines before being accepted by partners and sent to beneficiary countries	<ul style="list-style-type: none"> <li>• The DG ECHO's partner is provided with the list of the medical donations before taking receipt of them.</li> <li>• The nature and the quantity of each pharmaceutical product are checked for compliance with the needs and the rational use within the beneficiary country by the partner who is sending it.</li> </ul>	<ul style="list-style-type: none"> <li>• Donated medicines and medical supply arrive and are managed easily at destination.</li> <li>• No disposal following the donation is to be undertaken</li> </ul>	
Medical waste management appears in the project proposals sent for DG ECHO funding as an item line in the budget.	<ul style="list-style-type: none"> <li>• The waste management is included in the pharmaceutical staff's job description.</li> <li>• Staff members are trained on this issue.</li> <li>• Advocacy to national authority is carried out to include this task in the job description of local public sector staff.</li> </ul>	<ul style="list-style-type: none"> <li>• Sub-standard drugs are routinely handled (destroyed) in compliance with national and/or WHO standards at least once a year.</li> </ul>	
When the cost of transport of drugs for their disposal is likely to be significant, i.e. by air, this is to be foreseen in the budget presented to DG ECHO.	<ul style="list-style-type: none"> <li>• Return of sub-standard medicines is taken into account and funds and facilities made available.</li> </ul>	<ul style="list-style-type: none"> <li>• No sub-standard drugs are left by the partner in the field at the end of its project.</li> </ul>	

# 1. INTRODUCTION

## 1.1 WHY THE QA OF MEDICINES AND MEDICAL SUPPLIES IS A PRIORITY

8. "Quality assurance is a wide-ranging concept covering all matters that individually or collectively influence the quality of a product. It is the totality of the arrangements made with the object of ensuring that pharmaceutical products are of the quality required for their intended use."<sup>2</sup>

9. It is often considered that the procurement is the crucial point of QA of medicines. Of course, this step is very important, because the source of the raw materials (active ingredient, excipients - an inert substance used to give a pharmaceutical preparation a suitable form or consistency), as well as the way the final pharmaceutical product is manufactured determines the intrinsic quality of each medicine.

10. Nonetheless, the selection and QA of the medicines to be provided in a country affected by an emergency is of key importance because, if the medicine is not well known by the health professionals who will prescribe it, it will not achieve its intended use.



**Medicine Management Cycle**

11. Furthermore, each medicine is a chemical compound that has a time 'life' when out

<sup>2</sup> A model QA system for procurement agencies – draft 5 – WHO – Nov 2004.



of the factory. The climatic conditions it is subjected to during transport and/or storage thus influences the quality and the stability of this chemical compound.

12. At the end of its life, this compound is a potential toxic which has to be managed carefully with the aim of protecting the environment, as well as the health of the public.

13. The use of [multi-source](#) essential medicines has widely contributed to their accessibility to populations in developing countries, as well as in cases of emergencies. The challenge remains one of providing an acceptable level of health care at a reasonable cost for populations in the developing world, including the ever growing number of displaced communities. Although the manufacture and availability of [generic essential medicines](#) offers a practical way of achieving this aim, the quality of these products tends to be jeopardized by overriding considerations of cost.<sup>3</sup>

14. The Indian pharmaceutical industry is the first generic producer and the 4<sup>th</sup> largest producer in the world with 23,000 registered manufacturers. Among these, a wide range of QA systems can be found in use - from 'garage' operations to very well established industries.

15. Sub-standards drugs can have different causes:

- Storage and climatic conditions damage drugs (instability);
- Raw materials for drugs are of poor quality or counterfeited;
- Manufacturers do not respect minimum acceptable pharmaceutical requirements. (An extreme case is when the drug does not correspond to the drug mentioned on the label, or when the drug does not contain an active ingredient.);
- The marketing of fake, counterfeit drugs by taking advantage of the original drug's reputation (In some cases, everything is done to mislead the user who believes s/he is buying the original medicine/drug. See more details on this increasing problem in the Concept Paper); and
- Drugs are expired.



Broken tablets were blister-packed with intact tablets. In the case of a well controlled production line, the broken tablets should have been eliminated. This is an example of sub-standard quality.

The consequence of this sub-standard quality manufacture is that some tablets do not have the right quantity of active ingredient.



These tablets, sophisticatedly packed, should be synonymous for security. However, analysis of these capsules revealed a complete lack of the antibiotic mentioned on the label, and the presence of an unidentified white powder.

This type of counterfeit is dangerous as it does not cure, and the risk of infection can increase. This kind of product is even more dangerous if it contains toxic substances which can lead to tragic consequences for the patients.

Furthermore, counterfeiting leads to consequences on the image of the pharmaceutical industry, which is fraudulently copied.

### Examples of sub-standard drugs

<sup>3</sup>

“Generic drugs: the hidden issues of quality and cost”, WHO Drug Information, Volume 14, N<sup>o</sup>. 2, 2000.



## 1.2 MAIN OBJECTIVE OF THESE GUIDELINES

16. These guidelines are intended to: increase capacity on the part of humanitarian Partner NGOs of DG ECHO; and to better inform partners as to what their responsibilities and liabilities are, with respect to the QA of medicines and medical supplies.

17. These guidelines propose recommendations to DG ECHO's Partner NGOs as to how to manage each of the four steps of the medicine management cycle during emergency situations, and thus, to assist them to operate in accordance with international standards.

18. Here below is a non-exhaustive list of standards in the area of the QA of medicines:

- The International Conference on Harmonisation (ICH) provides standards for Japan, the US and the European Union;
- The Pharmaceutical Inspection Co-operation Scheme (PIC/S);<sup>4</sup>
- The European Medicines Agency (EMA) provides standards for EU countries;
- The World Health Organization (WHO) provides standards for all member states.

19. Furthermore, [national standards](#), national pharmaceutical legislation and pharmaceutical regulations in each country are essential for the QA of locally manufactured, imported, exported or distributed medicines, and should always be followed, where existing.

20. For the purpose of these DG ECHO guidelines, the WHO standards are chosen as the benchmark in humanitarian situations worldwide, other guidelines e.g. certain national guidelines may also be appropriate, when the medicines are purchased locally, for example.

## 1.3 DEFINITION OF THE EMERGENCY PHASES USED

21. The categorisation of interventions along these lines largely coincides with the duration of DG ECHO funding decisions, illustrated by the following:

- Acute emergency: 0 to 3 months after the onset of the crisis, which corresponds to the duration of a primary emergency funding decision: 3 months;
- Post-acute emergency: 1 to 9 months after the onset of the crisis, in line with the duration of an emergency funding decision from DG ECHO which is 6 months; and
- Chronic emergency: from 6 months onwards, in line with an ad-hoc decision for 12 months and a Global Plan of up to 18 months duration.<sup>5</sup>

<sup>4</sup> Participating regulatory authorities are those from Australia, Austria, Belgium, Canada, Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Lichtenstein, Malaysia, the Netherlands, Norway, Portugal, Rumania, the Slovak Republic, Spain, Sweden, Switzerland, the United Kingdom, and the United States.

<sup>5</sup> A review of water and sanitation issues relating to the funding of humanitarian operations under the EC humanitarian regulation – Model Guidelines for mainstreaming Water and Sanitation in emergencies, protracted crisis, LRRD and Disaster Preparedness operations – 2005 – [http://europe.eu.int/comm/DGECHO/evaluation/thematic\\_en.htm#qualitymanag](http://europe.eu.int/comm/DGECHO/evaluation/thematic_en.htm#qualitymanag)



## **2. THE NEED: WHY DG ECHO IS CONCERNED ABOUT THE QA OF MEDICINES AND MEDICAL SUPPLIES IN DG ECHO-FUNDED ACTIVITIES**

22. DG ECHO funds partners in the health sector to implement humanitarian actions in emergency areas. Those actions include selection, procurement, delivery and dispensing of medicines in the beneficiary countries. DG ECHO's partners are thus involved in the medicine management cycle, possibly not always having the necessary technical expertise in the pharmaceutical area.

23. There are numerous reports (see foot notes) of an unacceptable prevalence of substandard, including counterfeit pharmaceutical products, in international trade. Developing countries are the ones most frequently exposed to such products which may be inefficacious and/or toxic products, and which threaten to erode confidence in the health care system.<sup>6</sup>

24. Recently, the international press has reported upon the use of poor quality or fake drugs resulting in serious and sometimes fatal consequences; such news is an indication that this major problem is gaining recognition worldwide.

### **2.1 CONSEQUENCES OF USING POOR QUALITY DRUGS**

25. The use of poor quality drugs bears serious health consequences such as treatment failure, adverse reactions, drug resistance, increased morbidity and mortality. It can erode public confidence in a country's health programme and waste scarce resources. Counterfeit drugs can damage public trust, resulting in reduced investment in the pharmaceutical industry.<sup>7</sup>

### **2.2 DG ECHO QA OF MEDICINES AND MEDICAL SUPPLIES REQUIREMENTS IN ACUTE, POST-ACUTE AND CHRONIC PHASES OF HUMANITARIAN EMERGENCIES**

26. DG ECHO is cognisant of the difficult circumstances under which Partner NGOs are frequently working in at field level. DG ECHO does not allow less strict QA procurement procedures in cases of dire emergency when Humanitarian Procurement Centres (HPCs) or other pre-qualified suppliers may take too long to deliver or may not be able to reach the disaster areas. An alternative solution to this dilemma is the pre-positioning of stocks of medicines and medical supplies for use in such emergencies, be it in bulk or in the form of pre-packed kits. Partners may have to pre-finance these supplies themselves and seek to have such investments on their part taken into account for reimbursement under DG ECHO's financing decisions and operation contracts, where they are subsequently used in DG ECHO financed projects.

27. DG ECHO expects that its partners use the lessons learned from their previous QA experiences to select, even in acute, post-acute, and/or chronic emergencies, their providers and products judiciously. For example, in the post-acute phase, partners are expected to get back to their regular procurement channels with established and proven QA standards.

<sup>6</sup> [http://www.fip.org/pdf/GPP97\\_en.PDF](http://www.fip.org/pdf/GPP97_en.PDF)

<sup>7</sup> A review of drug quality in Asia with a focus on anti-infectives – Feb 2004 – USP.



### 3. WHAT ARE PARTNER NGOS EXPECTED TO DO ?

#### 3.1 RAPID ASSESSMENT OF THEIR QA OF MEDICINES AND MEDICAL SUPPLIES SITUATION - IDENTIFICATION OF GAPS

28. With the aim of assessing the actual QA practices as applied by DG ECHO's partners, a link to an online questionnaire was sent to the 60 partners who used 20% or more of their DG ECHO budget on medical interventions on a certain time period. Responses were collected from February 15<sup>th</sup> to March 1<sup>st</sup>, 2006.

29. 38% of the partners approached responded to the on-line survey. Given the responses, there is room for improvement as the partners themselves identified major gaps they see in QA; these gaps are now addressed and to a degree can be covered by using these Guidelines.

30. The questionnaire used is attached in Annex I of the accompanying Concept Paper and the key-findings are highlighted in each of the respective chapters below.

#### 3.2 NORMATIVE ASPECTS IN THE APPLICATION OF WHO QA MINIMUM STANDARDS IN ALL STAGES OF THE MANAGEMENT CYCLE OF MEDICINES AND MEDICAL SUPPLIES

##### 3.2.1 SELECTION

**Selection involves reviewing the prevalent health problems, identifying treatments of choice, choosing the individually needed medicines and dosage forms, quantifying the medicine requirements and deciding which medicines will be made available at each level of the health care system.**

31. Most of the partners use the WHO or the [National Essential Medicines Lists](#) (EML), but only 52% of them actually assess the needs and 70% use emergency kits.

##### 3.2.1.1 DEFINING THE REQUIRED QUANTITY

32. According to the nature of the available data to quantify the needs for pharmaceutical products, the WHO distinguishes 2 methods for quantitative estimation<sup>8</sup>:

<sup>8</sup>

Estimating Drug Requirements - A Practical Manual (WHO/DAP; 1995; 158 pages) [http://www.who.int/medicinedocs/library.fcgi?e=d-0edmweb--00-1-0--010---4---0--0-10l--1en-5000---50-about-0---Estimating Drug Requirements - A Practical Manual \(WHO/DAP; 1995; 158 pages\) 01131-0011N%40%2F2%5BmSa9ee80c740000000043e740be-OutfZz-8-0-0&a=d&c=edmweb&cl=CL1.1.3&d=Jh2931e](http://www.who.int/medicinedocs/library.fcgi?e=d-0edmweb--00-1-0--010---4---0--0-10l--1en-5000---50-about-0---Estimating+Drug+Requirements+-+A+Practical+Manual+(WHO/DAP;+1995;+158+pages)+01131-0011N%40%2F2%5BmSa9ee80c740000000043e740be-OutfZz-8-0-0&a=d&c=edmweb&cl=CL1.1.3&d=Jh2931e)



- The patient morbidity-standard treatment method, also called the morbidity method, starts from two sets of data;
    - The number of episodes of each health problem treated by the type or types of facilities for which drug requirements are to be estimated; and
    - Average standard treatment schedules agreed on for each health problem defined<sup>9</sup>.
  - The adjusted consumption method, also called the consumption method. This method starts from the existing consumption of the drugs concerned. For each type of health facility, a number of ‘standard or average’ facilities are identified, which have a reasonably representative workload, acceptable drug supply, and rational prescribing and consumption. The health facility’s drug consumption is reviewed, and for any drug whose consumption is considered inappropriate, the quantity is adjusted upwards or downwards to an appropriate level. The adjusted quantities of drugs used per “standard” facility are converted into standard quantities per 1,000 treatment episodes, and these are then used to estimate the drug quantities required for each facility of the type concerned, according to its expected number of treatment episodes, as in the previous method.
33. Both methods are time-consuming and call for the performance of a needs assessment in the country or region to determine the actual needed quantity.
34. During the acute emergency phase, it is sometimes impossible to calculate needs with these methods, thus it can be more effective to use either emergency kits for 10,000 persons/3 months or to follow standard lists (See Annex IV).
35. Thereafter, the needs will be assessed as soon as possible after the acute emergency and the list of the pharmaceutical products to be procured will be adapted to the properly assessed quantity.

#### **3.2.1.2 CHOICE OF THE MEDICINES TO BE USED AT EACH LEVEL OF THE HEALTH CARE SYSTEM**

36. In most countries, the selection is already made at the national pharmaceutical level and is based on the WHO EML.
37. The selection of pharmaceutical products should be based on the national formulary or on the National EML. The pharmaceutical product, its form and dosage should also be compliant with the recommended list for each level of the health care system.
38. If a National EML is not available, the selection should comply with the WHO EML.

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<sup>9</sup>

According to WHO: The quantity of drugs given as a standard treatment for each health problem, multiplied by the number of treatment episodes of that problem, gives the total quantity of drugs required for it.

### 3.2.1.3 LOGISTICAL REQUIREMENTS

39. At this same stage, when the medicines, their form, dosage and their quantities are being selected, the specific packaging required for the pharmaceutical products should be carefully listed, as well as the quantities to be ordered.

40. This concerns in particular the required packaging for ‘dangerous materials’ so that it complies with transport industry regulations and standards as well as the cold chain requirements; these should be assessed depending on the delivery point chosen, the transport means, and the time to reach the final destination.

### 3.2.2 PROCUREMENT

**Procurement includes selecting procurement methods, managing tenders, establishing contractual terms with providers, assuring drug quality, obtaining best prices, and ensuring adherence to contractual terms.**

41. It is important to note that while 87% of the surveyed partners who responded advised that they selected their medicine sources, only 22% of them said that the [pre-qualification](#) of the products they required was linked to the manufacturing site for that particular product.

42. 52% of the partners who responded have a logistician in the organisation in charge of the procurement of medicines, while only 26% of them have a pharmacist carrying out this function.

43. 74% of the partners who responded use HPCs for their procurement, IDA and UNICEF being the two first choices for them.

44. Different situations are found in the emergency field:

- International procurement;
- Local procurement;
- Procurement through HPCs; and
- Combinations of some of the above choices.

40. In the opinion of the consultants, when DG ECHO’s Partner NGOs procure medicines to be sent to the beneficiary country, they must be considered as acting as procurement agencies and should thus comply with the ‘WHO Model Quality Assurance System For Procurement Agencies’. This document can be found at: [Pre-qualification of Procurement Agencies](#). Person(s) in charge of the procurement of medicines and medical supplies should ensure that they are familiar with this internet site.

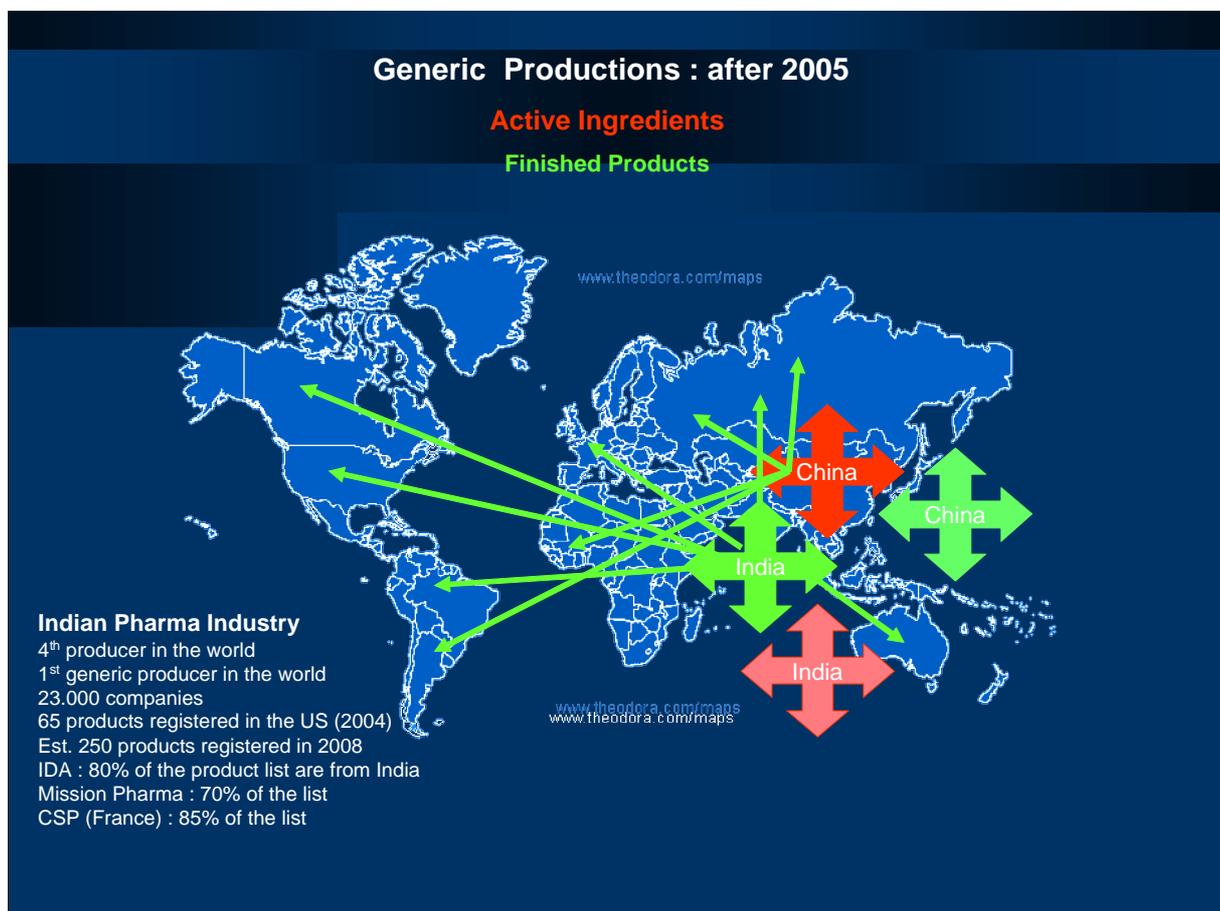
41. Pharmaceutical competences are essential in order to properly manage the procurement of medicines and medical supplies.

42. WHO standards are based on the pre-qualification of suppliers and are applicable to:
- Medicines;
  - Nutraceuticals;
  - Diagnostic kits; and
  - Medical devices.

### 3.2.2.1 LOGISTICAL REQUIREMENTS

43. Local procurement is to be encouraged as far as the quality of medicines can be assessed and is found to be acceptable. When humanitarian organisations procure from local manufacturers, the latter should be at least recognised by the national drug authorities.

44. At present, active ingredients and finished multi-source pharmaceutical products are mainly synthesised and/or manufactured in India and China.





45. Procurement in these markets is high risk, because regulations may possibly be weak or non-existent in the countries of origin (e.g. India, China and even Europe for products being exported), as well as in the countries of destination (developing countries).

46. While QA is the responsibility of the national drug regulatory authorities through existing registration processes, the agencies procuring medicines and medical supplies must ensure that quality products are supplied to their clients.

#### THE PRINCIPLES FOR 'PRE-QUALIFICATION'

47. Pre-qualification procedures should be based on the following principles:

- Reliance on the information supplied by the relevant National [Drug Regulatory Authority](#) (DRA);
- Evaluation of product data and information submitted by manufacturers, including product formulation, manufacturing and test data and their results;
- General understanding of the production and [quality control](#) activities of the manufacturers and suppliers and of their commitment to the principles of [Good Manufacturing Practices](#) (GMP);
- Assessment of consistency in the production processes and quality control activities through compliance with GMP, as described in the respective WHO publication<sup>10</sup> and supplementary WHO GMP guidelines;
- Availability of appropriate quality systems and Standard Operating Procedures (SOPs);
- Random sampling and testing of pharmaceutical products supplied;
- Adequate purchasing mechanisms (see WHO's MQAS);
- Good Storage Practices (GSP);
- Good Distribution Practices (GDP);
- Monitoring of customers' complaints and follow-up to remedy the shortcomings;
- Adequate handling of complaints and recalls; and
- Ongoing monitoring and re-qualification.

48. Several manufacturing sites can exist for the same pharmaceutical product. Since the GMP include standards of specific premises and equipment, the pre-qualification of products should be linked to the manufacturing site that was pre-qualified for that particular product.

<sup>10</sup>

*"Quality assurance of pharmaceuticals: a compendium of guidelines and related materials"*. WHO, Geneva, Volume 1 and 2 (Updated Edition), 1997. and *"Good manufacturing practices and inspection"*, WHO, Geneva, 2004.



49. It is essential to understand that a manufacturer can be qualified for one product, but not for another. Moreover, the manufacturer may produce the same product in different sites with unequal quality. For this reason, one is speaking of the qualification of the product/manufacturer/site entity (see Annex V).

#### THE CASE OF MEDICAL SUPPLIES

50. In the survey, only 56% of the DG ECHO's partners, who responded, that carry on a medical activity advised that they follow any standard for medical devices such as syringes, needles, and gauze...etc

51. The purchaser should at least require from the supplier one of the following quality standards:

- ISO13485/ ISO13488
- EN46001/ EN46002
- Japan QS Standard for medical devices 1128
- United States QS (21 CFR part 820)
- ISO9001/ISO9002
- ISO9001: 2000

52. Medical devices should:

- Meet essential requirements as described by the Global Harmonization Task Force (GHTF)<sup>11</sup>;
- Be produced in conformity with ISO standards and/or other equivalent standards as recognised by the GHTF.
- Be marketing their products according to at least one of the regulatory authorities: MPALS License (Australia), Device License (Canada), CE Mark (EU), Device License (Japan), and 510 k Device Letter (USA).

#### RE-QUALIFICATION AND MONITORING

53. Re-qualification of suppliers should occur at regular intervals. Routine re-inspection of manufacturers should take place at least once every three years. Furthermore, routine evaluations of product information or equivalents such as circulation of questionnaires should be carried out every three years as well. Non-routine evaluations and/or inspections

<sup>11</sup> GHTF, SG1- N041R6 – essential principles of safety and performance medical devices (including *In Vitro* diagnostic devices), 2004. and GHTF SG1(PD) - N043R6 – labelling for medical devices (including *In Vitro* diagnostic devices), 2004. [http://www.hc-sc.gc.ca/dhp-mps/compl-conform/int/part/ghtf\\_tc-tm\\_e.html](http://www.hc-sc.gc.ca/dhp-mps/compl-conform/int/part/ghtf_tc-tm_e.html)



should be carried out whenever necessary, e.g. when the manufacturer changes the formula, the manufacturing method, or the manufacturing site, and also if any product supplied was considered not to be in compliance with the agreed specification of the product, or if a significant complaint was received.

54. As part of the on-going monitoring programme, random samples of batches of pharmaceutical products supplied by pre-qualified manufacturers should be taken for independent testing to check final product specifications.

#### PROCUREMENT METHODS

55. In the opinion of the consultants, the WHO statement that open tendering is not appropriate for health sector goods, is fully supportable as it may be difficult to establish - before a contract is awarded - whether unknown bidders will be able to supply the required quality in required quantities on a sustained basis.

56. The consultants consider that, procurement agencies should use 'restricted tenders'<sup>12</sup>, conducted by direct invitation to all pre-qualified suppliers. (Please note, DG ECHO's procurement rules as set out under Annex V of the Framework Partnership Agreement have to be respected by the partners.)

57. The tender should include precise technical specifications<sup>13</sup> including:

- Pharmaceutical product specifications; and
- Package specifications.
- Labelling instructions;
- Case identification;
- Unique identifier; and
- Standards of Quality Control for supplies.

#### PRICES

58. The International Drug Prices Indicator<sup>14</sup> is regularly updated and provides a spectrum of prices from pharmaceutical suppliers and procurement agencies, based on their current catalogues or price lists. It also contains prices obtained from international development organisations and government agencies and represents an essential tool to be used by humanitarian organisations to compare prices.

<sup>12</sup> Also called 'closed bid' or 'selective tender'.

<sup>13</sup> An example can be found at <http://siteresources.worldbank.org/PROCUREMENT/Resources/health-ev4.pdf> p.117 to 120.

<sup>14</sup> International Drug Prices Indicator Guide - Management Sciences for Health (MSH), in collaboration with WHO, 2004. [http://erc.msh.org/dmpguide/pdf/DrugPriceGuide\\_2004\\_En.pdf](http://erc.msh.org/dmpguide/pdf/DrugPriceGuide_2004_En.pdf)



59. When comparing the costs of pharmaceutical products, the cost of the whole treatment -not just the cost per unit- should be taken into consideration. Since the choice may also be influenced by other factors such as transportation charges, storage requirements and shelf-life, the total cost should be considered.

#### CONTRACTUAL AGREEMENTS

60. The team's consultants consider that, a Memorandum of Understanding (MoU) between the buyer and the supplier should always be used. It should stipulate that the purchaser of the products has to ensure that only pre-qualified products (same formula, same manufacturing methods and manufacturing site, etc. as submitted in the product information) will be delivered by the supplier. The responsibilities of each party should be clearly defined in the agreement including reference to the above-mentioned aspects.

61. Furthermore, the agreement should have clauses regarding liability and compensation in case of breach of contract.<sup>15</sup>

#### MONITORING OF COMPLAINTS

62. Complaints should be handled in accordance with pre-established written procedures. Any complaint concerning a pharmaceutical product or batch of products supplied by the manufacturer should be thoroughly investigated. The nature of the complaint should be communicated to the manufacturer.

63. A written report of the complaint, investigation, recommendations for action where relevant, and outcome should be made available to the procurement agency.

#### 3.2.2.2 INTERNATIONAL SUPPORT TO DRUG QA

64. WHO has an ongoing pre-qualification project focussing on HIV/AIDS, TB and malaria medicines. The list of these pre-qualified drugs is regularly re-assessed and is published on the WHO website.<sup>16</sup>

65. It is envisaged that in the near future pre-qualification will also be done for reproductive health pharmaceutical products.

66. The qualified product linked to its manufacturing site and company (or product/supplier pair) found on the WHO website, should be respected by all the partners when procuring pharmaceutical products for those diseases.

#### 3.2.2.3 PROCURING THROUGH A QUALIFIED HPC

67. A single-bid procedure can be used to procure from HPCs provided they are recognised by DG ECHO and qualified at least by the respective national drug authority where they operate and, preferably, also by an external qualifying body.

<sup>15</sup> An example of such contract can be found at <http://siteresources.worldbank.org/PROCUREMENT/Resources/health-ev4.pdf>, p.142

<sup>16</sup> <http://mednet3.who.int/prequal/>



68. If a partner buys through one of the recognised HPCs, it is important to note that the above described pre-qualification of the product/supplier pair is to be carried out under the HPCs' responsibility. Moreover, the technical specifications collected, including the product information related to the quality of each product must be available for customer partners for inspection on demand.

69. A MoU is strongly recommended to regulate the partnership between the HPC and the DG ECHO partner, based on the same grounds, as described above regarding the contractual agreements (see paragraph 60). This MoU arrangement would have to be voluntarily entered into between the HPC and a partner, but it should be considered a good practice.

70. Purchasing through HPCs can be very convenient for humanitarian actions when emergencies occur in regions of intervention where HPCs or their subsidiaries are operating. The HPCs could make available pre-positioned or buffer stocks. Partners can develop an in-depth partnership with the HPCs who can assist with forecasting the partners' needs and thus assist with inventory management. Further, HPCs that are operating in a beneficiary country should share their experience about the local manufacturers' qualifications, in order to improve their and the manufacturers services to DG ECHO's partners. A good example of such practices exists in East Africa, where a de facto manufacturing capacity is present and also where ASRAMES operates in Goma, CHMP and IDA in Nairobi.

#### **3.2.2.4 WHAT CAN THE PARTNER DO WHEN THE MEDICINES IT NEEDS DO NOT TO MEET THE INTERNATIONAL STANDARDS ?**

71. This could be the case when partners are faced with 'orphan' drugs (drugs used for rare diseases or those difficult to find in the market place) or with new pharmaceutical products where, for example, stability studies are still ongoing. In the former case, the Expression of Interest (EoI) launched by a procurement agency may receive only one or two submissions; in the latter case, significant pre-qualification documentation is still pending. The choice to procure these medicines should be made by the partner; a committee that includes medical doctors and pharmacists of the partner's organisation should be created in order to assess the benefit/risk ratio and to decide on the use or non-use of the molecule.

72. Another situation where medicines fail to reach international standards could occur in countries where the import of medicines is banned and where national standards are possibly weaker than the international standards. HPCs or specialised partners that perform pre-qualifications are important actors in improving manufacturing conditions of local producers. They can visit production plants and can advise local producers on how to improve their production processes with the aim of progressively reaching international standards and thus increasing the quality of their final pharmaceutical products and sales as well. The findings of these inspections should be shared with local DG ECHO partners for them to procure from the best local supplier. (The HPCs and partners have to be prudent to avoid any risk of libel in reporting, i.e. they have to stick to facts.)



73. Furthermore, as far as possible and as necessary, external support should be provided to the best local producers among these local manufacturers to improve the quality of their products. (See [best practices in Annex I](#)).

### 3.2.3 DISTRIBUTION

**Distribution includes clearing customs, stock control, store management, and delivery to drug depots and health facilities.**

74. Most of DG ECHO's partners do not store pharmaceutical products themselves and instead request the supplier to deliver the order directly to the recipient country, either to an intermediate storage location or to the points of use.

75. The supplier (the manufacturer, the wholesaler, the distributor or the HPC) is responsible for the pharmaceutical products up to their delivery point. This pharmaceutical responsibility has to be specifically designated to a pharmaceutically trained person in the partner's field team.

76. The principles established in the WHO's guidelines for Good Trade and Distribution Practice<sup>17</sup>, as well as in the WHO Guide to Good Storage Practices for pharmaceuticals<sup>18</sup> should be followed.

77. In emergency situations, the following points must be carefully considered:

- Receiving of stocks;
- Post-procurement quality control; and
- Distribution system.

<sup>17</sup> WHO Expert Committee on Specifications for Pharmaceutical Preparations, *Thirty-eighth report*. Geneva, Switzerland: World Health Organisation, 2003, Annex 2 (Technical Report Series No. 917)

<sup>18</sup> WHO Expert Committee on Specifications for Pharmaceutical Preparations, *Thirty-seventh report*. Geneva, Switzerland: World Health Organisation, 2003, Annex 9 (Technical Report Series No. 908)



### 3.2.3.1 RECEIVING OF STOCKS

78. This step requires a control to confirm that what is received is compliant with the specification requirements that were established at time of ordering in terms of quality, quantity, form, dosage and packaging. Non compliant products should not be accepted. The batch number is to be used for tracing at this stage.

#### Receiving of stocks:

- All incoming materials and finished products should be quarantined immediately after receipt until they are released for use or distribution. Imported pharmaceutical products should be quarantined until test results confirm that the pharmaceutical products meet all of the requirements, specifications, terms and conditions of the purchase order.
- A review of certificates of analysis should be made to confirm that what has been delivered is what has been ordered and is certified by the manufacturer to meet specification.
- Upon receipt each incoming delivery should be checked for correspondence between the order, the delivery note, and the supplier's labels.
- The consignment should be examined for integrity of package and seal, and for uniformity of the containers. Should the delivery comprise more than one batch, it should be subdivided according to the supplier's batch number.
- Containers should be cleaned where necessary and labelled, if required, with the prescribed data, e.g. label description, batch number, type and quantity.
- Each container should be carefully inspected for possible contamination, tampering and damage, and any suspect containers or the entire delivery should be quarantined.
- Damage to containers and any other problem that might adversely affect the quality of a material should be recorded and investigated.

79. Toxic substances and flammable materials should be stored in suitably designed, separate places, in closed containers in closed areas, taking into account the relevant national legislation. Provision should be made for the proper and safe storage of waste materials awaiting disposal.

### 3.2.3.2 POST-PROCUREMENT QUALITY CONTROL

80. Procedures for the receipt of medicines / medical supplies should include random sampling using independent laboratory analysis to ensure that pharmaceutical products meet the required standards and specification. Representative samples should be taken directly from the containers of the consignment. Sampling should be performed in accordance with a written procedure (SOP) that every partner should have. Products may also be randomly sampled at the end of the distribution chain and sent for independent analysis.

### 3.2.3.3 THE DISTRIBUTION SYSTEM

81. A well managed distribution system should achieve the following objectives:

- Maintain a constant supply of medicines;



- Keep pharmaceutical products in good condition throughout the distribution process;
- Minimise pharmaceutical products losses due to spoilage and expiry;
- Maintain accurate inventory records;
- Rationalise pharmaceutical products' storage points;
- Use available transport resources as efficiently as possible;
- Reduce theft and fraud; and
- Provide information to forecast needs of pharmaceutical products.

82. Materials and pharmaceutical products should be transported in such a way that the integrity of the material and pharmaceutical products is not negatively affected and storage conditions are maintained.

83. That means that in emergency situations where transportation to the health facilities have to be done by air freight, a logistical coordination should be implemented by the partners to organise the grouping of freight in order to avoid that, the pharmaceutical products stay at the receiving airport under conditions where there is no control of temperature levels.

84. In cases of medical emergencies (such as a sudden outbreak of a contagious disease or a natural disaster that requires the urgent transport of medicines), DG ECHO partners in charge of flight management should give priority to the transport of the medicines and supplies needed to respond to the emergency.

85. The cold chain represents the first priority to keep the pharmaceutical products in good condition through the distribution process. If, as is normal practice, the temperature-sensitive products are sent by the supplier in cold boxes including freeze packs, it is important to foresee the equipment needed to maintain the required temperature level during storage, as well as an independent energy supply (generators, solar panel, etc.). Normally, the temperature sensitive products are stored in fridges in the warehouse, while the freeze packs are frozen to be used during the follow-on distribution.

86. The use of devices to monitor conditions such as temperature levels in the warehouse and during transportation is recommended as essential. Records should be held available for review.

87. Dangerous materials such as ethanol, methanol, chloramine, ether, etc. cannot be transported when they are incorrectly packaged or are not in compliance with lawful regulations because they will almost certainly be rejected by transporters. Hence, it is very important to tackle this issue before the distribution phase.

88. Special packaging requirements are needed either for air transport, ship and/or road transport. Companies that offer special packaging service should be identified and



engaged early enough. When such services are not available in the emergency area the special packaging should be requested at the previous phase (procurement).

89. Ideally, such packaging should be done in the field to allow all the needed flexibility in the dispatching of medical supplies. Indeed, it could be necessary to divide a bulk packaging (bulk break) in several smaller packages for laboratory reagents or chloramine or other substances such as methanol, with the aim of distributing rational quantities to several peripheral health facilities.

90. Specific requirements for narcotic medicines should also be followed before the distribution phase to avoid bottle-necks. (Significant paperwork is needed for their customs clearance).

### 3.2.4 RATIONAL USE

**Rational use includes diagnosing, prescribing, dispensing, and proper consumption by the patient.**

91. The rational use of drugs requires that patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community.

92. From the survey, 87% of DG ECHO partners that responded advised that they train their local health workers in the rational prescription of medicines and consider it the best way to promote the rational use of drugs.

93. DG ECHO's partners are also encouraged to develop quality controls in the clinics by monitoring and regularly auditing the prescriptions and dispensing practices of the staff, based on the following criteria:

- Use of the correct drug;
- Appropriate indication of the same (i.e., the reason to prescribe is based on sound medical considerations);
- Use of the most appropriate drug, considering its efficacy, safety, suitability for the patient, and cost;
- Use of the appropriate dosage, administration route, and duration of treatment;
- The patient can use that drug safely (i.e. contraindications do not exist, and the likelihood of an adverse reaction is minimal);
- Drug is correctly dispensed including giving appropriate information to the patients about the prescribed medicines; and
- The patient understands the need and adheres to the treatment.

### 3.2.4.1 PHARMACOVIGILANCE

94. It is worrisome to note that only 35% of the survey respondents advised that they have mechanisms in place to report the adverse effects of medicines.

95. The safety of a medicine is also linked to the regular reporting of the observed adverse effects by the users. This is called pharmacovigilance and is a crucial aspect that needs to be considered at the user's level. Physicians, pharmacists and nurses can play an important role in promoting such a reporting and in providing additional information (for example, on co-medication and previous drug use).

96. The WHO has announced<sup>19</sup>, the publication of "*The safety of medicines in public health programmes, pharmacovigilance an essential tool*". The purpose of this publication is ultimately to help each patient to receive the optimum therapy - and on a population basis, to help ensuring the acceptance and effectiveness of public health programmes.

97. DG ECHO's partners are strongly recommended to promote medicine safety by reporting the detected adverse effects of medicines their staff prescribes to national authorities and to the WHO Collaborating Centre for International Drug Monitoring (the Uppsala Monitoring Centre<sup>20</sup>).

#### How to report Adverse Drug Reactions (ADRs):

Local Case Report Forms (CRF) should be obtained from the National Drug Regulatory Authority. Some countries have included CRF in their National Formularies (British National Formulary, Formularies of South Africa, Zimbabwe, etc.). There are different Case Report Forms in different countries, but all of them have at least four sections which should be completed:

##### Section I – Patient information

- Patient identifier;
- Age at time of event or date of birth;
- Gender; and
- Weight.

##### Section II – Adverse event or product problem

- Description of event or problem;
- Date of event;
- Date of this report;
- Relevant tests/laboratory data (if available);
- Other relevant patient information/history; and
- Outcomes attributed to adverse event.
- Name (INN and brand name);

##### Section III – Suspected medication(s)

- Dose, frequency & route used;
- Therapy date;
- Diagnosis for use;
- Event abated after use stopped or dose reduced;
- Batch number;
- Expiration date;
- Event reappeared after reintroduction of the treatment; and
- Concomitant medical products and therapy dates.

##### Section IV – Reporter

- Name, address and telephone number (plus email when pertinent); and
- Specialty and occupation.

The completed Case Report Form should be sent to the national or regional ADR centre or to the manufacturer of the suspected product.

98. To do it in a proper way, and to contribute to the effectiveness of this process, the partners should follow the WHO Adverse Reaction Terminology that was developed 30 years ago for this purpose<sup>21</sup>.

<sup>19</sup> WHO Pharmaceutical newsletter, N°1, 2006, p.16.

<sup>20</sup> <http://www.who-umc.org/>

<sup>21</sup> WHO adverse Reaction Terminology: Terminology for coding clinical information in relation to drug therapy, December 2003, p.9. <http://www.umc-products.com/graphics/3149.pdf>



### 3.2.4.2 DRUG AND MEDICAL SUPPLIES DONATIONS

99. Eleven humanitarian organisations advised in the survey that they accept donated medicines; of these, only eight stated that they apply the “*WHO Guidelines for Drug Donations*”<sup>22</sup>.

100. Each humanitarian crisis leads to a flood of medicines and medical supplies donations from a lot of well-disposed people and rich countries. Guidelines have been developed by WHO in cooperation with the major international agencies active in humanitarian relief, (this started as far back as 1996 and they are regularly updated), but these are largely not consulted and not followed.

101. Pharmaciens sans Frontières Comité International (PSF-CI) produced a movie (<http://www.psfci.org/new/index.htm>) on the observed consequences of these practices after the Asian Tsunami in Banda Aceh in December 2004; it very appropriately called the documentary “*The Second Tsunami*”.

102. Some solutions on how to tackle this problem are proposed in the accompanying Concept Paper, but overall it can be stipulated that it would be best to avoid accepting these donations outright as this practice causes more problems and risks than benefits to recipients<sup>23</sup>. Furthermore, countries and organisations that continuously bypass the Guidelines should be sanctioned.

### 3.2.4.3 DISPOSAL OF PHARMACEUTICAL PRODUCTS

103. 70% of the responding partners stated that they have a disposal policy for sub-standard medicines and medical supplies, but only 48% of them advise that these policies are in line with the national guidelines following the WHO recommendations.

104. The waste disposal of pharmaceutical products is to be considered as a part of their rational use, i.e. the right way to manage their demise. Improper disposal may be hazardous as it can lead to contamination of water supplies or local water sources used by nearby communities or wildlife.

105. Furthermore, expired drugs may come into the hands of scavengers and children, e.g. if a landfill is insecure. Pilfering from a stockpile of waste drugs or during sorting may result in expired drugs being diverted to the market for resale or being terribly misused.

106. Most pharmaceutical products past their expiry date, become less efficacious and a few may even cause different adverse drug reactions. There are some categories of expired drugs or defective disposal practices that carry a clear public health risk. For example, non-biodegradable antibiotics, anti-cancer drugs and disinfectants should not be disposed of into the sewage system as they may kill bacteria necessary for the treatment of sewage; they should also not be flushed into water courses as they may damage aquatic life or contaminate drinking water.

107. For these reasons, all DG ECHO partners should include these aspects of the drugs and medical supply management in their activities complying with the WHO guidelines for safe disposal of unwanted pharmaceuticals in and after emergencies<sup>24</sup> and within the realm of national regulations.

<sup>22</sup>

Guidelines for drug donations, revised 1999, Interagency guidelines WHO/EDM/PAR/99.4

<sup>23</sup>

Possible challenges include: risks for the public health, expensive storage, transport payments, and, above all, the exorbitant cost of disposing of these toxic substances as waste in generally poorly equipped countries.

<sup>24</sup>

Guidelines for Safe Disposal of Unwanted Pharmaceuticals in and after Emergencies, Interagency Guidelines, WHO/EDM/PAR/99.2



## 4. Monitoring & Evaluation

108. The partners are recommended to produce standard operating procedures for selection, procurement, distribution and rational use for medicines and medical supplies.

109. Staff should be designated to be in charge of the pharmaceutical management and their job descriptions should clearly describe each step, referring to SOPs, regarding performance, monitoring and evaluation of the drug management at headquarters and in the field.

110. Training, when needed, is to be carried out for staff by experienced personnel within the partner's organisation or by external trainers.

111. Controls should be performed yearly on their own procedures, using the activities and results indicators proposed in these Guidelines or equivalents.

112. Corrective actions should be planned for and carried out when needed. Where problems have been identified, a follow-up visit should be made by an appropriately qualified official of the partner's organisation.



# ANNEX I – GOOD AND POOR PRACTICES ENCOUNTERED

## AI.1 GOOD PRACTICES

### AI.1.1 A MODEL THAT SHOULD BE REPLICATED: A COMPREHENSIVE SUPPORT OF DG ECHO-FUNDED MEDICAL NGOS IN THE MANAGEMENT OF THEIR MEDICINES

1. Due to the protracted civil war, the health system of Southern Sudan is extremely weak and a reliable pharmaceutical supply chain does not exist.
2. In this context, in 1995, Pharmaciens Sans Frontières Comité International (PSF-CI) set up a central store in Lokichoggio which enabled them to reduce the logistical costs, as well as assuring access to high quality essential drugs for the beneficiaries of the Southern Sudan controlled territory. Through pharmaceutical expertise and technical support, to this day, PSF-CI helps NGO partners to ensure a constant availability of essential drugs and to avoid the wastage of drugs.
3. Several medical NGOs' budget for medicines, medical devices and equipment are in fact to a large degree managed by this pharmaceutical NGO which: pre-qualifies its product/supplier pairs; procures and stores the pharmaceutical products in place; and makes them ready for the medical NGOs to come and collect them when needed, from Lokichoggio.

**This programme managed EUR 930,000 of pharmaceutical supplies in 2006, and was the procurer for eight medical NGOs.**

4. PSF-CI also takes an interest in the health care services of partners by insisting on their rational use of drugs, writing correct prescriptions, and compliance with patients' needs. It also gets involved in the stock management of the NGOs, providing them with tools and advice in this area. They further have developed guidelines in collaboration with the local MOH, with WHO and other implementing agencies.
5. Finally, they assist the NGOs in forecasting their needs and in the ordering of medicines, thanks to a careful follow-up and monitoring from the very start of the partnership they know the average rates of the NGOs stock consumption, on the one hand, and the public health profile of the population they serve, on the other.
6. Furthermore, PSF/CI aims at promoting local manufacturers and suppliers in East Africa. Almost 80% of the essential drugs, logistical and medical materials, and services used for this project are provided by Kenyan suppliers.
7. In its ten years in Southern Sudan, through, not only the provision of drugs, but also the monitoring, supervision and training of its partners on-site, PSF/CI has greatly contributed to a better level of access to high quality drugs at affordable prices.



**A recent review of this programme emphasised:**

- **The high relevance of this programme;**
- **The cost effectiveness of this central structure in Lokichoggio;**
- **The QA of the supplies;**
- **The attention to the NGOs needs;**
- **The flexibility offered thanks to the experience of the partner; and**
- **The monitoring carried out after delivery.**

**AI.1.2 A NATIONAL ASSOCIATION ACTIVE IN PUBLIC HEALTH, IN A 25 YEARS OLD CONFLICT ZONE, MEASURES UP TO THE CHALLENGE**

8. The Association Régionale d'Approvisionnement en Médicaments Essentiels (ASRAMES), a medicines and medical supply procurement centre, already in existence since more than ten years, is located in Goma, North Kivu, and the Democratic Republic of Congo. It has also now developed relevant additional activities in this remote region.

**North Kivu DRC, Post-conflict Zone: 5 million Inhabitants, 60,000 km<sup>2</sup>, 407 Public Health Centres, 57 Referral Health Centres and Hospitals.**

9. Training and technical assistance activities on health and medicines management were developed by ASRAMES using bilateral funding. When the funding stopped, a subsidiary NGO, CIF<sup>25</sup> Santé was set up to monitor and train regional health workers on the rational management of drugs, and to improve the quality assurance of the medicines procured once 'downstream' i.e. after their delivery to the places of use.

10. Solar installations were started by ASRAMES in health facilities, especially in the Eastern DRC where the electricity supply is unreliable or non-existent. Over time, this section also became an independent, subsidiary NGO called BIOSOL<sup>26</sup>. Today, it sells, installs, maintains and gives training on solar systems. They have already installed and are maintaining 500 systems in health facilities in the region. The annual turnover began at EUR 17,700 in 2001 and had grown to EUR 160,400 by 2004. This very dynamic NGO is now expanding its activities to the biomedical engineering area, because this is also a bottle-neck to the sound functioning of vital equipment in the health facilities in the region.

11. Air transport is the only transport for medicines and medical supplies in the large region of Eastern DRC. NGOs encounter major problems in transporting material considered as dangerous by IATA regulations (see III.2.3.c on the distribution system in these Guidelines). ASRAMES has shown its willingness to develop special packaging for these

<sup>25</sup> Conseil Information et Formation  
<sup>26</sup> Biomédical - Solaire

materials in its premises, so as to offer this needed service to its partners and thus facilitate the transport of such essential products as chloramine, methanol, ethanol, ether, etc.

12. On top of that, ASRAMES keeps the only available stocks of medicines and medical supplies in this region. In 2004, EUR 4,121,038 worth of medicines and medical supplies were delivered; of that amount, EUR 3,106,956 was sold to NGOs and EUR 1,014,082 was for public health centres.

13. A very dynamic and motivated team runs ASRAMES, a team that is willing to adapt or improve its performance when needed; the right human resources are already employed and they have just moved to brand-new, completely adequate facilities.

### **AI.1.3 A WIN-WIN SITUATION WHEN PARTNERS AND HPCs WORK TOGETHER IN THE IMPROVEMENT OF THE QA OF MEDICINES AND MEDICAL SUPPLIES**

14. Two good practices are described here as examples of possible synergies between humanitarian actors.

15. One of DG ECHO's partners was looking for a very rare medicine to treat the Kala Azar<sup>27</sup> and only found it in one HPC. The analysis of the quality dossier was not convincing to the medical NGO; and it was decided that a joint HPC-NGO team would conduct a new pharmaceutical visit of the manufacturer. The visit report was also jointly prepared by the team. In the report, the HPC and the NGO's requirements were clearly set out, practical advice was also given to the manufacturer to improve the quality of the drug in such a way as to be qualified by the medical NGO.

16. The same joint team second visit to the manufacturer found the expected quality improvement for this medicine and thus a benefit for all the actors involved in treating this illness was attained, i.e., the HPC, the medical NGO, the manufacturer, the other humanitarian organisations that need this medicine and, of course, the patients.

17. An HPC located in Europe has, since a long time, been passing-on its know how to developing countries. This in the areas of QA of national medicines and medical supplies, of appropriate procurement, in the quality of imported medicines and in their proper storage and distribution systems. In this way, they are contributing to decrease dependency and fostering sustainable development in developing countries.

18. Thanks to a presence in Europe and in Kenya with a subsidiary, this HPC is able to transfer the latest information technology on the procurement of medicines from the North with the knowledge of the South's concrete field realities..

19. The HPC trains the staff in the head quarters using a supervised learning-by-doing method and shares all their know-how and information.

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<sup>27</sup>

This conducts to death if not treated with the medicine.



20. Before implementing such training, a questionnaire is sent out and the objectives of the training are carefully defined with the future trainees. The human resources from the developing country spend some days in the HPC in France working within the French team in their daily work focusing on the particular interests of the trained person. Each employee of this HPC has the function of a trainer in its job description. Adapted solutions to the specific conditions of the country where the trainee will implement the learned lessons are actively discussed.

21. When the trainee gets back to her/his country, s/he keeps in email contact with a designated member of the HPC team who will follow-up on the needs of the trainee.

22. This kind of peer support from the North to the South has turned out to be very relevant. In this context, this kind of learning would benefit ASRAMES which received confirmation recently that it will be in charge of the entire 9<sup>th</sup> EDF budget for medicines and medical supplies in their region.

**Training areas covered :**

- **Implementation of pharmaceutical policy;**
- **Quality control of medicines;**
- **Implementation of the Quality Assurance system;**
- **Implementation of tools and methods for the distribution of medicines;**
- **Management of a hospital pharmacy; and**
- **Support in the implementation of programmes.**

#### **AI.1.4 WINDFALL BENEFIT FROM DG ECHO'S RECOGNITION OF HPCS**

23. One NGO interviewed used the DG ECHO example of single-sourcing from recognised HPCs to convince its funders to accept the same principle.

## **AI.2 POOR PRACTICES**

### **AI.2.1 A LACK OF PHARMACEUTICAL COMPETENCIES**

24. Some NGOs in the emergency field consider that the quality of medicines is circumscribed to its packaging, its expiry date and the language on the label. They do not know much about the standards to be applied during their manufacture; some of the same NGOs wonder when and how to decide to carry out quality controls of the medicines they receive. All these shortcomings are due to the fact that very few have any pharmaceutical personnel.



### **AI.2.2 MISMANAGING THE PRODUCTS OF GOOD WILL OF DONORS IN AN EMERGENCY**

25. One year and three months after the Tsunami, and despite the huge stock of medicines of the 4,000 tonnes<sup>28</sup> received still stored in the Aceh Provincial Health Office (PHO) warehouse, some NGOs were locally procuring and importing drugs, and government health centres were using their regular budget to procure medicines as if these stocks did not exist. This is mainly due:

- To gross ineptitude of the local system (the PHO pharmacy department is not proactive enough in having the health centres, districts, and hospitals of the province tap on this soon to expire stock); this results in hardly any orders coming to the warehouse (only two in the month of February);
- To a lack of coordination between NGOs in the province and PSF (who sorted and properly stored the medicines with DG ECHO funding);
- A good number of batches are expiring soon (on top of the 60% of the original 4,000 tonnes that were deemed unusable immediately after reception) and the supply in stock surpasses what they can use in Aceh province. Authorities have banned sending the medicines to other provinces; and
- Moreover, 1,200 tonnes of discarded medicines are waiting to be destroyed and are still stored in the same warehouse; the estimated cost: EUR 2.4 million.

### **AI.2.3 THE IRRATIONAL USE OF MEDICINES: TOO FREQUENT**

26. An NGO carried out a study on the rational use of drugs in public health facilities in four districts in Aceh Province<sup>29</sup>. This work showed that:

- Some patients' records had neither data on the patient's age, gender, diagnosis, or on the medicines prescribed. Often only signs and symptoms were used in the charts, rather than a diagnosis. Concerning the medication, the name of the drug was used, but without stating the strength, the dosage, the route of administration, and/or the number of units prescribed and/or dispensed.
- None of the prescribed medicines was in the latest edition of the national formulary issued by the MOH; neither was this document nor the standard treatment guidelines available in most of the health facilities studied.
- The dispensing practices showed that, patients did not receive correct information about their medication, nor were drugs adequately labelled.

<sup>28</sup>

For 2 millions inhabitants, that means 2 kg per inhabitant!

<sup>29</sup>

"Study on Rational Use of Drugs in Public health Facilities in Four Districts in Aceh Province", A joint Applied Health Research by MoH, PHO, DHO's, WHO, Merlin. Rochman Arif, Husnia Rubiana Th-Akib, Bayugo Y, Badoy TJ. Draft.



## ANNEX II – DEFINITIONS

<b>Active pharmaceutical ingredient</b>	A substance or compound that is intended to be used in the manufacture of a pharmaceutical product as a therapeutically active compound (ingredient).
<b>Drug</b>	Any substance or pharmaceutical product for human or veterinary use that is intended to modify or explore physiological systems or pathological states for the benefit of the recipient. In this document, the terms drug, medicine and pharmaceutical product are used interchangeably.
<b>Drug regulatory authority</b>	A national body that administers the full spectrum of drug regulatory activities, including at least all of the following functions in conformance with national drug legislation: <ul style="list-style-type: none"> <li>• <a href="#">Marketing authorisation</a> of new products and variation of existing products;</li> <li>• Quality control laboratory testing;</li> <li>• Adverse drug reaction monitoring;</li> <li>• Provision of drug information and promotion of rational drug use;</li> <li>• Enforcement operations;</li> <li>• Monitoring of drug utilisation; and</li> <li>• Essential medicines.</li> </ul>
<b>Essential medicines</b>	Those medicines that satisfy the priority health care needs of the population. They are selected with due regard to public health relevance, evidence on efficacy and safety, and comparative cost-effectiveness. Essential medicines are intended to be available within the context of functioning health systems at all times in adequate amounts, in the appropriate dosage forms, with assured quality and adequate information, and at a price the individual and the community can afford.
<b>Generic products</b>	The term generic product has somewhat different meanings in different jurisdictions. Use of this term is therefore avoided as much as possible, and the term multi-source pharmaceutical product (see below) is used instead. Generic products may be marketed either under the approved non-proprietary name or under a brand (proprietary) name. They may be marketed in dosage forms and/or strengths different from those of the innovator products (see below). Where the term generic product is used, it means a pharmaceutical product, usually intended to be interchangeable with the innovator product, which is usually manufactured without a license from the innovator company and marketed after expiry of the patent or other exclusivity rights. The term should not be confused with generic names for APIs.
<b>Good Manufacturing Practice (GMP)</b>	That part of quality assurance which ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorisation.
<b>Marketing Authorisation</b>	<p>An official document issued by the competent drug regulatory authority for the purpose of marketing or free distribution of a product after evaluation for safety, efficacy and quality. It must set out, inter alia, the name of the product, the pharmaceutical dosage form, the quantitative formula (including excipients) per unit dose (using INNs or national generic names where they exist), the shelf-life and storage conditions, and packaging characteristics. It specifies the information on which authorisation is based (e.g. "The product(s) must conform to all the details provided in your application and as modified in subsequent correspondence"). It also contains the product information approved for health professionals and the public, the sales category, the name and address of the holder of the authorisation, and the period of validity of the authorisation.</p> <p>Once a product has been given marketing authorisation, it is included on a list of authorised products - the register - and is often said to be "registered" or to "have registration". Market authorisation may occasionally also be referred to as a "license" or "product license".</p>



<b>Multi-source (generic) pharmaceutical product</b>	Pharmaceutically equivalent products that may or may not be therapeutically equivalent. Multi-source pharmaceutical products that are therapeutically equivalent are interchangeable.
<b>National list of essential pharmaceutical products</b>	The list of essential pharmaceutical products that has been defined, adopted and published at country level. It normally caters for all health facilities, including the main hospitals.
<b>National standards</b>	Includes laws, regulations, standards, ordinances or other requirements enacted or promulgated by an official body at any level of government, as well as guidelines, recommendations or other pronouncements of professional organisations of pharmacy.
<b>Pharmacovigilance</b>	The science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problems.
<b>Pre-qualification</b>	The activities undertaken in defining a product or service need, seeking expressions of interest from enterprises to supply the product or service, and examining the product or service offered against the specification and the facility where the product or service is prepared against common standards of Good Manufacturing Practice (GMP). The examination of the product or service and of the facility where it is manufactured is performed by trained and qualified inspectors against common standards. Once the product is approved, and the facility is approved for the delivery of the specified product or service, other Procurement Agencies are informed of the approval. Pre-qualification is required for all pharmaceutical products regardless of their composition and place of manufacture/registration, but the amount and type of information requested from the supplier for assessment by the Procurement Agency may differ.
<b>Quality control</b>	Quality control is concerned with sampling, specifications and testing, and with the Procurement Agency's documentation and acceptance/rejection procedures which ensure that the necessary and relevant tests are actually carried out and that starting materials, intermediates and finished products are not accepted for use, sale or supply until their quality has been judged to be satisfactory.



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