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PROPOSED UPDATED TEXT FOR

WHO GOOD MANUFACTURING PRACTICES FOR PHARMACEUTICAL PRODUCTS: MAIN PRINCIPLES

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DRAFT FOR COMMENTS

Please address any comments on this proposal by 29 March 2013 to Dr S. Kopp, Medicines Quality Assurance Programme, World Health Organization, 1211 Geneva 27, Switzerland, fax: (+41 22) 791 4730 or e-mail: kopps@who.int with a copy to gaspardm@who.int.

We are sending out our working documents electronically only and they are also laced on the Medicines web site for comment. If you do not already receive our documents please let us have your e-mail address (to bonnyw@who.int) and we will add it to our electronic mailing list.

SCHEDULE FOR THE PROPOSED ADOPTION PROCESS OF DOCUMENT QAS/13.517: PROPOSED UPDATED TEXT FOR WHO GOOD MANUFACTURING PRACTICES FOR PHARMACEUTICAL PRODUCTS: MAIN PRINCIPLES

WHO Expert Committee on Specifications for Pharmaceutical Preparations recommended update of good manufacturing practices for pharmaceutical products: main principles	8-12 October 2012
Drafting of newly updated paragraphs by Dr A.J. van Zyl, South Africa.	November-December 2012
Working document sent out for comment	January 2013
Compilation of feedback	April 2013
Discussion with expert group/inspectors	May-June 2013
Recirculation, if necessary	
Presentation to forty-eighth meeting of the WHO Expert Committee on Specifications for Pharmaceutical Preparations	October 2013
Any further action as necessary	…

1. INTRODUCTION

During 2012 the Secretariat was made aware that the current good manufacturing practices (GMP) for pharmaceutical products: main principles published as Annex 3 in the WHO Technical Report Series, No. 961, 2011, would need updating. (http://www.who.int/medicines/areas/quality_safety/quality_assurance/production/en/index.html → Quality assurance of pharmaceuticals: a compendium of guidelines and related materials)
The WHO Expert Committee on Specifications for Pharmaceutical Preparations discussed the need for an update during its forty-seventh meeting and agreed to pursue this accordingly.

Attached please find a table with the current and newly proposed text. The paragraphs that would need to be updated have been identified as being in the following sections:

Section 1
Section 2
Section 7
Section 17

Proposed updated text for

WHO good manufacturing practices for pharmaceutical products: main principles

1. Pharmaceutical quality system

Current WHO good manufacturing practices (GMP) text as published in WHO Technical Report Series, No. 961, 2001, Annex 3.	Proposed WHO text – 2013
1. **Quality assurance** 1.1 *Principle.* QA 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. QA, therefore, incorporates GMP and other factors, including those outside the scope of this guide such as product design and development. 1.2 The system of QA appropriate to the manufacture of pharmaceutical products should ensure that: (a) pharmaceutical products are designed and developed in a way that takes account of the requirements of GMP and other associated codes such as those of good laboratory practice (GLP) and good clinical practice (GCP); (b) production and control operations are clearly specified in a written form and GMP requirements are adopted; (c) managerial responsibilities are clearly specified in job descriptions; (d) arrangements are made for the manufacture, supply and use of the correct starting and packaging materials; (e) all necessary controls on starting materials, intermediate products, and bulk products and other in-process controls, calibrations, and validations are carried out; (f) the finished product is correctly processed and checked, according to the defined procedures; (g) pharmaceutical products are not sold or	**1. Pharmaceutical quality system** 1.1 *Principle.* Quality management is a wide-ranging concept covering all matters that individually or collectively influence the quality of a product. It is the totality of the arrangements made with the object of ensuring that pharmaceutical products are of the quality required for their intended use. Quality management, therefore, incorporates good manufacturing practices (GMP) and other factors, including those outside the scope of this guide such as product design and development. 1.2 GMP applies to the life-cycle stages from the manufacture of investigational medicinal products, technology transfer, commercial manufacturing through to product discontinuation. The pharmaceutical quality system (PQS) can extend to the pharmaceutical development life-cycle stage and should facilitate innovation and continual improvement and strengthen the link between pharmaceutical development and manufacturing activities. All parts of the PQS should be adequately staffed with competent personnel, and should have suitable and sufficient premises, equipment and facilities. 1.3 The PQS appropriate to the manufacture of pharmaceutical products should ensure that: (a) product realization is achieved by designing, planning, implementing, maintaining and continuously improving a system that allows the consistent delivery of products with appropriate quality attributes; (b) product and process knowledge is managed throughout all life-cycle stages;

supplied before the authorized persons (see also sections 9.11 & 9.12) have certified that each production batch has been produced and controlled in accordance with the requirements of the marketing authorization and any other regulations relevant to the production, control and release of pharmaceutical products; (h) satisfactory arrangements exist to ensure, as far as possible, that the pharmaceutical products are stored by the manufacturer, distributed, and subsequently handled so that quality is maintained throughout their shelf-life; (i) here is a procedure for self-inspection and/or quality audit that regularly appraises the effectiveness and applicability of the QA system; (j) deviations are reported, investigated and recorded; (k) there is a system for approving changes that may have an impact on product quality; (l) regular evaluations of the quality of pharmaceutical products should be conducted with the objective of verifying the consistency of the process and ensuring its continuous improvement; and (m) there is a system for QRM. 1.3 The manufacturer must assume responsibility for the quality of the pharmaceutical products to ensure that they are fit for their intended use, comply with the requirements of the marketing authorization and do not place patients at risk due to inadequate safety, quality or efficacy. The attainment of this quality objective is the responsibility of senior management and requires the participation and commitment of staff in many different departments and at all levels within the company, the company's suppliers, and the distributors. To achieve the quality objective reliably there must be a comprehensively designed and correctly implemented system of QA incorporating GMP and QC. It should be fully documented and its effectiveness monitored. All parts of the QA system should be adequately staffed with competent	(c) pharmaceutical products are designed and developed in a way that takes account of the requirements of GMP and other associated codes such as those of good laboratory practice (GLP) and good clinical practice (GCP); (d) production and control operations are clearly specified in a written form and GMP requirements are adopted; (e) managerial responsibilities are clearly specified in job descriptions; (f) arrangements are made for the manufacture, supply and use of the correct starting and packaging materials, the selection and monitoring of suppliers and for verifying that each delivery is from the approved supply chain; (g) all necessary controls on starting materials, intermediate products, and bulk products and other in-process controls, calibrations and validations are carried out; (h) the finished product is correctly processed and checked, according to the defined procedures; (i) pharmaceutical products are not sold or supplied before the authorized persons (see also sections 9.11 & 9.12) have certified that each production batch has been produced and controlled in accordance with the requirements of the marketing authorization and any other regulations relevant to the production, control and release of pharmaceutical products; (j) processes are in place to assure the management of outsourced activities; (k) satisfactory arrangements exist to ensure, as far as possible, that the pharmaceutical products are stored by the manufacturer, distributed and subsequently handled so that quality is maintained throughout their shelf-life; (l) there is a procedure for self-inspection and/or quality audit that regularly appraises the effectiveness and applicability of the PQS; (m) products and processes are monitored with a view to taking preventive action to avoid potential deviations occurring in the future. Deviations are reported, investigated and recorded;

personnel, and should have suitable and sufficient premises, equipment and facilities. 1.4 QRM is a systematic process for the assessment, control, communication and review of risks to the quality of the medicinal product. It can be applied both proactively and retrospectively. 1.5 QRM should ensure that: — the evaluation of the risk to quality is based on scientific knowledge, experience with the process and ultimately links to the protection of the patient; and — the level of effort, formality and documentation of the QRM process is commensurate with the level of risk.	(n) arrangements are in place for the prospective evaluation and approving of planned changes and their approval prior to implementation taking into account regulatory notification and approval where required. After implementation of any change, an evaluation is undertaken to confirm the quality objectives were achieved and that there was no unintended deleterious impact on product quality; (o) regular evaluations of the quality of pharmaceutical products should be conducted with the objective of verifying the consistency of the process and ensuring its continuous improvement; (p) a state of control is established and maintained by developing and using effective monitoring and control systems for process performance and product quality; (q) continual improvement is facilitated through the implementation of quality improvements appropriate to the current level of process and product knowledge; (r) there is a system for quality risk management (QRM); (s) an appropriate level of root cause analysis is applied during the investigation of deviations, suspected product defects and other problems. Most likely root cause(s) should be identified and appropriate corrective actions and/or preventative actions (CAPAs) should be identified and taken. The effectiveness of CAPAs should be monitored and assessed. 1.3 The manufacturer must assume responsibility for the quality of the pharmaceutical products to ensure that they are fit for their intended use, comply with the requirements of the marketing authorization and do not place patients at risk due to inadequate safety, quality or efficacy. The attainment of this quality objective is the responsibility of senior management and requires the participation and commitment of staff in many different departments and at all levels within the company, the company's suppliers and the distributors.

	1.4 Senior management has the ultimate responsibility to ensure an effective PQS is in place, adequately resourced and that roles, responsibilities, and authorities are defined, communicated and implemented throughout the organization. Senior management's leadership and active participation in the PQS is essential. This leadership should ensure the support and commitment of staff at all levels and sites within the organization to the PQS. 1.5 There should be periodic management review, with the involvement of senior management, of the operation of the PQS to identify opportunities for continual improvement of products, processes and the system itself. 1.6 The PQS should be defined and documented. A quality manual or equivalent documentation should be established and should contain a description of the quality management system including management responsibilities. **Quality risk management** 1.7 QRM is a systematic process for the assessment, control, communication and review of risks to the quality of the medicinal product. It can be applied both proactively and retrospectively. 1.8 QRM should ensure that: — the evaluation of the risk to quality is based on scientific knowledge, experience with the process and ultimately links to the protection of the patient; — the level of effort, formality and documentation of the QRM process is commensurate with the level of risk.
Product quality review 1.6 Regular, periodic or rolling quality reviews of all medicinal products, including export-only products, should be conducted	**Product quality review** 1.6 Regular, periodic or rolling quality reviews of all medicinal products, including export-only products, should be conducted

with the objective of verifying the consistency of the existing process, the appropriateness of current specifications for both starting materials and finished product to highlight any trends and to identify product and process improvements. Such reviews should normally be conducted and documented annually, taking into account previous reviews, and should include at least: (i) a review of starting materials and packaging materials used for the product, especially those from new sources; (ii) a review of critical in-process controls and finished product results; (iii) a review of all batches that failed to meet established specification(s) and their investigation; (iv) a review of all significant deviations or non-conformances, the related investigations and the effectiveness of resultant corrective and preventive actions taken; (v) a review of all changes made to the processes or analytical methods; (vi) a review of dossier variations submitted, granted or refused; (vii) a review of the results of the stability monitoring programme and any adverse trends; (viii) a review of all quality-related returns, complaints and recalls and the investigations performed at the time; (ix) a review of adequacy of any other previous corrective actions on product process or equipment; (x) for new dossiers and variations to the dossiers, a review of postmarketing commitments; (xi) the qualification status of relevant equipment and utilities, e.g. heating, ventilation and air-conditioning (HVAC), water, or compressed gases; and (xii) a review of technical agreements to ensure that they are up to date. The manufacturer and marketing authorization holder, where different, should evaluate the results of this review and an assessment should be made whether	with the objective of verifying the consistency of the existing process, the appropriateness of current specifications for both starting materials and finished product to highlight any trends and to identify product and process improvements. Such reviews should normally be conducted and documented annually, taking into account previous reviews, and should include at least: (i) a review of starting materials and packaging materials used for the product, especially those from new sources; (ii) a review of critical in-process controls and finished product results; (iii) a review of all batches that failed to meet established specification(s) and their investigation; (iv) a review of all significant deviations or non-conformances, the related investigations and the effectiveness of resultant corrective and preventive actions taken; (v) a review of all changes made to the processes or analytical methods; (vi) a review of dossier variations submitted, granted or refused; (vii) a review of the results of the stability monitoring programme and any adverse trends; (viii) a review of all quality-related returns, complaints and recalls and the investigations performed at the time; (ix) a review of adequacy of any other previous corrective actions on product process or equipment; (x) for new dossiers and variations to the dossiers, a review of post-marketing commitments; (xi) the qualification status of relevant equipment and utilities, e.g. heating, ventilation and air-conditioning (HVAC), water or compressed gases; (xii) a review of technical agreements to ensure that they are up to date. The manufacturer and marketing authorization holder, where different, should evaluate the results of this review and an assessment should be made as to whether corrective and preventive action or any revalidation should

corrective and preventive action or any revalidation should be undertaken. Reasons for such corrective actions should be documented. Agreed corrective and preventive actions should be completed in a timely and effective manner. There should be management procedures for the ongoing management and review of these actions and the effectiveness of these procedures should be verified during self-inspection. Quality reviews may be grouped by product type, e.g. solid dosage forms, liquid dosage forms, or sterile products, where scientifically justified. Where the marketing authorization holder is not the manufacturer, there should be a technical agreement in place between the various parties that defines their respective responsibilities in producing the quality review. The authorized person responsible for final batch certification, together with the marketing authorization holder, should ensure that the quality review is performed in a timely manner and is accurate.	be undertaken. Reasons for such corrective actions should be documented. Agreed corrective and preventive actions should be completed in a timely and effective manner. There should be management procedures for the ongoing management and review of these actions and the effectiveness of these procedures should be verified during self-inspection. Quality reviews may be grouped by product type, e.g. solid dosage forms, liquid dosage forms, or sterile products, where scientifically justified. Where the marketing authorization holder is not the manufacturer, there should be a technical agreement in place between the various parties that defines their respective responsibilities in producing the quality review. The authorized person responsible for final batch certification, together with the marketing authorization holder, should ensure that the quality review is performed in a timely manner and is accurate.

2. **Good manufacturing practices for pharmaceutical products**	**2. Good manufacturing practices for pharmaceutical products**
2.1 GMP is that part of QA which ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorization. GMP are aimed primarily at diminishing the risks inherent in any pharmaceutical production. Such risks are essentially of two types: cross-contamination (in particular of unexpected contaminants) and mix ups (confusion) caused by, for example, false labels being put on containers. Under GMP: (a) all manufacturing processes are clearly defined, systematically reviewed in the light of experience, and shown to be capable of consistently manufacturing pharmaceutical products of the required quality that comply with their specifications; (b) qualification and validation are performed; (c) all necessary resources are provided, including: (i) appropriately qualified and trained personnel; (ii) adequate premises and space; (iii) suitable equipment and services; (iv) appropriate materials, containers and labels; (v) approved procedures and instructions; (vi) suitable storage and transport; (vii) adequate personnel, laboratories and equipment for in-process controls; (d) instructions and procedures are written in clear and unambiguous language, specifically applicable to the facilities provided; (e) operators are trained to carry out procedures correctly; (f) records are made (manually and/or by recording instruments) during manufacture to show that all the steps required by the defined procedures and instructions have in fact been taken and that the quantity and	2.1 GMP is that part of quality management which ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorization. GMP is concerned with both production and quality control. GMP are aimed primarily at diminishing the risks inherent in any pharmaceutical production. Such risks are essentially of two types: cross-contamination (in particular of unexpected contaminants) and mix ups (confusion) caused by, for example, false labels being put on containers. Under GMP: (a) all manufacturing processes are clearly defined, systematically reviewed in the light of experience, and shown to be capable of consistently manufacturing pharmaceutical products of the required quality that comply with their specifications; (b) qualification and validation are performed; (c) all necessary resources are provided, including: (i) appropriately qualified and trained personnel, (ii) adequate premises and space, (iii) suitable equipment and services, (iv) appropriate materials, containers and labels, (v) approved procedures and instructions, (vi) suitable storage and transport, (vii) adequate personnel, laboratories and equipment for in-process controls; (d) instructions and procedures are written in clear and unambiguous language, specifically applicable to the facilities provided; (e) procedures are carried out correctly and operators are trained to do so; (f) records are made (manually and/or by recording instruments) during manufacture to show that all the steps required by the defined procedures and instructions have in fact been taken and that the quantity and quality of the product are as expected. Any significant deviations are fully recorded and investigated

quality of the product are as expected; any significant deviations are fully recorded and investigated; (g) records covering manufacture and distribution, which enable the complete history of a batch to be traced, are retained in a comprehensible and accessible form; (h) the proper storage and distribution of the products minimizes any risk to their quality; (i) a system is available to recall any batch of product from sale or supply; (j) complaints about marketed products are examined, the causes of quality defects investigated, and appropriate measures taken in respect of the defective products to prevent recurrence.	with the objective of determining the root cause and appropriate corrective and preventive action implemented; (g) records covering manufacture and distribution, which enable the complete history of a batch to be traced, are retained in a comprehensible and accessible form; (h) the proper storage and distribution of the products minimizes any risk to their quality and takes account of good distribution practice (GDP); (i) a system is available to recall any batch of product from sale or supply; (j) complaints about marketed products are examined, the causes of quality defects investigated and appropriate measures taken in respect of the defective products to prevent recurrence.

Proposed updated text for

WHO good manufacturing practices for pharmaceutical products: main principles

7. **Contract production and analysis**

Current WHO good manufacturing practices (GMP) text as published in WHO Technical Report Series, No. 961, 2001, Annex 3.	Proposed WHO text
7.1 *Principle*. Contract production and analysis must be correctly defined, agreed and controlled in order to avoid misunderstandings that could result in a product or work or analysis of unsatisfactory quality.	7.1 *Principle*. Contract production and analysis must be correctly defined, agreed and controlled in order to avoid misunderstandings that could result in a product or work or analysis of unsatisfactory quality.
General	**General**
7.2 All arrangements for contract production and analysis, including any proposed changes in technical or other arrangements, should be in accordance with the marketing authorization for the product concerned.	7.2 All arrangements for contract production and analysis, including any proposed changes in technical or other arrangements, should be in accordance with the marketing authorization for the product concerned.
7.3 The contract should permit the contract giver to audit the facilities of the contract acceptor.	7.3 The contract should permit the contract giver to audit the facilities and activities of the contract acceptor or mutually agreed subcontractors.
7.4 In the case of contract analysis, the final approval for release must be given by the authorized person.	7.4 In the case of contract analysis, the final approval for release must be given by the authorized person.
The contract giver	**The contract giver**
7.5 The contract giver is responsible for assessing the competence of the contract acceptor in successfully carrying out the work or tests required, for approval for contract activities, and for ensuring by means of the contract that the principles of GMP described in this guide are followed.	7.5 The PQS of the contract giver should include the control and review of any outsourced activities. The contract giver is responsible for assessing the legality, suitability and competence of the contract acceptor to successfully carry out the work or tests required, for approval for contract activities, and for ensuring by means of the contract that the principles of GMP incorporating QRM principles are followed.
7.6 The contract giver should provide the contract acceptor with all the information necessary to carry out the contracted operations correctly in accordance with the	

marketing authorization and any other legal requirements. The contract giver should ensure that the contract acceptor is fully aware of any problems associated with the product, work or tests that might pose a hazard to premises, equipment, personnel, other materials or other products. 7.7 The contract giver should ensure that all processed products and materials delivered by the contract acceptor comply with their specifications or that the product has been released by the authorized person.	7.6 The contract giver should provide the contract acceptor with all the information necessary to carry out the contracted operations correctly in accordance with the marketing authorization and any other legal requirements. The contract giver should ensure that the contract acceptor is fully aware of any problems associated with the product, work or tests that might pose a hazard to premises, equipment, personnel, other materials or other products. 7.7 The contract giver should review and assess the records and the results related to the outsourced activities. The contract giver should ensure that all processed products and materials delivered by the contract acceptor have been processed in accordance with GMP and the marketing authorization; comply with their specifications and that the product has been released by the authorized person. 7.8 The contract giver should monitor and review the performance of the contract acceptor including the implementation of any needed improvement.
The contract acceptor 7.8 The contract acceptor must have adequate premises, equipment, knowledge, and experience and competent personnel to carry out satisfactorily the work ordered by the contract giver. Contract manufacture may be undertaken only by a manufacturer who holds a manufacturing authorization. 7.9 The contract acceptor should not pass to a third party any of the work entrusted to him or her under the contract without the contract giver's prior evaluation and approval of the arrangements. Arrangements made between the contract acceptor and any third party should ensure that the manufacturing and analytical information is made available in the same way as between the original contract giver and contract acceptor.	**The contract acceptor** 7.8 The contract acceptor must have adequate premises, equipment, knowledge, experience and competent personnel to carry out satisfactorily the work ordered by the contract giver. Contract manufacture may be undertaken only by a manufacturer who holds a manufacturing authorization. 7.9 The contract acceptor should not pass to a third party any of the work entrusted to him or her under the contract without the contract giver's prior evaluation and approval of the arrangements. Arrangements made between the contract acceptor and any third party should ensure that the manufacturing and analytical information is made available in the same way as between the original contract giver and contract acceptor.

7.10 The contract acceptor should refrain from any activity that may adversely affect the quality of the product manufactured and/or analysed for the contract giver.	7.10 The contract acceptor should refrain from any activity (including unauthorized changes outside the terms of the contract) that may adversely affect the quality of the product manufactured and/or analysed for the contract giver. 7.12 The contract acceptor should understand that his or her activities may be subject to inspection by competent authorities.
The contract 7.11 There must be a written contract between the contract giver and the contract acceptor which clearly establishes the responsibilities of each party. 7.12 The contract must clearly state the way in which the authorized person, in releasing each batch of product for sale or issuing the certificate of analysis, exercises his or her full responsibility and ensures that each batch has been manufactured in, and checked for, compliance with the requirements of the marketing authorization. 7.13 Technical aspects of the contract should be drawn up by competent persons suitably knowledgeable in pharmaceutical technology, analysis and GMP. 7.14 All arrangements for production and analysis must be in accordance with the marketing authorization and agreed by both parties. 7.15 The contract should describe clearly who is responsible for purchasing, testing and releasing materials and for undertaking production and QC, including in-process controls, and who has responsibility for sampling and analysis. In the case of contract analysis, the contract should state whether or not the contract acceptor should take samples at the premises of the manufacturer. 7.16 Manufacturing, analytical, distribution records and reference samples should be kept	**The contract** 7.11 There must be a written contract between the contract giver and the contract acceptor which clearly establishes the responsibilities of each party, covering the outsourced activities, the products or operations to which they are related, communication processes relating to the outsourced activities and any technical arrangements made in connection with it. 7.12 The contract must clearly state the way in which the authorized person, in releasing each batch of product for sale or issuing the certificate of analysis, exercises his or her full responsibility and ensures that each batch has been manufactured in, and checked for, compliance with the requirements of the marketing authorization. 7.13 Technical aspects of the contract should be drawn up by competent persons suitably knowledgeable in pharmaceutical technology, analysis and GMP. 7.14 All arrangements for production and analysis must be in accordance with the marketing authorization and agreed by both parties. 7.15 The contract should describe clearly who is responsible for contracted activities, e.g. knowledge management, technology transfer, supply chain, subcontracting, testing and releasing materials and, undertaking production and quality control (QC), including in-process controls, and who has

by, or be available to, the contract giver. Any records relevant to assessing the quality of a product in the event of complaints or a suspected defect must be accessible and specified in the defect/recall procedures of the contract giver. 7.17 The contract should describe the handling of starting materials, intermediate and bulk products and finished products if they are rejected. It should also describe the procedure to be followed if the contract analysis shows that the tested product must be rejected.	responsibility for sampling and analysis. In the case of contract analysis, the contract should state whether or not the contract acceptor should take samples at the premises of the manufacturer. 7.16 Manufacturing, analytical, distribution records and reference samples should be kept by, or be available to, the contract giver. Any records relevant to assessing the quality of a product in the event of complaints or a suspected defect or to investigating in the case of a suspected falsified product must be accessible and specified in the procedures of the contract giver. 7.17 The contract should describe the handling of starting materials, intermediate and bulk products and finished products if they are rejected. It should also describe the procedure to be followed if the contract analysis shows that the tested product must be rejected.

WHO good manufacturing practices for pharmaceutical products: main principles

17. **Good practices in quality control**

Current WHO good manufacturing practices (GMP) text as published in WHO Technical Report Series, No. 961, 2001, Annex 3.	Proposed WHO text
17.1 QC is the part of GMP concerned with sampling, specifications and testing, and with the organization and documentation which ensure that the necessary and relevant tests are actually carried out and that materials are not released for use, nor products released for sale or supply, until their quality has been judged to be satisfactory. QC is not confined to laboratory operations, but may be involved in many decisions concerning the quality of the product.	17.1 QC is the part of GMP concerned with sampling, specifications and testing, and with the organization and documentation which ensure that the necessary and relevant tests are actually carried out and that materials are not released for use, nor products released for sale or supply, until their quality has been judged to be satisfactory. QC is not confined to laboratory operations, but may be involved in many decisions concerning the quality of the product.
17.2 The independence of QC from production is considered fundamental.	17.2 The independence of QC from production is considered fundamental.
17.3 Each manufacturer should have a QC function. The QC function should be independent of other departments and under the authority of a person with appropriate qualifications and experience, who has one or several control laboratories at his or her disposal. Adequate resources must be available to ensure that all the QC arrangements are effectively and reliably carried out. The basic requirements for QC are as follows: (a) adequate facilities, trained personnel and approved procedures must be available for sampling, inspecting, and testing starting materials, packaging materials, and intermediate, bulk, and finished products, and where appropriate for monitoring environmental conditions for GMP purposes; (b) samples of starting materials, packaging materials, intermediate products, bulk products and finished products must be taken by methods and personnel approved of by the QC department; (c) qualification and validation; (d) records must be made (manually and/or by recording instruments) demonstrating that	17.3 Each manufacturer should have a QC function. The QC function should be independent of other departments and under the authority of a person with appropriate qualifications and experience, who has one or several control laboratories at his or her disposal. Adequate resources must be available to ensure that all the QC arrangements are effectively and reliably carried out. The basic requirements for QC are as follows: (a) adequate facilities, trained personnel and approved procedures must be available for sampling, inspecting, and testing starting materials, packaging materials, and intermediate, bulk, and finished products, and where appropriate for monitoring environmental conditions for GMP purposes; (b) samples of starting materials, packaging materials, intermediate products, bulk products and finished products must be taken by methods and personnel approved of by the QC department; (c) qualification and validation; (d) records must be made (manually and/or

all the required sampling, inspecting and testing procedures have actually been carried out and that any deviations have been fully recorded and investigated; (e) the finished products must contain ingredients complying with the qualitative and quantitative composition of the product described in the marketing authorization; the ingredients must be of the required purity, in their proper container and correctly labelled; (f) records must be made of the results of inspecting and testing the materials and intermediate, bulk and finished products against specifications; product assessment must include a review and evaluation of the relevant production documentation and an assessment of deviations from specified procedures; (g) sufficient samples of starting materials and products must be retained to permit future examination of the product if necessary; the retained product must be kept in its final pack unless the pack is exceptionally large. 17.4 QC as a whole will also have other duties, such as to establish, validate and implement all QC procedures, to evaluate, maintain, and store the reference standards for substances, to ensure the correct labelling of containers of materials and products, to ensure that the stability of the active pharmaceutical ingredients (APIs) and products is monitored, to participate in the investigation of complaints related to the quality of the product, and to participate in environmental monitoring. All these operations should be carried out in accordance with written procedures and, where necessary, recorded. 17.5 QC personnel must have access to production areas for sampling and investigation as appropriate.	by recording instruments) demonstrating that all the required sampling, inspecting and testing procedures have actually been carried out and that any deviations have been fully recorded and investigated; (e) the finished products must contain ingredients complying with the qualitative and quantitative composition of the product described in the marketing authorization; the ingredients must be of the required purity, in their proper container and correctly labelled; (f) records must be made of the results of inspecting and testing the materials and intermediate, bulk and finished products against specifications; product assessment must include a review and evaluation of the relevant production documentation and an assessment of deviations from specified procedures; (g) sufficient reference samples of starting materials and products must be retained to permit future examination of the product if necessary; the retained product must be kept in its final pack unless the pack is exceptionally large. 17.4 QC as a whole will also have other duties such as to establish, validate and implement all QC procedures, to evaluate, maintain, and store the reference standards for substances, to ensure the correct labelling of containers of materials and products, to ensure that the stability of the active pharmaceutical ingredients (APIs) and products is monitored, to participate in the investigation of complaints related to the quality of the product and to participate in environmental monitoring. All these operations should be carried out in accordance with written procedures and, where necessary, recorded. 17.5 QC personnel must have access to production areas for sampling and investigation as appropriate.

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