GLOSSARY

Definitions given below apply to the words as used in this guide. They may have different meanings in other contexts.

ACTION LIMIT

Established criteria, requiring immediate follow-up and corrective action if exceeded.

AIR-LOCK

An enclosed space with two or more doors, and which is interposed between two or more rooms, e.g. of differing class of cleanliness, for the purpose of controlling the air-flow between those rooms when they need to be entered. An air-lock is designed for and used by either people or goods.

ALERT LIMIT

Established criteria giving early warning of potential drift from normal conditions which are not necessarily grounds for definitive corrective action but which require follow-up investigation.

BATCH (OR LOT)

A defined quantity of starting material, packaging material or product processed in one process or series of processes so that it could be expected to be homogeneous.

Note To complete certain stages of manufacture, it may be necessary to divide a batch into a number of sub batches, which are later brought together to form a final homogeneous batch. In the case of continuous manufacture, the batch must correspond to a defined fraction of the production, characterised by its intended homogeneity.

For control of the finished product, the following definition has been given in Directive 75/318/EEC: 'For the control of the finished product, a batch of a proprietary medicinal product comprises all the units of a pharmaceutical form which are made from the same initial mass of material and have undergone a single series of manufacturing operations or a single sterilisation operation or, in the case of a continuous production process, all the units manufactured in a given period of time'.

BATCH NUMBER (OR LOT NUMBER)

A distinctive combination of numbers and/or letters which specifically identifies a batch.

BIOGENERATOR

A contained system, such as a fermenter, into which biological agents are introduced along with other materials so as to effect their multiplication or their production of other substances by reaction with the other materials. Biogenerators are generally fitted with devices for regulation, control, connection, material addition and material withdrawal.

BIOLOGICAL AGENTS

Micro-organisms, including genetically engineered micro-organisms, cell cultures and endoparasites, whether pathogenic or not.

BULK PRODUCT

Any product which has completed all processing stages up to, but not including, final packaging.

CALIBRATION

The set of operations which establish, under specified conditions, the relationship between values indicated by a measuring instrument or measuring system, or values represented by a material measure, and the corresponding known values of a reference standard.

CELL BANK

Cell bank system: A cell bank system is a system whereby successive batches of a product are manufactured by culture in cells derived from the same master cell bank. A number of containers from the master cell bank are used to prepare a working cell bank. The cell bank system is validated for a passage level or number of population doublings beyond that achieved during routine production.

Master cell bank: A culture of [fully characterised] cells distributed into containers in a single operation, processed together in such a manner as to ensure uniformity and stored in such a manner as to ensure stability. A master cell bank is usually stored at - 70°C or lower.

Working cell bank: A culture of cells derived from the master cell bank and intended for use in the preparation of production cell cultures. The working cell bank is usually stored at - 70°C or lower.

CELL CULTURE

The result from the in-vitro growth of cells isolated from multicellular organisms.

CLEAN AREA

An area with defined environmental control of particulate and microbial contamination, constructed and used in such a way as to reduce the introduction, generation and retention of contaminants within the area.

Note The different degrees of environmental control are defined in the Supplementary Guidelines for the Manufacture of sterile medicinal products.

CLEAN/CONTAINED AREA

An area constructed and operated in such a manner that will achieve the aims of both a clean area and a contained area at the same time.

CONTAINMENT

The action of confining a biological agent or other entity within a defined space.

Primary containment: A system of containment which prevents the escape of a biological agent into the immediate working environment. It involves the use of closed containers or safety biological cabinets along with secure operating procedures.

Secondary containment: A system of containment which prevents the escape of a biological agent into the external environment or into other working areas. It involves the use of rooms with specially designed air handling, the existence of airlocks and/or sterilisers for the exit of materials and secure operating procedures. In many cases it may add to the effectiveness of primary containment.

CONTAINED AREA

An area constructed and operated in such a manner (and equipped with appropriate air handling and filtration) so as to prevent contamination of the external environment by biological agents from within the area.

CONTROLLED AREA

An area constructed and operated in such a manner that some attempt is made to control the introduction of potential contamination (an air supply approximating to grade D may be appropriate), and the consequences of accidental release of living organisms. The level of control exercised should reflect the nature of the organism employed in the process. At a minimum, the area should be maintained at a pressure negative to the immediate external environment and allow for the efficient removal of small quantities of airborne contaminants.

COMPUTERISED SYSTEM

A system including the input of data, electronic processing and the output of information to be used either for reporting or automatic control.

CROSS CONTAMINATION

Contamination of a material or of a product with another material or product.

CRUDE PLANT (VEGETABLE DRUG)

Fresh or dried medicinal plant or parts thereof.

CRYOGENIC VESSEL

A container designed to contain liquified gas at extremely low temperature.

CYLINDER

A container designed to contain gas at a high pressure.

EXOTIC ORGANISM

A biological agent where either the corresponding disease does not exist in a given country or geographical area, or where the disease is the subject of prophylactic measures or an eradication programme undertaken in the given country or geographical area.

FINISHED PRODUCT

A medicinal product which has undergone all stages of production, including packaging in its final container.

HERBAL MEDICINAL PRODUCT

Medicinal product containing, as active ingredients, exclusively plant material and/or vegetable drug preparations.

INFECTED

Contaminated with extraneous biological agents and therefore capable of spreading infection.

IN-PROCESS CONTROL

Checks performed during production in order to monitor and if necessary to adjust the process to ensure that the product conforms its specification. The control of the environment or equipment may also be regarded as a part of in-process control.

INTERMEDIATE PRODUCT

Partly processed material which must undergo further manufacturing steps before it becomes a bulk product.

LIQUIFIABLE GASES

Those which, at the normal filling temperature and pressure, remain as a liquid in the cylinder.

MANIFOLD

Equipment or apparatus designed to enable one or more gas containers to be filled simultaneously from the same source.

MANUFACTURE

All operations of purchase of materials and products, Production, Quality Control, release, storage, distribution of medicinal products and the related controls.

MANUFACTURER

Holder of a Manufacturing Authorisation as described in Article 16 of Directive 75/319/EEC.

MEDIA FILL

Method of evaluating an aseptic process using a microbial growth medium. (Media fills are synonymous to simulated product fills, broth trials, broth fills etc.).

MEDICINAL PLANT

Plant the whole or part of which is used for medicinal purpose.

MEDICINAL PRODUCT

Any substance or combination of substances presented for treating or preventing disease in human beings or animals.

Any substance or combination of substances which may be administered to human beings or animals with a view to making a medical diagnosis or to restoring, correcting or modifying physiological functions in human beings or in animals is likewise considered a medicinal product.

PACKAGING

All operations, including filling and labelling, which a bulk product has to undergo in order to become a finished product.

Note Sterile filling would not normally be regarded as part of packaging, the bulk product being the filled, but not finally packaged, primary containers.

PACKAGING MATERIAL

Any material employed in the packaging of a medicinal product, excluding any outer packaging used for transportation or shipment. Packaging materials are referred to as primary or secondary according to whether or not they are intended to be in direct contact with the product.

PROCEDURES

Description of the operations to be carried out, the precautions to be taken and measures to be applied directly or indirectly related to the manufacture of a medicinal product.

PRODUCTION

All operations involved in the preparation of a medicinal product, from receipt of materials, through processing and packaging, to its completion as a finished product.

QUALIFICATION

Action of proving that any equipment works correctly and actually leads to the expected results. The word *validation* is sometimes widened to incorporate the concept of qualification.

QUALITY CONTROL

See Chapter 1.

QUARANTINE

The status of starting or packaging materials, intermediate, bulk or finished products isolated physically or by other effective means whilst awaiting a decision on their release or refusal.

RADIOPHARMACEUTICAL

“Radiopharmaceutical” shall mean any medicinal product which, when ready for use, contains one or more radionuclides (radioactive isotopes) included for a medicinal purpose (Directive 89/343/EEC extending the scope of Directives 65/65/EEC and 75/319/EEC to radiopharmaceuticals and laying down additional provisions.

RECONCILIATION

A comparison, making due allowance for normal variation, between the amount of product or materials theoretically and actually produced or used.

RECORD

See Chapter 4.

RECOVERY

The introduction of all or part of previous batches of the required quality into another batch at a defined stage of manufacture.

REPROCESSING

The reworking of all or part of a batch of product of an unacceptable quality from a defined stage of production so that its quality may be rendered acceptable by one or more additional operations.

RETURN

Sending back to the manufacturer or distributor of a medicinal product which may or may not present a quality defect.

SEED LOT

Seed lot system: A seed lot system is a system according to which successive batches of a product are derived from the same master seed lot at a given passage level. For routine production, a working seed lot is prepared from the master seed lot. The final product is derived from the working seed lot and has not undergone more passages from the master seed lot than

the vaccine shown in clinical studies to be satisfactory with respect to safety and efficacy. The origin and the passage history of the master seed lot and the working seed lot are recorded.

Master seed lot: A culture of a micro-organism distributed from a single bulk into containers in a single operation in such a manner as to ensure uniformity, to prevent contamination and to ensure stability. A master seed lot in liquid form is usually stored at or below - 70°C. A freeze-dried master seed lot is stored at a temperature known to ensure stability.

Working seed lot: A culture of a micro-organism derived from the master seed lot and intended for use in production. Working seed lots are distributed into containers and stored as described above for master seed lots.

SPECIFICATION

See Chapter 4.

STARTING MATERIAL

Any substance used in the production of a medicinal product, but excluding packaging materials.

STERILITY

Sterility is the absence of living organisms. The conditions of the sterility test are given in the European Pharmacopoeia.

SYSTEM

Is used in the sense of a regulated pattern of interacting activities and techniques which are united to form an organised whole.

VALIDATION

Action of proving, in accordance with the principles of Good Manufacturing Practice, that any procedure, process, equipment, material, activity or system actually leads to the expected results (see also qualification).