Aseptic Dispensing for NHS Patients

A Guidance Document for Pharmacists in the United Kingdom

ACKNOWLEDGMENTS

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ASEPTIC DISPENSING FOR NHS PATIENTS

Contents

1. INTRODUCTION

1.1 Background

Recently there has been a significant growth in the aseptic preparation of medicines under the control of pharmacists in hospitals. This work has developed in dedicated facilities based both in pharmacy departments and adjacent to patient areas.

The general reduction of manufacturing activity in hospital pharmacy has led to units operating a more limited range of such facilities. It is becoming common for aseptic dispensing to be undertaken alone.

Whereas previously independent inspection of such activities was often incorporated into visits by Regional Quality Controllers or the Medicines Inspectorate, there has been a reduction in this monitoring. Further there appears to have been a decrease in the activity levels of local Quality Controllers, probably associated with the lower production outputs. Whilst there have been a significant number of documents published which refer to the standards appropriate to the various aseptic dispensing activities, their status and availability to those responsible for these services is variable. All this pointed to the need for standards in practice to be reviewed.

A review was instituted by the Health Departments' Chief Pharmacists with the intention of examining, updating and issuing guidance on the approach which providers should adopt in undertaking aseptic dispensing for NHS patients.

1.2 Process

Standard, procedures and service audit documents relating to all aseptic activities available in the United Kingdom were collected and reviewed. Material published in Europe, the USA, Canada and Australia was also considered. Evidence was also collected from selected practising hospital specialists in the four home territories. A workshop involving representatives from each of the home territories, MCA, Regional Pharmacists and specialists pharmacists in CIVAS, Cytotoxic, Paediatric, Production, Quality Control, Radiopharmacy and TPN services considered the issues. A draft working document was circulated to the workshop participants and some other specialists and the final version prepared after consideration of the comments received.

1.3 Outcome

The fundamental conclusion was that guidance contained within existing documents set acceptable standards, but that these standards were not always applied in practice. The formal status and distribution of documents was not consistent between and within the home countries.

The final guidance document provides users with pointers to key issues, which should be considered by any pharmacist responsible for an aseptic dispensing activity. The document should not be used alone, but in conjunction with the relevant items in the bibliography, which is specific to each home country.

2 SCOPE

2.1 From the perspective of the Medicines Act, Aseptic Dispensing should be seen as two separate but linked activities. The supply or issue of a finished product to the patient or to the person responsible for its administration is *dispensing*. The manipulation of the product leading to this final presentation is *preparation*. This document is essentially focused on the preparation stage and covers all activities up to the point of issue although some aspects eg. product stability are relevant to the post-issue phase. The requirements arising under a Section 10 exemption from the Medicines Act are applicable to preparation activities as well as dispensing.

2.2 These guidelines are intended to be used in all situations where parenteral products are being prepared in non-licensed units which are run exclusively under the control of a pharmacist whether they are located in the pharmacy department facilities or in other departments.

2.3 Their purpose is to provide managers with a template on which to develop their local services so that preparation is carried out to a high standard and the products issued have an assurance of quality to the level of safety patients may legitimately expect.

2.4 The contents of this document provide a broad indication of the aspects to which consideration needs to be given and highlight the basic tenets for each. Those using the document should refer to other current guidance documents which give specific details relating to standards applicable for aseptic activities. Details of some sources are listed in Appendix 2. Reference may also be needed to any specific local policies and management arrangements which affect the way in which services are run.

2.5 Activities covered by the guidance in this document include

Aseptic Dispensing
Dispensing of Parenteral Cytotoxic products
Dispensing of Radiopharmaceuticals
Central Intravenous Additive Services
Total Parenteral Nutrition preparation

3. POLICIES

3.1 The principles established in "The Rules Governing Medicinal Products in the European Community Vol IV Guide to Good Manufacturing Practice for Medicinal Products" and the "Standards of Good Professional Practice" of the Royal Pharmaceutical Society of Great Britain and the Pharmaceutical Society of Northern Ireland should be adopted.

3.2 Medicines prepared as stock in anticipation of a prescription for parenteral administration under a Section 10 exemption to the Medicines Act 1968 in units which do not possess a "special" manufacturers license for that activity are required to meet the following criteria:

i. The preparation is done by or under the supervision of a pharmacist
ii. The preparation uses closed systems
iii. Licensed sterile medicinal products are used as ingredients or the sterile ingredients are manufactured in licensed facilities
iv. Products will have an expiry date of no more than one week. The shelf life should be supported by stability data.
v. All activities should be in accordance with defined NHS guidelines

(from "Guidance to the NHS on the Licensing Requirements of the Medicine Act").

The same criteria should also be considered appropriate for preparation for dispensing directly to named patients.

3.3 Aseptic preparation provides the lowest level of assurance of sterility of all the methods used to produce parenteral products. It should only be selected when other methods which include final product sterilisation cannot be used.

3.4 A general policy statement should be published to cover each of the aseptic dispensing activities undertaken locally and be available to all staff involved in the preparation and issue of the products. This should refer to the principles on which the service provision is based, the status of the document and time interval for its review.

3.5 Specific policies, incorporating reference to appropriate standards, should exist for each activity and highlight the need for a quality system which would include inter alia

- detailed, approved, operational procedures to cover all facets of the activity
- defined responsibilities, competencies, training and performance of staff involved in the activity
- control of all materials, including containers, devices and packaging, used in the processes
- appropriate provision and use of special clothing (for operator and product protection)
- provision, maintenance and correct performance of facilities and equipment, including disposables, for the whole range of activities carried out
- consistent approach to product presentation including labelling
- full documentation of systems and processes and other product related issues such as customer complaints
- validation of all procedures
- comprehensive quality assurance with independent approval
- reference to other legislative requirements, where necessary, eg. COSHH, Ionising Radiation Regulations, etc

4. PROCESS DESIGN

4.1 Assuming the appropriateness of the prescription has been confirmed, the responsible pharmacist needs to know how (methods and route), when, and where the product will be administered and to draw up an appropriate specification.

4.2 The responsible pharmacist should also know the range of functions which can be appropriately carried our using the available facilities, equipment and staff.

4.3 In combining the product specification with the facility design capacity the responsible pharmacist should design a process leading to provision of a suitable product. This will include establishment of the critical stages in the process which need to be validated and writing a process control document incorporating the full procedures required and the associated quality assurance. A primary objective in the procedures should be to minimise the number of manipulations during which product integrity is compromised.

4.4 In most circumstances the processes in use will be common to a range of products or the same product, with perhaps some minor variations, and will be used regularly. Thus established, validated activities should be used for most if not all stages in preparation of the patient's medicine.

5. PROCESS VALIDATION

5.1 A fully validated process provides a high level of confidence that a product from the process will meet the requirements for content, strength and purity. In situations such as aseptic dispensing, where limited or no final product testing is undertaken, the use of validated systems is vital.

5.2 Validation requirements include all stages up to completion of the administration to the patient. It is therefore a requirement that data relating to product stability should be assessed as part of the process.

5.3 Once established deviation from a validated process should not be permitted.

5.4 The responsible pharmacist may authorise use of a product made outside validated arrangements if there is an urgent patient need. Any deviation should be recorded as a quality exception report and retained as part of the audited documentation system. This option should be seen as exceptional and the responsible pharmacist should either undertake the preparation personally or directly supervise the procedure. If it is likely that further doses of such products are required, where feasible, steps should be taken to fully validate the process before they are dispensed.

5.5 Wherever possible quantifiable rather than qualitative measures should be used eg. environmental limits should show pressure differences in pascals not just that it is positive, microbial assessments should show numbers and basic morphological characteristics of organisms not just presence. Each class or type of procedure should be separately validated and repeated after any change, including introduction of a new operator, or at suitable intervals.

5.6 Operational characteristics of key equipment such as laminar air flow cabinets and isolators should be confirmed in writing by the contractor as part of planned preventative maintenance, after each full service and subsequent to other significant events such as breakdown.

5.7 Any equipment used in the process or in monitoring the process which shows quantifiable data should be calibrated and checked at appropriate intervals for continuing accuracy.

5.8 Where disposable equipment such as transfer sets, filters, syringes, etc are used the validation process must confirm their operational characteristics particularly with respect to system integrity, chemical stability (absorption, adsorption or leaching) and chemical interaction. If sources of such equipment are changed or the equipment is updated by the manufacturers, the process should be revalidated.

5.9 Cleaning procedures should be regularly validated especially where hazardous materials eg. cytotoxics, antibiotics, are being processed.

5.10 Continuing correct operation of system failure indicators should be confirmed at regular intervals.

5.11 Process validation checks requiring further manipulation or interpretation eg. microbiological monitoring, should be undertaken by suitably experienced staff in appropriately equipped facilities, using methods appropriate to pharmaceutical products.

5.12 Full documentation of validation activities should be established and maintained.

6. ASEPTIC PROCESSING

6.1 Written procedures should be available for all aseptic dispensing activities. When a product is required on a single occasion a standard procedure can be used but all normal process activities should be covered in it.

6.2 Processes should be undertaken in suitable, defined and validated conditions by appropriately qualified and fully trained staff. Consideration should be given to the special requirements when any hazardous product is manipulated.

6.3 If common facilities are used for different product types, care must be taken to segregate adequately the activities by time and, where appropriate, specific cleaning arrangements so that cross-examination is avoided. If alternating product types due to workload demand or timing occurs regularly, early consideration should be given to permanently separating the product types by use of a separate clean room or isolator.

6.4 All components for the product should be assembled prior to processing and manipulations undertaken as a single operation. Activities within the critical zone should not be compromised by breaks in processes to add further components.

6.5 Processes should be organised to make best use of the facilities and equipment eg. within laminar air flow cabinets operator technique and arrangement of materials should ensure that manipulations take place in uninterrupted airflow.

7. PERSONNEL

7.1 A pharmacist with appropriate skills and experience should be responsible for managing each aseptic dispensing activity. The responsible pharmacist should have knowledge of and current experience in the following topics:

a. the principles of Good Manufacturing Practice
b. the principles of pharmaceutical mircobiology
c. basic formulation and product design
d. the chemical, pharmaceutical and clinical properties of the ingredients of the products handled in the unit
e. process validation
f. documentation, general quality control and quality assurance
g. procedures for the preparation, compounding and storage of sterile products
h. methods and equipment in use for parenteral drug administration
i. aseptic technique and sources and types of contamination
j. environmental monitoring, facilities management, equipment operation and raw material control.

Additionally some specialised knowledge may be required for specific aseptic activities eg. of Ionising Radiation Regulations in radiopharmacy.

7.2 Day to day professional supervision of activities, including approval of the product for use, in units with fully validated systems can be undertaken by pharmacists with more limited experience and training. However any pharmacist exercising such responsibilities must have appropriate training and a clear understanding of the processes and of the requirement to follow the written procedures.

7.3 In the absence of the responsible pharmacist, another pharmacist with similar qualities should deputise or the activity should be temporarily restricted to the level appropriate to the skills available.

7.4 All staff working in aseptic dispensing operations should be fully trained in the techniques required for the range of product types and equipment being handled. Further, they should have formal skills assessment appropriate to the preparation processes prior to handling real products and these skills should be updated and re-evaluated at appropriate and regular intervals. Training programmes to meet deficiencies identified for individual or groups of staff should be provided without undue delay.

7.5 Staff should also be trained in the general requirements relating to process controls, disinfection, cleaning, good manufacturing practice, health and hygiene and other relevant topics.

7.6 Staff handling cytotoxic drugs or other products which may cause adverse effects should be apprised of the risks, of their responsibilities to inform line management of relevant changes in their personal circumstances (eg. becoming pregnant) and the need to comply with other written procedures such as exposure records and checks required by local Occupational Health Departments.

7.7 Engineers, fitters and others who may undertake maintenance of equipment or deal with breakdowns should be suitably trained in the functioning of the equipment, and the nature of the work for which it is being used, including the basic principles of Good Manufacturing Practice.

8. FACILITIES AND EQUIPMENT

8.1 Facilities for aseptic dispensing should be designed, constructed and operated in a manner appropriate to the activities undertaken in them and with respect to the equipment installed so that, by segregation and process control, maximum protection can be afforded to the product and, where necessary, to the operator.

8.2 Equipment should be specific for the tasks to be undertaken. Where possible, moveable equipment not in use for the product being prepared should be removed from the area.

8.3 A planned preventative maintenance programme should exist, covering all the key equipment, to standards agreed with the responsible pharmacist. Comprehensive breakdown, service and maintenance records should be kept. Engineers, fitters etc carrying our maintenance work should be instructed to inform supervisory staff which work is to be undertaken particularly where plant, or access to it, is remote from the unit.

8.4 Performance criteria for facilities and equipment should be established and records made of status prior to and during use. Operation, cleaning, maintenance and fault logs should be developed and maintained for all facilities and equipment.

8.5 Manipulation of products should be undertaken in conditions meeting Grade A (in laminar or non-laminar flow) of the EC standard. Air quality, flow direction and rate across the critical zone should be established and routinely monitored. Where the equipment is not designed to provide laminar flow, air patterns in the critical areas should be established to ensure adequate flow rates and no dead zones.

8.6 Quality of air, airflow patterns and pressure differences to the adjacent areas should be appropriate to the facility type, equipment used and the product being handled. Detailed advice relevant to the specific requirements for the different aseptic activities should be obtained from the publications listed in the bibliography.

8.7 The principles of operation for isolators should be the same as for clean rooms. Isolators provide only a partial barrier and the transfer of materials into the work zones is a critical phase. Transfer processes into the operational zones should be validated and appropriately monitored.

8.8 Operation of any facility which is not kept continuously running should be validated to establish the time required for the unit to achieve the required air quality standard.

8.9 All surfaces, in a clean room or isolator should be of a suitable material and quality for the work to be undertaken. All areas should be designed to be readily cleanable and enable effective disinfection. Isolators, particularly models which, by design, have areas which are difficult to sanitise, may also be sterilised on re-commissioning and at appropriate intervals.

8.10 Cleaning processes should be fully documented and validated. Cleaning/sanitization of equipment, materials and containers should be undertaken prior to the manipulation and preparation activities with particular care of transfers into the critical zones. Cleaning materials should generate low levels of particles and be reserved specifically for use in the aseptic area. Cleaning/sanitization solutions should be appropriate for the surfaces and should be demonstrably active throughout their shelf life.

8.11 Laminar flow cabinets and isolators used for products which are hazardous to the operator may operate at negative pressure to the immediate surrounding zone. Validation of such equipment should incorporate checks against extraneous air inflow from the surrounding zone. The equipment should also possess capacity for safe changing of filters.

8.12 Computer software used to generate formulae eg. control processes etc should be validated. Access to any operating systems should be restricted to the appropriate grade of authorised personnel only.

8.13 Disposable compounding equipment should be changed at least daily if not after each session.

8.14 Access to the critical areas of the preparation facilities during the periods when products are being manipulated should be restricted to those directly involved in the processes. Staff temporarily attached or visitors should have access limited to non-operational periods and then only for valid purposes.

9. PROTECTIVE CLOTHING

9.1 Clothing including masks, gloves and foot covering should be shown to be appropriate for the purposes of preventing contamination of the environment and product from operator-shed particles and for protecting the operator from any hazards associated with the product. In the wider context, use of clothing also highlights the critical nature of the processes.

9.2 Clean, undamaged, sterile, lint free clothing and sterile gloves should be used in clean rooms. Dedicated clothing together with head covering and footware or overshoes should be worn by isolator operators. Staff spraying items into a clean room or isolator hatch should wear suitable gloves and clothing. A mask may also be needed if the operator's head is near the hatch aperture during the transfer process.

9.3 Cross contamination via environment or product should be minimised by reserving clothing for use in a single operational area. In clean rooms clothing should be replaced on a sessional basis (or daily if justified by monitoring), or immediately following a contamination event or damage. In isolator areas frequency of changing may be reduced as long as environmental standards are shown to be maintained.

10. DOCUMENTATION

10.1 Good comprehensive documentation is an essential feature of the quality assurance system. Documents used for any purpose should be clearly and unambiguously phrased, legible and contain all the detail necessary for staff to undertake the task in hand.

10.2 All the procedures used in aseptic dispensing, the preparation of every product individually and all the associated records should be available as written documents. It should also enable the establishment and maintenance of an audit trail for any product including, through quality exception reports, those made outside the standard operational procedures.

10.3 All documentation should be prepared, approved and regularly reviewed by appropriately qualified staff.

10.4 Entries made during processing or as records should be by authorised staff only.

10.5 Data held electronically should comply with relevant legislation, should have access restricted to authorised staff only and, for records, should not be open to modifications after initial entry is confirmed unless such modifications retain details of the original entry.

10.6 Retention of documentation should be specified in both form and period to meet legislative and operational requirements.

10.7 A control system should exist to ensure that only up-to-date documentation and programs are used.

11. STARTING MATERIALS AND COMPONENTS

11.1 All materials, devices and containers should be from approved sources. Where products used are not themselves licensed they should be from a unit holding a manufacturer's licence. QC approval of any non-licensed products should be obtained before the product is used.

11.2 Containers, equipment and devices used in the preparation process or for the final product should be validated as part of the process checks. They should provide adequate protection to physical or chemical threats to the integrity of the product. They should not react with any components of the product or allow passage of other harmful substances into the product eg. by leaching of chemicals from labels through the wall of the container.

12. STORAGE AND HANDLING

12.1 Components and finished products, process materials and disposable equipment should all be stored before use or issue in conditions which provide appropriate protection and under which any deterioration (chemical, physical or microbiological) is minimised and integrity maintained.

12.2 The external surfaces of components, intermediate or final product containers, of disposable apparatus, and of other equipment, eg. filters must be protected before being used in a process to minimise the transfer of particles into critical operation areas.

12.3 The conditions of storage and the performance of the equipment used for storage, particularly refrigerators, should be established, maintained and monitored regularly if not continuously.

12.4 Handling of components and other potential sources of particulate contamination in or near the manipulation facility should be minimised.

12.5 To minimise the consequences of any ingress of live micro-organisms into the product during preparation, the product should be refrigerated (4-8°) between the time of preparation and use except where such conditions would adversely affect the product by for example, causing precipitation be exceeding solubility limits. The need for these products to be kept cold should not be subordinated to other storage requirements which may exist eg. the security of products containing Controlled Drugs.

13. LABELLING

13.1 Labelling should be used to identify finished or intermediate products and labels should be applied to the container as soon as possible after manipulations are completed.

13.2 A standard operating policy approved by the responsible pharmacist should exist to ensure that style and presentation of labels are standardised and consistent and meet current requirements. Information on labels should be comprehensive, legible and, where possible, capable of being read while the product is being administered. It should be checked against the original order/prescription as accurate and complete and be approved by an appropriately trained member of the supervisory staff.

13.3 Written control procedures should ensure that labels are adequately segregated and reconciled so that mislabelling is avoided.

13.4 The label will identify the product as part of the audit trail and for this purpose as well as to ensure appropriate use should contain all the necessary information regarding the patient (if not prepared as a stock item), content, administration, storage, expiration and origin (including, where possible, a lot number).

13.5 Scope to incorporate data on to labels eg. batch number, expiry date or to modify design, particularly when these are held on a data base, should be restricted to suitably authorised staff.

14. PRODUCT SHELF LIFE

14.1 By the nature of aseptically prepared products there is no guarantee that all final containers will be free of viable micro-organisms, although in well controlled and validated processes the probability of contamination will be low. Therefore the overall aim should be to minimise the time between preparation of the injection and its administration so that the opportunity for any live micro-organisms in the product to multiply are restricted. If there are no chemical or physical reasons why shelf life should be less, a maximum shelf life of 1 week is recommended.

14.2 The setting of an arbitrary shelf life should be avoided by testing the stability of the product in its container against appropriate chemical, physical and microbiological parameters. Data available from manufacturers, official compendia or other reliable sources may be used but it must be carefully and reliably compared to ensure that transfer to the local situation is justified. Where such a process is used to set product parameters, further testing should be done to confirm that the shelf life given is justified. Such work may need to be repeated if significant changes are made to the product constituents, the preparative process, the equipment, the final container or the storage conditions.

15. QUALITY ASSURANCE AND RELEASE OF FINISHED PRODUCTS

15.1 A comprehensive quality assurance programme set up by the responsible pharmacist in conjunction with the Quality Controller is essential for all aseptic preparation activities. Individual product quality is generally not tested as would be the case in batch produced materials and therefore confidence that the patient will receive a medicine of suitable content, strength and purity is dependent on the controls built into the processes, the assessment of the raw materials and packaging components and the performance of staff and equipment.

15.2 Quality assurance activity should particularly concentrate on those aspects of product manipulation and processing at which the integrity of the system is at greatest risk.

15.3 The release of a finished product for use should be undertaken by suitably qualified and authorised member of staff. Release requirements should include visual inspection of the product and full compliance with the controls laid down in the approved operational documents for validated systems. Where product release and issue for use are simultaneous (cf 1.1) the release should be undertaken by a pharmacist.

15.4 Results of some tests undertaken during the preparative processes may not be available prior to final product release or use. This is particularly likely for microbiological monitoring. Despite not affecting the use of the product, such testing is important and contributes to the overall quality assurance of the operation.

15.5 Sampling from final containers should be avoided unless the product is surplus to requirements. Samples may be taken at the end of the compounding operation before final seals are in place. They may be used to confirm accurately the chemical composition of solutions but

there is limited value in testing them microbiologically unless the whole volume in the container is used. Further, sampling of the final container is another threat to the integrity of the product and if undertaken would need to be incorporated in the validation system. The test for sterility is an important test not only for validation purposes but also for routine control. A sampling scheme should be in place such that extra containers are prepared on a routine basis and subjected to a validated test for sterility. The test should as far as reasonably practicable follow the requirements of the British Pharmacopoeia.

15.6 For aseptically prepared products, no guarantee exists that conditions under which any dose was prepared were exactly the same. Monitoring, particularly microbiological controls, needs therefore to be undertaken for every session of work. Settle plates in the critical zone will provide basic data but should be regularly supplemented by other tests eg. finger dabs, swabs, air sampling etc to provide a satisfactory level of confidence.

15.7 Regular review of quality control activities and systems should be undertaken.

15.8 Where testing is carried out in laboratories outside the facility, the responsible pharmacist should ensure that the tester is fully conversant with the technical background and requirements in aseptic processing, uses up-to-date methods appropriate to pharmaceutical products, appropriately qualified and experienced staff and undertakes the work in suitable facilities.

16. SERVICE AUDIT

16.1 An assessment of the overall activity and performance of sections undertaking aseptic preparative work should be an established feature of the management of these services.

16.2 It should be undertaken by suitably trained and experienced staff who have not been directly involved in the day to day running of the service and are independent of it managerially. Written reports of such audits should be submitted to the senior pharmacy manager and be available for service users and commissioners.

16.3 Where the audit is undertaken by a relatively inexperienced auditor (one who undertakes a limited number or range of audits) then, at appropriate intervals, probably not less than every two years, an auditor from an appropriately qualified external organisation, such as the MCA or a region wide quality assurance service, should be used so that a different perspective can be taken of the activity.

16.4 Senior pharmacy managers should remedy deficiencies without delay and timetable action on priority issues. Any deficiency which could be regarded as a threat to acceptable product quality should lead to immediate cessation of the on-site activity until remedied.

Appendix 1

GLOSSARY

Approved Sources

Suppliers of raw materials, components, containers and consumables assessed and approved by Quality Control.

Appropriately Qualified

Minimum competencies will be specified for staff undertaking defined tasks. Staff whose current qualification and training are assessed as meeting the defined minimum competencies will be deemed to be appropriately qualified.

Authorised

Formally approved within the existing Standard Operational Procedures.

Audit Trail

The process by which all activities in the preparation of a batch or individual product can be shown to have occurred, including the identification of staff involved, the identification of raw materials, containers, components and other significant consumables and the processing records.

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.

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.

Closed system

Preparation by addition of sterile ingredients to a pre-sterilised closed container via a system closed to the atmosphere (a hypodermic needle inserted through a rubber closure is commonly part of a closed system. Use of a solution from an ampoule may be considered part of a closed system provided the ampoule is opened within the contained work station, only one withdrawal is made and the contents are added immediately to the closed container).

Critical zone

That part of the controlled work space where containers are opened and the product is exposed. Particulate and microbiological contamination should be reduced to levels appropriate to the intended use.

Critical processes

Those activities during which the integrity of the product or the particulate level in the critical zone is threatened.

Dispensing

The activity of supplying the product in its appropriate form to the patient pursuant to a doctor's prescription. This includes issue by the pharmacist to a person authorised to administer the product or cause it to be administered to the patient.

Independent assessor

An assessor who does not report managerially to the responsible pharmacist. He/She may be accountable to the senior pharmacy manager (as long as the latter is not also the responsible pharmacist), or be employed by another NHS or non-NHS organisation.

Licensed

Possessing a license from the Licensing Authority to operate as a manufacturer of pharmaceutical products.

Operational characteristics

The measurement and assessment of the performance of a piece of equipment, system etc. This may include fixed and variable physical and chemical considerations eg. dead space, volume delivered, chemical absorption.

Preparation

The manipulation of raw materials and components within the pharmacy to make a final product for dispensing or in anticipation of dispensing in accordance with a prescription given by a practitioner.

Responsible pharmacist

The pharmacist responsible for the whole of the services within an aseptic services section.

Senior Pharmacy manager

The pharmacist responsible for the pharmacy services within a Trust or in a directly managed unit.

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.

Appendix 2

ASEPTIC DISPENSING

SOURCE DOCUMENTS – FOR ALL TERRITORIES

PUBLISHER	TITLE	DATE OF ISSUE	SOURCE
MCA	Rules and Guidance for Pharmaceutical Manufacturers	1993	HMSO
Commission of the Eur. Communities	The Rules Governing Medicinal Products in the European Communities Vol. IV: Good Manufacturing Practice for Medicinal Prod.	1992	HMSO
MCA	Guidance to the NHS on the Licensing Requirements of the Medicines Act	9/92	MCA
Reg QC Sub-Comm of RPhO's	The Design and Monitoring of Isolators: A Specification for Pharmaceutical Applications	9/93	Local Specialist QC pharmacist
HMSO	Isolators for Pharmaceutical Applications; ed Lee and Midcalf	12/94	HMSO
Reg QC Sub-comm of RPhO's	The Quality Assurance of Aseptic Preparation Service (National guidelines on the design, operation and monitoring of aseptic preparation services in NHS hospitals)	1/93	Local specialist QC pharmacist
Joint WP Radioph and QC Sub-comm	Quality Assurance of Radio-pharmaceuticals	10/93	Mrs Barbara Parsons Sterile Production Unit Pharmacy Department Northampton General Hospital NHS Trust Cliftonville Northampton NN1 5BD
Radcliffe Med Press	Cytotoxics Handbook ed Allwood and Wright 2nd Edition	1993	Any good bookshop
National CIVAS Gp	Centralised Intravenous Additives Services Manual	4/93	Dr Richard Needle Pharmacy Support Unit Essex Rivers Healthcare NHS Trust Colchester General Hospital Turner Road Colchester CO4 5JL (price £4.00)
National TPN Gp	Pharmaceutical Services: Quality Audit Scheme of Total Parenteral Nutrition Services	7/94	Mr Bruce McElroy Pharmacy Department Royal Shewsbury Hospital Mytton Oak Royal Shrewsbury SY3 8BR (price £2.50)

ENGLAND

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SOURCE DOCUMENTS

PUBLISHER	TITLE	DATE OF ISSUE	SOURCE
RPSGB	Medicines, Ethics and Practice	Current Edition	RPSGB
RPhO's Sp Inter Gp	Standards for Pharmaceutical Services in Health Authorities, Units and Trusts in England	12/91	Mr Jeff Watling Queen Alexander Hospital Cosham Portsmouth PO6 3LY (price £2.50)

SCOTLAND

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SOURCE DOCUMENTS

PUBLISHER	TITLE	DATE OF ISSUE	SOURCE
RPSGB	Medicines, Ethics and Practice	Current Edition	RPSGB
CAPO Gp	Standards for Pharmaceutical Care in Health Board Premises and NHS Trusts in Scotland	1992	Dr N McNulty CAPO Greater Glasgow Health Board 112 Ingram Street Glasgow G1 1ET

WALES

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SOURCE DOCUMENTS

PUBLISHER	TITLE	DATE OF ISSUE	SOURCE
RPSGB	Medicines, Ethics and Practice	Current Edition	RPSGB
DGM(93)119	Standards of Pharmaceutical Services	1993	Dr. G.B.A. Veitch Chief Pharmaceutical Advisor Welsh Office Cathays Park Cardiff CF1 3NQ
WHC(88)65	Policy for Safe Handling of Cytotoxic Drugs	1988	As above
Welsh Ph Qual Ass	MCA Guidelines on the Implications of the Loss of Crown Immunity	2/93	Mr. V. Fenton-May Welsh Pharmaceutical Quality Assurance Services St Mary's Hospital Corbett Road Penarth CF6 1QX

NORTHERN IRELAND

ASEPTIC DISPENSING

SOURCE DOCUMENTS

PUBLISHER	TITLE	DATE OF ISSUE	SOURCE
PSNI	Medicines, Ethics and Practice	Current Edition	PSNI
CAPO's	Standards for Managed Services in Health and Personal Social Services Boards in NI	12/88	Directors of Pharmaceutical Services of H&SS Boards
Pharm Dir Grp (NI)	Monitoring the Quality of Pharmaceutical Services in NHS Trusts/DMUs	1993	Directors of Pharmaceutical Services of of H&SS Boards