

**GUIDANCE FOR THE PURCHASE AND SUPPLY OF
UNLICENSED MEDICINAL PRODUCTS
NOTES FOR PRESCRIBERS AND PHARMACISTS**

NHS PHARMACEUTICAL QUALITY ASSURANCE COMMITTEE

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GUIDANCE FOR THE PURCHASE AND SUPPLY OF UNLICENSED MEDICINAL PRODUCTS

NOTES FOR PRESCRIBERS AND PHARMACISTS

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GUIDANCE FOR THE PURCHASE AND SUPPLY OF UNLICENSED MEDICINAL PRODUCTS

NOTES FOR PRESCRIBERS AND PHARMACISTS

INTRODUCTION

The use of unlicensed medicines, or the use of licensed medicines for unlicensed indications (off-label), are matters of concern to all prescribers and pharmacists. This paper gives recommendations to prescribers and pharmacists involved in the use or procurement of unlicensed medicines and gives guidance on the assessment of their quality. Specific reference is made to unlicensed medicines in both the second wave of the Medicines Management Framework (Standard 12) and the Controls Assurance Standard for Medicines Management (Criterion 6).

For good clinical reasons the use of unlicensed medicines and the use of licensed medicines for unlicensed indications is widespread in hospitals. Were this practice to be curtailed the treatment of many patients would be impeded. It is therefore important that all prescribers and pharmacists should be aware of the associated medico-legal implications.

Whilst licensed medicinal products are subject to stringent control by the Medicines and Healthcare products Regulatory Agency (MHRA), neither prescriber nor pharmacist can make the same assumptions of quality, safety and efficacy about unlicensed products.

The manufacture and sale or supply of medicinal products was first brought under legal control by The Medicines Act 1968. This was subsequently incorporated into European law by EEC Directive 65/65.

Article 3 of Directive 65/65/EEC states that no medicinal product may be placed on the market unless a marketing authorisation (more commonly known as a product licence in the UK) has been issued. Article 2.1 of the same Directive ensures that full control of manufacturing and marketing (covered by chapters II to V) applies to medicinal products on the market.

However article 2.4 of 65/65/EEC gives an exemption from the full controls in Chapters II to V for medicinal products to fulfil special needs, supplied in response to a bona fide unsolicited order, formulated in accordance with the specifications of an authorised health care professional, and for use by his/her individual patients on his/her direct personal responsibility.

In the UK legislation, SI No.3144/1994, the section on marketing authorisations states that it is illegal to either place on the market or wholesale deal any relevant medicinal product without a marketing authorisation unless it is covered by an exemption. Schedule 1 of SI No.3144/1994 gives the details of the conditions for this exemption and this is printed as an Appendix to Guidance Note 14, the MHRA advice on interpretation of legislation on unlicensed medicines.

This legislation only applies to relevant medicinal products, which includes all licensed medicines and “specials”. Products extemporaneously prepared in the pharmacy in response to a prescription are not defined as relevant medicinal products. UK manufacturers of relevant medicinal products are required to hold a manufacturer’s licence (ML). Unlicensed products manufactured in the UK must be labelled with the ML number. In the case of licensed products the ML number forms the first portion of the product licence number (see below) and is therefore generally not stated separately.

Products which are unlicensed in the UK, may thus be identified by the absence of a licence number prefixed by PL (product licence), MA (marketing authorisation), EMEA (European Medicines Evaluation Agency) or EU (European Union). If they have been manufactured in the UK they will have a licence number prefixed by ML (manufacturer’s licence).

Thus, whilst it is the right of a practitioner to use any material for any purpose in the treatment of his/her own patients, he/she does so on his/her own responsibility and prescribers should always be aware of the licence status of the medicines they use.

Because of the lack of external scrutiny via the licensing process, the use of unlicensed medicines within each organisation needs to be controlled and monitored as discussed under "RECOMMENDATIONS TO PRESCRIBERS" AND "RECOMMENDATIONS TO PHARMACISTS". The risk assessment process, clinical governance and peer review, for example through Drug and Therapeutics Committees, are particularly useful tools for exercising this control.

MEDICINES WITH A PRODUCT LICENCE

The product licence defines the therapeutic or diagnostic purposes (the clinical indications) for which a product may be marketed. The manufacturer may then promote and sell the product for these purposes. These clinical indications are based on data submitted by the manufacturer as part of the product licence application. The Medicines and Healthcare products Regulatory Agency also considers other data to approve the manufacturing processes, shelf-life, etc.

If a prescriber uses a licensed medicine for an unlicensed indication (ie outwith the terms of its product licence or ‘off-label’) then the manufacturer is unlikely to be found liable for any harm caused by that medicine, unless the harm is directly attributable to a defect in it, rather than the way in which it was prescribed.

The use of medicines, licensed only for use in adults, for the treatment of children falls into this category. The joint Royal College of Paediatrics and Child Health and the Neonatal and Paediatric Pharmacists Group issued a policy statement entitled ‘the use of unlicensed medicines or licensed medicines for unlicensed applications in paediatric practice’ in February 2000. This was circulated to Chief Executives of NHS Trusts in October 2000 together with two versions of a generic patient information leaflet (one for parents/carers and the other for older children). Further information can be obtained from the Royal College of Paediatrics and Child Health, at 50 Hallam Street, London W1N 6DE, E-mail: enquiries@rcpch.ac.uk.

UNLICENSED MEDICINES

The majority of medicines sold or supplied against a prescription are covered by a product licence. However some are not, and they can be classified as follows:

(i) Medicines prepared by a manufacturer but not on sale in this country.

Such medicines may be awaiting the grant of a UK product licence, be undergoing clinical trial, be manufactured for export or may have been withdrawn from the UK market. It is usually possible to obtain supplies of these medicines from the manufacturer, or through a specialist importer. Since the medicines are not licensed, the responsibility for their use, together with liability for any consequences, rests with the prescriber. Examples of wording used to denote marketing authorisations used in other countries is given in Appendix 1.

Pharmacists are advised to ensure that the prescriber is aware of this – written notification which the prescriber signs and returns is often used.

If the medicine is to be used for the treatment of a particular patient, it may usually be obtained from the manufacturer on what is commonly referred to as an “individual patient basis”. The manufacturer has no justification for demanding individual patients’ names, and hospitals divulging such information may be breaking patient confidentiality. The hospital should, however, keep detailed records of the purchase and administration.

(ii) Medicines prepared for a specified patient in accordance with a prescriber’s instructions.

This broadly includes any form of extemporaneous dispensing, including TPN compounding, IV additives and cytotoxic reconstitution services.

Pharmacies are exempted from the need to hold a manufacturer’s licence, provided that medicines are prepared by or under the supervision of a pharmacist in accordance with a practitioner’s prescription. This is often referred to as a Section 10 exemption and the products would not generally be labelled with a ML or PL number.

(iii) Unlicensed medicines obtained from a hospital or a commercial supplier with a manufacturer’s “specials” licence.

Such medicines, widely known as “specials”, can be supplied against an order or prescription by a hospital manufacturing unit or commercial manufacturer holding a manufacturer’s “specials” licence.

Such “specials” will be labelled with the manufacturer’s licence (ML) number.

A “specials” manufacturer cannot advertise any product by name nor publish a catalogue or price list. He/she may advertise his/her service but not solicit orders.

(iv) Re-packed medicines

The product licence for a medicine regulates not only its formulation and manufacture but also the container in which it is sold. When a medicine is removed from its original container and re-packed, either during a dispensing operation or for the assembly of small packs for use as ward stocks, it technically becomes an unlicensed product (the term de-licensed is sometimes used). This is of little significance to prescribers, as the medicine has been manufactured and sold in accordance with a product licence. These guidelines are therefore not intended to apply to such medicines. Its significance will further decrease as the trend towards patient packs continues.

Such operations can be performed “in-house” on a small scale or can be commissioned from a packaging unit holding a manufacturer’s “specials” licence, which covers assembly activities or a manufacturer’s (assembly) licence. In these latter cases they will be labelled with the manufacturer’s licence (ML) number.

For both (iii) and (iv) above the premises of the manufacturer are regularly inspected by the Medicines Inspectorate to ensure that quality of standards and procedures is maintained. However, individual products are not assessed as they are when a product licence is applied for.

Because “specials” have no product licence they cannot be offered for sale by a manufacturer, but must be procured or commissioned by a purchaser.

As “specials” are not licensed for the specific use for which they are being procured, it is in the interests of the purchaser to ensure that the manufacturer is supplied with a detailed specification appropriate to that use AND that the medicine received complies with this specification. This will require an in-house assessment of quality, which might involve carrying out some quality control testing (see Appendix 2).

Quality controllers should be involved in drawing up these specifications to give advice on requirements such as formulation, production method, packaging, expiry and analytical testing. It is acceptable for this specification to be based on, or to include, data on formulation, analysis and stability by the “specials” manufacturer.

RISK MANAGEMENT

Because unlicensed medicines have not been formally assessed through the licensing process for safety, quality and efficacy, the risks associated with their use cannot be presumed to have been evaluated, either implicitly or explicitly.

There will generally be two stages of risk assessment.

(i) Prescribing/requesting

Prior to the approval being given for an unlicensed medicine to be used for the first time, a clinical risk assessment needs to be carried out. This assessment might also need to be reviewed for each repeat request or periodically and this will be defined in the trust policy.

This stage of assessment can be considered primarily as an assessment of safety and efficacy. It will be necessary to present some evidence as to the benefits offered by the preparation together with a consideration of possible licensed alternatives. Any evidence of side effects, contra-indications and precautions in use need to be detailed.

It is common to assign products/usage to risk groups (eg. high, medium, low). Risk assessments can be made on a number of criteria or a combination of criteria and will probably differ from organisation to organisation. For example, the route of administration, probable legal category (if the product were to be licensed) or therapeutic index could give one indication of risk. Whether the active ingredient(s) are in common or historical usage in other products, whether they have been withdrawn on safety grounds and whether imported and in common usage or licensed abroad would give another measure. There may also be risks associated with certain groups of patient, eg. paediatrics, neonates or immunosuppressed patients. The trust policy will define how the different risk groups are to be treated. For example, there might be tighter prescribing restrictions on certain groups, re-evaluation of risk and need might differ and the level of record keeping might vary.

(ii) Procurement/receipt

This stage of assessment can be considered primarily as an assessment of quality. Risk assessments would again be made on the basis of a range of criteria although there may be some overlap with the previous section. A quality risk assessment would generally be based on criteria relating to the supply. As in the previous section, the specific product supply can be assigned to a risk group based on a number of criteria. For example, quality related risks could be assessed on the basis of knowledge of and confidence in the manufacturer, historical analytical testing data, certificate of analysis information, audit and whether the product is licensed in its country of origin. The trust policy will define how the different risk groups are to be treated. For example, there might be a requirement to subject certain groups (eg. high risk) to a full quality control analysis. There needs to be an on-going review of these assessments in the light of experience. Thus, the first supply from a new manufacturer might be considered 'high risk' and require close scrutiny. After a number of satisfactory supplies, the risk might be

reassigned to a lower group. This assessment might also need to be reviewed for each repeat request or periodically and this will be defined in the trust policy.

Risks associated with transmissible spongiform encephalopathies (TSE), need to be given some consideration. For a number of years, for licensed medicines, the MHRA have required evidence of compliance with the TSE guideline as part of the licensing process and the user could safely assume that any potential risk had therefore been addressed. As unlicensed medicines have not been through the licensing process the same assumption could not be made and there was an onus on the user to seek an assurance that the product had been manufactured in accordance with the TSE guideline.

In 2003, SI 2003 No. 1680 came into force. This states that no person shall import or market an unlicensed product unless that product has been manufactured in accordance with the TSE guideline. It might therefore now be presumed that if an unlicensed medicine is supplied, which proves to carry a risk from TSE and any harm to a patient is caused, that the person importing or marketing that product would be held liable.

Notwithstanding SI, 2003 No. 1680, it must still be recognised that individual unlicensed medicinal products do not go through the same independent scrutiny as licensed products and that, in the short term, manufacturers of unlicensed medicines might not have been able to obtain all the necessary evidence of compliance for all their products. It is therefore recommended that, at least for a period of time, certification of compliance with the TSE guideline be obtained from each manufacturer for their products and these are held on file.

WARNING

A practitioner prescribing an unlicensed product or for an unlicensed indication, does so on his/her own responsibility. Consequently he/she carries the burden of the patient's welfare and in the event of adverse reactions he/she may be called upon to justify his/her actions.

A pharmacist will share responsibility:

- 1 as the purchaser of the product, particularly where this involves specifying the product to be purchased;
- 2 if his/her actions or omissions have contributed to the harm.

RECOMMENDATIONS TO PRESCRIBERS

- 1 It is important to remember that whenever an unlicensed medicine is prescribed or a licensed medicine is prescribed for an unlicensed indication, the prescriber is **PROFESSIONALLY ACCOUNTABLE** for his/her judgement in so doing, and may be called upon to justify his/her actions.
- 2 Similarly a pharmacist who is responsible for the manufacture or preparation of an unlicensed medicine in response to a prescription is **PROFESSIONALLY ACCOUNTABLE** for any harm caused by a defect in the medicine which is attributable to his/her own actions or omissions.
- 3 Before an unlicensed medicine is to be prescribed for the first time or before 'off-label' usage, there needs to be a critical, evaluation of evidence or peer review (risk assessment). This will generally involve approval through the Drug and Therapeutics Committee. The mechanism for this will vary from one organisation to another and will be described in detail in the trust policy.
- 4 Some unlicensed medicines cannot be manufactured or prepared within a hospital pharmacy and must be purchased from a "specials" manufacturer. This may result in some delay in obtaining the supply and might involve discussions between the prescriber and pharmacist in order to draw up a suitable product specification.
- 5 A hospital consultant having extensive knowledge of medicines used in a particular speciality, may feel confident in using licensed medicines for unlicensed indications. However, this decision should be explained to the patient's general practitioner if the latter is requested so to prescribe.
- 6 A general practitioner is not obliged to prescribe in such circumstances.
- 7 A dispensing doctor who orders unlicensed medicines from a "specials" manufacturer carries the same responsibility as a pharmacist procuring a special.

See **"RECOMMENDATIONS TO PHARMACISTS"**

RECOMMENDATIONS – TO PHARMACISTS

1 Establish a clear trust policy.

It is recommended that this policy be written within pharmacy and formally ratified by the Drug and Therapeutics Committee. Within the policy, a senior pharmacist should be designated as having overall responsibility for controlling the procurement and supply of unlicensed medicines. It is, however, not unusual for several pharmacists to be involved in the procurement of an unlicensed medicine and everyone from the ward/clinical pharmacist, who may first receive the request, through to the person who signs the order or authorises the invoice should be involved in the decision making process. The policy should detail inter alia the responsibilities of all staff involved in the supply of unlicensed medicines.

A record should be kept, including:

- name of product;
- specification;
- prescriber's name, if appropriate;
- manufacturer and (if different) supplier;
- date ordered;
- quantity ordered;
- batch number received.

In addition, SI 1994/3144 states that any person selling or supplying an unlicensed medicine is obliged to maintain and keep for a period of at least five years, a record of that supply (see 3.7 below). This is confirmed by MAL 81, which refers to an "Obligation on person selling or supplying medicinal products (the manufacturer or wholesale dealer) to maintain certain records". The extent of record keeping appropriate to the issue of unlicensed medicines within an organisation needs to be defined following an assessment of risk and the need to have an audit trail in the event of a product recall or adverse reaction. Any requirement for record keeping should be written into the policy. More detailed guidance on writing a trust policy is contained in Appendix 3.

2 Ensure that the prescriber is always aware that a medicine he/she has requested is only available as an unlicensed product. A signed request form may be appropriate, but it is for each hospital to establish a suitable local policy and procedure.

Where a particular unlicensed medicine is to be ordered for the first time, there needs to be a critical, evidence based evaluation for its use (risk assessment). An appropriate forum for this evaluation is the Drug and Therapeutics Committee, although it is recognised that, when items are needed urgently, they may need to be reviewed retrospectively. The role of the pharmacist in assessing the evidence and challenging use is important and the designated pharmacist should be involved in the Drug and Therapeutics Committee

evaluation process. A pro-forma order form can be a useful aid to documenting the decision making process.

Ask whether a similar, licensed medicine would be acceptable (see Guidance Note 14).

Ask whether a similar unlicensed medicine already in use in the trust would be acceptable.

Where a consultant requests an unlicensed medicine confirm whether junior medical staff will be permitted to prescribe it. If a member of the junior medical staff requests an unlicensed medicine this request should be refused and referred to the appropriate consultant.

3 Follow the steps below in the procurement of the product:

3.1 Ensure that the manufacturer of the unlicensed product holds the appropriate licence.

In particular, a manufacturer's "specials" licence may only cover a restricted range of products:
eg terminally sterilised products, but not aseptically prepared ones;
solid dosage forms, but excluding antibiotics.

3.2 Consider any available audit reports on the manufacturer.

3.3 BEFORE placing an order prepare a specification for the product.

As well as the formula, include details such as container type, sterilisation requirements, environmental conditions, assay limits etc. The regional quality assurance specialist can provide technical assistance, also advising whether samples will be required for testing before the product is used. It should be recognised that any holder of a manufacturer's "specials" licence has a responsibility for ensuring that their products are manufactured under appropriate environmental conditions and that, where applicable, they are correctly sterilised. Part of the specification may therefore be a statement that the product should be made in accordance with the requirements of the Rules and Guidance for Pharmaceutical Manufacturers and Distributors, 2002.

An appropriately validated shelf-life should be applied. Where the product is procured from a "specials" manufacturer and is part of their normal product range, the shelf-life may have been validated by the manufacturer. They might also be able to offer advice based on knowledge of similar products. If the product is a novel formulation advice from the local or regional quality assurance specialist should be obtained before assigning a shelf-life. If the product is likely to be used regularly, this should be followed up by a valid stability study. Purchasers need to be aware that stability studies are expensive to perform and be prepared to build this into the cost of the product.

It is acceptable to base a specification on information given by the manufacturer. However, in all cases, this specification should then become a condition of the order.

- 3.4 Assurance should always be obtained from the manufacturer that the specification has been complied with. A certificate of analysis or certificate of conformity should be requested.
- 3.5 Operate a system whereby incoming unlicensed medicines are identified and quarantined by the storekeeper. Without such a system they could be mistaken for normal licensed products and placed in stock without the necessary controls being applied.
- 3.6 Upon receipt, the unlicensed medicine and associated documentation should be formally checked, and any testing deemed necessary should be carried out, before it is released for use by a nominated pharmacist (see Appendix 2). Certificates of analysis or conformity should be scrutinised and filed as part of a complete batch record.
- 3.7 On sale or supply, complete any records that need to be kept. Records should show:

- the source from which that person obtained the product;
- the person to whom and the date on which the sale or supply was made;
- the quantity of each sale or supply;
- the batch number of the batch of that product from which the sale or supply was made;
- details of any suspected adverse reaction to the product sold or supplied of which he/she is aware.

Any person required to keep such records must notify the licensing authority of any suspected adverse reaction and make the records described above available for inspection by the licensing authority at all reasonable times.

- 3.8 It may be appropriate to label the product to the effect that it is for use only by the patients of a particular prescriber.
- 4 Whenever an unlicensed medicine is reordered, confirm that it is to be used as originally agreed.
- 5 Monitor the usage of unlicensed medicines. The more they are used, the more likely it is that control of them will slip.
- 6 To underpin this monitoring of usage and to demonstrate adequate control of unlicensed medicines, as required by the Medicines Management Framework and the Controls Assurance Standard for Medicines Management, a system of

audit should be introduced. Suggested audit checklists are given in Appendix 4.

A more detailed consideration of the steps in section 3 above is provided in the Appendices.

This document is based on:-

- (i) The Medicines Act 1968;
- (ii) Rules and Guidance for Pharmaceutical Manufacturers and Distributors, 2002;
- (iii) Directive 65/65/EEC;
- (iv) The Medicines for Human Use (Marketing Authorisations etc) Regulations 1994, SI No.3144;
- (v) MCA Guidance Note No.14 “The Supply of unlicensed relevant medicinal products for individual patients”. Revised February 2000;
- (vi) Medicines Act Leaflet No. 81, 1995;
- (vii) The Unlicensed Medicinal Products for Human Use (Transmissible Spongiform Encephalopathies) (Safety) Regulations 2003, SI No. 1680;
- (viii) NHS Executive. Controls Assurance Standards. NHS Executive, October 2003;
- (ix) DoH. Medicines Management in NHS Trusts: Hospital Medicines Management Framework, 2003.

Non-UK Marketing Authorisation for Medicines

This appendix gives the wording and format used to denote the marketing authorisations (equivalent to the UK product licence) used in a range of countries from which imported medicinal products are most commonly sourced.

It must be noted that the presence of a non-UK marketing authorisation confers no status on the medicine in the UK.

AUSTRALIA

Prefix: Aust R
 Suffix: none
 eg. AUST R 16273

AUSTRIA

Prefix: Z. Nr
 Suffix: none
 eg. Z. Nr.: 1-18627

BELGIUM

Prefix: none
 Suffix: none
 eg: 922 IS 32 F3

EIRE

Prefix: PA
 Suffix: none
 eg: PA 40/78/1

FRANCE

Prefix: AMM
 Suffix: none
 eg: AMM 317 161.8

this also appears as a bar code on the outer pack
 but without the prefix

GERMANY

Prefix: Zul-Nr
 Suffix: none
 eg: Zul-Nr 808.00.01

GREECE

Prefixes: AP.ΕΓΚΑ - upper case
αρ.εγκα - lower case

Suffix: AP.ΑΔ.ΚΥΚΛΕ.Ο.Φ - upper case
Αρ.Αδ.Κυκλ.Ε.Ο.Φ - lower case
none

eg: AP.ΕΓΚΑ 29018/20.10.89 - new format
AP.ΕΓΚΑ Α6Α 2731/9871/73- old format

ITALY

Prefix: none
Suffix: Min Sanità
eg: 022760019 Min Sanità

this also appears as a bar code on the outer pack,
prefixed by “A”

NETHERLANDS

Prefix: RVG
Suffix: none
eg: RVG 09209

PORTUGAL

Prefix: Registo no.
Suffix: none
eg: Registo no. 8218313

this also appears on bar code label without prefix

SPAIN

Prefix: Reg DGFPS No
Suffix: none
eg: Reg DGFPS 56.920

this number sometimes does not appear on the outer pack, but
only on inner packaging (eg. tablet strip packs) without prefix

UNITED STATES

Prefix: NDC
Suffix: none
eg: NDC 54686-399-18

The Quality Assessment of Unlicensed Medicines

Introduction

This Appendix gives further consideration to the quality assessment for unlicensed medicines covered under the 'Recommendations to pharmacists' in the main document, and suggests minimum suitable measures.

However, in view of the diversity of products and suppliers, there must always be the freedom to exercise discretion locally as to the measures to be applied in the case of a particular product.

Recommendation 3 in the section entitled 'Recommendations to pharmacists', makes reference to measures associated with the following:

- 1 manufacturing licences;
- 2 audit reports;
- 3 specifications;
- 4 certificates of analysis or conformity;
- 5 formal checks on receipt of the product;
- 6 testing of products.

The extent to which each of these measures is desirable or can be achieved will vary from product to product, due to the wide variety of unlicensed medicines in use and the diverse sources of supply. The final decision as to whether a product is accepted for use will therefore depend upon the overall picture obtained.

Sources of unlicensed medicines

Sources of unlicensed medicines include the following:

Commercial "specials" manufacturer

A commercial manufacturer holding a manufacturer's "specials" licence.

'Ethical' company with a UK base

A company whose main business is the manufacture of licensed products, but who will supply unlicensed products for individual patient use.

Importer of licensed products from an EC country

An importer of medicines from an EC country where the product is licensed in that or another EC country

Importer of licensed products from a non-EC country

An importer of medicines licensed in countries outside the EC.

Importer of unlicensed medicines

An importer of unlicensed medicines (EC or non-EC)

NHS Hospital manufacturing unit

A hospital manufacturing unit, holding a manufacturer's "specials" licence.

General considerations

Before moving to a discussion of the individual quality control measures in relation to the various sources of supply, there are some general considerations that need to be taken in to account.

One factor which may influence the application of this guidance to some extent is the degree of risk attaching to the use of the product. For example, parenteral products may be considered to carry a greater degree of risk than oral products or topical applications. Products which have previously been licensed but have had licences withdrawn because of safety concerns would be regarded as higher risk than those whose licence had been voluntarily withdrawn for economic reasons.

The label should contain all the information necessary for the safe administration of the product. Where appropriate the route(s) of administration should be clearly stated.

Imported products which are not labelled in English carry a greater risk than those which are. Where the product has not been overlabelled in English there is the problem of obtaining an accurate translation, and where it has been overlabelled there is the problem of verifying that the translation is correct.

The degree of risk associated with the use of a product may also influence other matters of policy in relation to the handling of the product, eg the recording of patient names on issue, and the documentation of informed patient consent.

In some circumstances adequate testing is not practicable (eg insufficient or hazardous material, material requiring special facilities such as immunological or blood products or emergency situations for individual patients). In such cases, the prescribers/users of the product should be informed so that they can make a judgement in relation to the likely risk(s) versus benefit(s) to the patient.

Quality control measures in relation to sources of supply

1 Manufacturing licences

Where the source of supply is a **commercial "specials" manufacturer or hospital manufacturing unit**, it should be confirmed that the manufacturer holds the appropriate licence, and that this covers the types of product being purchased.

Products should not be obtained from manufacturers who claim or imply a Section 10 exemption for what is in effect the regular supply of “specials”.

Where the source of supply is an **importer** the licence status both of the product and the manufacturer should be ascertained. (This may not always be clear from numbering which appears on the label, especially if the label is in a foreign language – see Appendix 1.)

2 Audit of manufacturer

Reference should be made to any audit reports on the manufacturer held on file by the regional quality assurance specialist. The more recent the report, the more reliance can be placed upon it, since circumstances will change with time.

In practice, an audit report may be available for a **commercial “specials” manufacturer**, but is less likely to be held for a manufacturer of a product supplied by an **importer**.

Assurance regarding a **hospital manufacturing unit** is usually available, eg from local knowledge or through the regional quality assurance specialist.

Audits are occasionally carried out by purchasers on a **hospital manufacturing unit**, particularly where quantities of products are being regularly purchased.

Whilst the possession of a recent audit report on every manufacturer of purchased “specials” is desirable, audit visits are often not practicable, and where they are the resources to make them are very limited. Visits may particularly be made, however, when it is desirable to address particular issues with a company.

Some manufacturers produce company brochures which can provide useful information.

3 Specifications

(i) new products

When a product is being commissioned from a **commercial “specials” manufacturer**, or a **hospital manufacturing unit**, there should be agreement on the specification (Note 1) before the order is placed. If the product is already established in the range of the manufacturer, then (ii) below applies.

In the case of the other categories of supplier, the specification will already be established, and (ii) below applies.

(ii) established products

Where the product is an established product in the range of a manufacturer, a specification should nevertheless be obtained whenever possible, and confirmed to be appropriate to the intended use.

4 Certificates of analysis and certificates of conformity

(i) Certificates of analysis

A certificate of analysis (Note 2) is batch specific and provides documentary evidence to the purchaser that the batch in question has been tested and that satisfactory results have been obtained.

A certificate of analysis should therefore be obtained with every batch of an unlicensed medicine from all suppliers whenever possible. Certificates of analysis should be requested when orders are placed, as it may be much more difficult to obtain them retrospectively.

A certificate of analysis should state the results of all tests carried out, giving numerical results where a quantitative test is involved. It should also include a summary of the specifications as relevant to the tests, including numerical limits, unless the specification has been provided separately.

Certificates of analysis should be signed by an authorised signatory of the quality control department.

(ii) Certificates of conformity

Certificates of conformity state that batches of an unlicensed medicine supplied comply with the specification. They do not contain specific test results but should be batch specific and contain a statement of, or reference to, the specification. The current specification should be available, against which the certificate should be checked.

5 Formal checks on receipt of the product

A formal check on receipt should be carried out on all batches of unlicensed medicines from all suppliers. The checks may be carried out by authorised technical staff, however, approval for use should be by the quality controller or other designated pharmacist. Checks should include:

- (i) appearance of the product and packaging;
- (ii) information appearing on the label;
- (iii) a careful check of any certificates provided against the current specification.

If the label and/or information leaflet are in a foreign language, a translation should be obtained either from the importer or a specialist translator.

6 Testing of products

Testing in this context includes assay where feasible and other appropriate tests, though not necessarily full testing, as for example in a BP monograph. The obligation is on the purchasing organisation to satisfy themselves that an unlicensed medicine complies with their required specification. Testing might

also be deemed necessary to supplement a certificate of analysis for local usage.

- (i) testing of initial batches from a manufacturer until confidence established.

When a purchaser begins to purchase “specials” from a particular **commercial “specials” manufacturer**, initial batches should be tested until confidence in the manufacturer has been established. The number of batches to be tested will depend upon such factors as the results obtained, the audit report if available, the quality of the certificates of analysis provided, and the general standard of presentation of the products (packaging, labelling, appearance).

Results of testing of “specials” should be collected centrally through the Analytical Information Centre (AIC). Collated data available to regional quality assurance specialists may then be used locally to supplement the hospital’s own experience of the manufacturer and allow the amount of testing to be reduced.

A similar approach should be adopted with regard to “specials” from a **NHS hospital manufacturing unit**, although additional information on such units may be available which can also be taken into account. There are particular instances where testing may also be considered unnecessary, eg where a hospital has developed a product for a particular consultant, which has become established, and the usage of which has spread to other hospitals.

It will probably not be considered necessary to test a product from an **‘ethical’ company with a UK base**, or a product supplied by an **importer of licensed products from an EU country (Appendix 1)**, but this will be a matter of judgement.

Products supplied by an **importer of licensed products from a non-EU country** should ideally be tested, particularly if it has not proved possible to obtain the specification, unless the product is licensed in that country and the standards of manufacture and quality assurance are equivalent to those applied in the EU, eg products which are manufactured and licensed in countries with EU mutual recognition of inspection systems (Appendix 5).

Products supplied by an **importer** which are **unlicensed medicines** in the country of origin should ideally be tested, particularly if it has not proved possible to obtain the specification.

There may, however, be problems in testing products in the last two categories above since, for example, a convenient assay method may not be available, or the product may contain unknown ingredients which interfere with the assay of the active ingredient, or the product may be of a complex nature.

- (ii) testing of initial batches of each new product from a manufacturer

If the performance of a **commercial “specials” manufacturer**, or **hospital manufacturing unit**, is satisfactory in accordance with (i) above, and

confidence continues to be maintained, then it may not be necessary to test initial batches of new products from the manufacturer.

By analogy with (i) above, it will probably not be necessary to test a new product from a known manufacturer in the case of an **‘ethical’ company with a UK base**, or an **importer of licensed products from an EU country**.

Irrespective of the above, however, the testing of initial batches of new products may be advisable where there are concerns about the possible quality of the product, eg products that are believed to have problems with stability or possibly contain toxic impurities or degradation products.

A new product supplied by an **importer of licensed medicines from a non-EC country** should ideally be tested, particularly if it has not proved possible to obtain the specification, unless the product is licensed in that country and the standards of manufacture and quality assurance are accepted as equivalent to those applied in the EC, eg by virtue of a mutual recognition agreement with the MHRA (see Appendix 5).

A new product supplied by an **importer** which is an **unlicensed medicine** in the country of origin should ideally be tested, particularly if it has not proved possible to obtain the specification.

- (iii) routine testing of every batch of every product received

It should not be necessary to test routinely every batch of every product received. However, this remains at the discretion of the purchaser.

Summary of suggested minimum suitable measures

A summary of the suggested minimum suitable measures for the quality assessment of unlicensed medicines, is given in the model decision trees at the end of this document.

However, in the application of these measures the general considerations in this Appendix should be taken into account, and the freedom must remain locally to determine the measures to be applied in the case of particular products.

Final approval or rejection of the product

The approval of a product for use should be documented. When a product is rejected, the reasons for this should be recorded.

Note 1

Specifications for finished products should include the following elements, as in the Rules and Guidance for Pharmaceutical Manufacturers and Distributors, 2002, paragraph 4.13:

- (a) The designated name of the product and the code reference where applicable;
- (b) The formula or a reference to it;
- (c) A description of the pharmaceutical form and package details;
- (d) Directions for sampling and testing or a reference to procedures;
- (e) The qualitative and quantitative requirements, with the acceptance limits;
- (f) The storage conditions and any handling precautions, where applicable;
- (g) The shelf-life.

Note 2

UK Guidance on certificates of analysis is given at the end of the Guide to Good Manufacturing practice for medicinal products in Rules and Guidance for Pharmaceutical Manufacturers and Distributors 2002, p32.

APPENDIX 3

Trust Policy for the Use of Unlicensed Medicines

This appendix gives further guidance on the establishment of a trust policy for the prescribing, procurement, supply and use of unlicensed medicines. It is recognised that any trust policy must be written in such a way as to integrate with and be compatible with the individual trust's documentation system, policies and procedures. This additional guidance is therefore intended to indicate items which need to be included within the policy and how this might be formatted rather than simply to provide a sample policy.

Definition

A trust policy is a document that summarises the organisation's overall philosophy, intentions and approach to be used to ensure the safe and effective handling of unlicensed medicines. It is a high level document and should be approved by top level management within the organisation.

Scope

All activities relating to the use of unlicensed medicines should be covered. This includes controls on prescribing, procurement, quality assessment, issue, risk assessment and record keeping.

Format

The trust policy should be seen as a summary document. It should therefore be brief, concise and clear. Whilst it should contain sufficient information to stand alone, it should not repeat in detail information documented elsewhere. Where appropriate, reference should be made to existing documents and sources of information. It would not generally contain the day to day detail associated with procurement and supply as, unless the organisation had fairly limited use of unlicensed medicines, this would be contained in standard operating procedures (SOP's).

Content

The trust policy should contain information on the following, which are suggested as section headings.

1. Scope

This will generally be a fairly brief statement of the overall scope and purpose of the policy. A suitable example of wording may be:

“This policy document describes the trust policy for the procurement and use of unlicensed medicinal products (often called "specials"). These are unlicensed medicines which have been specially prepared by the holder of a manufacturer's “specials” licence or imported in response to or in anticipation

of the order of a doctor or dentist to meet the special needs of individual patients.”

It will also state whether other types of unlicensed products are covered, such as those prepared under a Section 10 exemption, clinical trials and off-label usage.

Where appropriate it will make general reference to relevant SOP's.

2. Introduction

This section will give a brief introduction into the licensing of medicinal products and marketing authorisations and the reasons and circumstances when products might be used without appropriate licences.

A suitable opening paragraph might be:

“In order to ensure that medicines are safe, effective and of appropriate quality, their manufacture and sale or supply is controlled by national and EU legislation. Accordingly no medicinal product may be placed on the market unless a marketing authorisation (formerly product licence) has been granted. In order to preserve prescriber's clinical freedom, the legislation gives some exemptions from full control. Thus, medicinal products that are not licensed may be prescribed in order to fulfil special needs in individual patients on the direct personal responsibility of the prescribing clinician.”

This would then be followed by examples of the types of product or usage which would be considered unlicensed (eg. Section 10, off-label, investigational products, imported products and repacked products).

This section should also contain a statement to the effect that unlicensed medicines should only be used when there is no pharmaceutically equivalent licensed product or suitable licensed alternative available at the time the patient needs it. A statement of liability can usefully be included in this section.

3. Types of unlicensed medicines

Under this section, the different categories of unlicensed medicine covered by the policy can be discussed in more detail together with any special issues relating to them.

Where the handling of the different categories of unlicensed medicines is dependent on a risk assessment, reference to this should be made in this section, although more detailed information will be included under the sections on prescribing and procurement. It is common to assign products/usage to risk groups (eg. high, medium, low) and this can be done on a range of criteria and will probably differ from organisation to organisation. This section should describe the general risk assessment principles and how they are applied to the different groups.

4. Consent and patient information

The trust's policy on obtaining the consent of the patient, carer or parent should be outlined here together with steps to be taken to inform patients. There is no explicit requirement to obtain consent on the basis of a medicine being unlicensed therefore the trust's policy on consent may be referred to.

Within this section, it has to be recognised that there are circumstances where involving the patient in decisions is inappropriate and impractical (eg. use of a stock line in theatres and emergency boxes). This needs to be described and the circumstances in which consent and information apply need to be outlined.

A statement outlining the trust's commitment to respecting the right of patients, carers and parents to participate in discussions regarding the health care of the patient should be included. Patients must be made aware that they are being prescribed an unlicensed medicine and should be given a generic patient information leaflet (PIL), a model of which is given as Appendix 6. In drawing up a PIL, it is important to ensure it is written in 'plain English' and it should therefore be referred to any such group within the trust, for comment and/or approval. Consideration might also need to be given to providing translations.

5. Key personnel and their roles and responsibilities

Within this section the key personnel involved in the prescribing and supply of unlicensed medicines should be described and their roles and responsibilities discussed.

The key personnel generally include:

- prescriber responsible for the care of the patient;
- trust designated pharmacist;
- pharmacy staff involved in the procurement process;
- clinical pharmacist;
- pharmacy staff involved in the dispensing process;
- nursing staff responsible for administration.

In this section, the roles and responsibilities of the Drugs and Therapeutics/ Medicines Management Committee should be described.

6. Prescribing/requesting

This section contains information on the process to be followed when prescribing or requesting unlicensed medicines. There will generally be a distinction between first time requests and repeat orders and the different types of unlicensed products or usage covered by the policy might to be discussed separately. Dependant upon the trust's documentation systems, this section might contain full details of the procedures to be followed or might contain an

overview together with a reference to any appropriate standard operating procedures (SOP's).

Circumstances where the request would be the subject of a risk assessment need to be discussed and details of this process and the criteria to be used need to be included. Reference to any appropriate risk assessment documentation needs to be made, and any associated forms may be included as appendices.

7. Procurement

This section contains information on the process to be followed for the procurement, receipt, quality assessment and issue of unlicensed medicines. Where appropriate, the various sources of unlicensed medicines covered by the policy (eg. imports, Section 10 preparation, manufacture by NHS or commercial holders of manufacturer's "specials" licences) would be described separately. Dependant upon the trust's documentation systems, this section might contain full details of the procedures to be followed or might contain an overview together with a reference to any appropriate SOP's.

Circumstances where procurement would be the subject of a risk assessment need to be discussed and details of this process and the criteria to be used need to be included. Reference to any appropriate risk assessment documentation needs to be made, and any associated forms may be included as appendices. Generally, each new supply would be subjected to a procurement risk assessment and where the processing of the product depends on the outcome of this assessment (for example the application of any in-house quality control testing) details of this need to be included.

8. Record keeping

In this section, details of all record keeping relating to the procurement and issue of unlicensed medicines are given. Dependant upon the trust's documentation systems, this section might contain full details of the records to be kept or might contain an overview together with a reference to any appropriate SOP's.

There will usually be sections describing receipt records and issue records and there might, where appropriate, be reference made to the records kept in relation to quality assessments.

Where the level of record keeping is dependent on the results of risk assessment, details of this would be included in this section.

The length of time for which records are to be retained will be defined or reference made to other trust policies. As a minimum, SI No.3144/1994 requires records to be kept for 5 years.

9. Adverse drug reactions and defective products

A brief description of the procedure to be followed for the reporting of ADR's will be included. Generally the same system of reporting as used for licensed products is used, and reference to the 'Yellow Card' system and any related trust SOP's should be given.

The reporting of suspected defective products is to be described. This will usually be the same as for licensed products and will generally involve reporting initially to the pharmacy department who will then report through regional quality control to the national AIC. Reference to any related SOP's will be made.

AUDIT SCHEME FOR THE PROCUREMENT AND SUPPLY OF UNLICENSED MEDICINAL PRODUCTS (SPECIALS)

HOSPITAL:

Date:

Management	Yes/No/Partial	Assess/Records	Comments
1 A clear trust policy has been established for the use of unlicensed medicinal products		Documents	(Ref p8 NHSPQAC)
2 The policy has been ratified by the trust Drugs and Therapeutics Committee or equivalent.		Documents	(Ref p8 NHSPQAC)
3 A senior pharmacist has been designated as having overall responsibility for controlling the procurement and supply of unlicensed medicines (preferably noted within the policy document).		Assess/Documents	(Ref p8 NHSPQAC)
4 The trust policy provides details in accordance with national guidelines, including: a. roles and responsibilities of all staff involved in the supply and use of unlicensed medicines b. how unlicensed medicines are approved for use c. how they are obtained d. issues of patient consent e. the quality assurance processes applied to unlicensed medicines f. prescriber liability g. continuation of supply on discharge (if required) h. record keeping requirements		Assess/Documents	(Ref p8 NHSPQAC)
5 The evaluation of the clinical need for unlicensed medicines is documented (in cases of urgency or long standing use this may be reviewed retrospectively)		Documents	(Ref p3 GN14, p8-9 NHSPQAC)

6	The evaluation of the clinical need for unlicensed medicines is evidence based, the designated pharmacist is involved in the evaluation process, there is input from Senior Clinicians, Clinical Pharmacists or the Drugs on Therapeutics Committee		Assess/Documents	(Ref p8-9 NHSPQAC)
7	Consideration is given in the evaluation process as to whether similar licensed medicines or similar unlicensed medicines already in established use, may be used as alternatives.		Assess/Documents	(Ref p3 GN14, p9 NHSPQAC)
8	A mechanism is in place to ensure prescribers are notified that they are prescribing an unlicensed medicine (this may be covered by a blanket trust waiver if a Drugs and Therapeutics approval process or formulary approach is used).		Assess/Documents/Records	(Ref p4-5 GN14, p8 NHSPQAC)
9	The prescribing of unlicensed medicines is restricted to senior medical staff only (this may be widened to all medical staff if a Drugs and Therapeutics approval process or formulary approach is used).		Assess/Documents/Records	(Ref p9 NHSPQAC)
10	A mechanism is in place to communicate with GP's that an unlicensed medicinal product is required to be continued in the community setting (a GP is not obliged to continue to prescribe in such circumstances)		Assess/Documents	(Ref p7 NHSPQAC)
11	A standard operating procedure is in place to establish the credentials and suitability of the manufacturer/supplier/importer of an unlicensed medicine prior to placing an order. This should include confirmation that the appropriate licence for the product type being procured, is held. Reference is made to regional QA specialists, any available supplier audits or information from the Analytical Information Centre database.		Documents	(Ref p9 NHSPQAC)
12	There is a procedure in place to establish compliance with the TSE guidelines.		Assess/Documents	(Ref p6 NHSPQAC)
13	Product specifications are available for all unlicensed medicines used (including established products)		Assess/Documents	(Ref p9, 16 NHSPQAC)

14	<p>Product specifications contain the following information:</p> <ul style="list-style-type: none"> a. the designated name of the product and the code reference where applicable b. the formula or reference to it c. a description of the pharmaceutical form and package details d. directions of sampling and testing or a reference to procedures e. the qualitative and quantitative requirements with acceptance limits f. the storage conditions and handling precautions where applicable g. the shelf life 		Documents	(Ref p20 NHSPQAC, p73 OG)
15	Certificates of analysis or certificates of conformity are requested when orders for unlicensed medicines are placed, unless otherwise justified.		Documents	(Ref p10 NHSPQAC)
16	The licensed status in the country of origin and the country of origin itself is established prior to placing an order with an appropriately licensed importer.		Documents/Procedures	(Ref p18-19 NHSPQAC)
17	English labeling, patient information leaflets and summary of product characteristics are requested (and obtained where available) for all imported medicines from non-English speaking countries.		Procedures/Assess	(Ref p17 NHSPQAC)
18	Patient names are not divulged to the manufacturers/suppliers of unlicensed medicines (breach of patient confidentiality). The use of code numbers, initial or a statement "for a patient of Dr" may represent suitable alternatives.		Assess	(Ref p3 NHSPQAC)

Receipt		Yes/No/Partial	Assess/Records	Comments
19	A system is operated whereby incoming unlicensed medicines can be readily identified by the storekeeper.		Assess/Documents	(Ref p10 NHSPQAC)
20	All Incoming unlicensed medicines are placed in quarantine until they can be evaluated by the quality controller or designated pharmacist.		Assess	(Ref p10 NHSPQAC)
21	Records are made on receipt of unlicensed medicines of the following, name of product, manufacturer (and supplier if different), date ordered, quantity ordered, date received, quantity received and batch number received.		Assess/Records	(Ref p8 NHSPQAC)
Quality Assurance		Yes/No/Partial	Assess/Records	Comments
22	<p>A formal check on receipt is carried out on all batches of unlicensed medicines from all suppliers by staff authorized in accordance with the trust policy. Checks should include:</p> <ul style="list-style-type: none"> a. the appearance of the product and packaging b. information appearing on the label c. careful scrutiny of any certificates provided 		Assess/Documents/Records	(Ref p17 NHSPQAC)
23	<p>Certificates of Analysis for unlicensed medicines are assessed for acceptability and must:</p> <ul style="list-style-type: none"> a. identify the organisation issuing it b. be authorised by a person competent to do so, stating qualifications and position c. name the material to which it refers and identify it by batch number d. state that the material has been tested, by whom and when this was done e. state the specification and/or acceptance limits f. give the test results obtained or state compliance with specification 		Records	(Ref p32 OG)

24	Certificates of conformity for unlicensed medicines are assessed for acceptability. They do not contain specific test results but must: a. identify the organisation issuing it b. be authorised by a person competent to do so stating qualification and position c. name the material to which it refers and identify it by batch number d. contain a statement of, or reference to, the product specification		Records	(Ref p17 NHSPQAC)
25	The current product specification is always available against which the certificate of analysis or conformity is checked.		Assess/Documents/Records	(Ref p17 NHSPQAC)
26	If the label and/or information leaflet are not in English a translation is always obtained (either from the supplier or a specialist translator).		Assess	(Ref p17 NHSPQAC)
27	If additional quality control testing (e.g. assay, identify test, sterility etc.) is deemed necessary, the testing methodologies and acceptance limits are always specified in a product specific QC procedure/document.		Assess/Documents/Records	(Ref p18-19 NHSPQAC)
28	The documentation associated with the release process is kept on file as a batch specific record (certificates of analysis, release forms, any test results, any risk assessment made, translations etc).		Records	(Ref p19 NHSPQAC)
29	The results of any product testing of unlicensed medicines are passed on to the Analytical Information Centre for incorporation into the database (this may be collated via regional quality control).		Assess/Documents/Records	(Ref p18 NHSPQAC)
30	The approval for use (release) of unlicensed medicine is by the designated pharmacist or an appropriate quality controller.		Assess/Documents/Records	(Ref p17 NHSPQAC)
31	The approval for use is documented. Likewise if a product is rejected the reasons for this are recorded.		Records	(Ref p19 NHSPQAC)

32	In circumstances where adequate testing is not practicable, the prescriber/user of the product is always informed so that the risk versus benefit to the patient can be assessed. This communication is always documented.		Assess/Documents/Records	(Ref p15 NHSPQAC)
Storage		Yes/No/Partial	Assess/Records	Comments
33	Segregation of unlicensed medicines is in accordance with the trust policy.		Assess/Documents	
34	Unlicensed medicines are stored in accordance with their labeled instructions.		Assess/Records	
35	All storage areas are monitored for temperature and appropriate records kept.		Assess/Records	(Ref p312-313 OG)
Record Keeping		Yes/No/Partial	Assess/Records	Comments
36	Records of receipt of unlicensed medicines are kept as described in 21 above.		Assess/Records	(Ref p8 NHSPQAC)
37	Records of issue are kept in accordance with the trust policy.		Records	(Ref p10 GN14, p10 NHSPQAC)
38	All records are kept for a minimum of 5 years and in accordance with the trust policy.		Assess/Documents/Records	(Ref p10 GN14)
39	Any suspected adverse reactions to unlicensed medicines are reported to the MHRA via the 'Yellow Card' scheme (indicating that the product is unlicensed).		Assess/Documents	(Ref p10 GN14, p10 NHSPQAC)
Consent/Information		Yes/No/Partial	Assess/Records	Comments
40	A system is in place, which ensures that consent is obtained and recorded in circumstances where this is required by the trust policy.		Assess/Documents/Records	
41	A mechanism is in place, which informs patients, where appropriate that they may receive unlicensed medicines during the course of their treatment.		Documents	
42	Where required by the trust policy, patients are supplied with a generic PIL outlining the use of unlicensed medicines and giving advice on obtaining further supplies.		Documents	

REFERENCES

- NHSPQAC - Guidance for the Purchase and Supply of Unlicensed Medicinal Products – Notes for Prescribers and Pharmacists. NHS Pharmaceutical Quality Control Committee. 3rd Edition, June 2004.
- GN14 - The supply of unlicensed relevant medicinal products for individual patients. MCA Guidance Note No. 14. Medicines and Healthcare products Regulatory Agency. Revised February 2000.
- OG - Rules and Guidance for Pharmaceutical Manufactures and Distributors 2002. London. The Stationery Office, 2002

APPENDIX 5

Countries accepted as having standards of manufacture and quality assurance equivalent to those applied in the UK by virtue of EU mutual recognition of inspection systems.

Australia

Canada

European Union Countries

Japan

New Zealand

Switzerland

MODEL PATIENT INFORMATION LEAFLETS FOR UNLICENSED MEDICINES

PATIENT INFORMATION LEAFLET

(Insert name of trust) NHS Trust**YOU HAVE BEEN GIVEN A SUPPLY OF:**

Currently, this product does not have a full U.K. pharmaceutical product licence. Medicines are often used in this way. This can be for many reasons, for example:

- It is awaiting the granting of a U.K. licence from the Government
- It is being tested in a clinical trial
- Usage of the medicine is low and therefore it is not economic for the makers to send the product for approval or it would be difficult to get enough patients to perform a clinical trial
- It has been withdrawn from the U.K. market

However, please be reassured that your doctor and pharmacist have thought very carefully about selecting the best medicine for you. If you have any concerns regarding this medicine please contact the pharmacy department.

(Insert name of trust) NHS TRUST



PATIENT INFORMATION LEAFLET

(Insert name of trust) NHS Trust**HOW TO OBTAIN A FURTHER SUPPLY**

- If you require a further supply of this medicine and if you do NOT have a further hospital appointment, please:
 - ◆ *Go to your GP to obtain a prescription and take it to your local pharmacy (chemist) along with this leaflet.*
 - ◆ *Return to the hospital pharmacy for a further supply*
- *(delete as appropriate)*
- You will probably need to give the pharmacist one or two weeks notice to obtain the supply for you, so it is important that you do not let your supply run out before going to the G.P.
- The pharmacist will be able to order it for you from:

(Insert name of trust) NHS TRUST

What Do I Do if I Want More Information?

If you

- * have any worries or concerns about any
 - medicine, or
 - information you have been given with the medicine,
- * are confused or not sure about any information or directions you have been given,
- * just want more information,

Please talk to your doctor or pharmacist. They have lots of knowledge and experience with medicines and will be pleased to answer your queries.

What If I Am Unhappy About Taking / Using a 'Special' Treatment?

If you have any concerns at all talk it over with your doctor or pharmacist. Tell them what you are worried about and why.

He/she can

- * give you more information about the treatment,
- * explain why it is believed to be the most suitable, and
- * discuss other treatments that may be available

Nobody can force you to take or use any treatment that you do not want.

'Special' Medicines

Information for Patients, Parents, Carers etc.

Most medicines prescribed in this country are approved for use by the government's Medicines and Healthcare Products Regulatory Agency.

This leaflet is intended to explain why doctors may sometimes prescribe treatments that are used outside this approval process.

Why Are Medicines Usually ‘Officially Approved’?

With a few exceptions medicines that are prescribed or sold in this country are approved for use by the government’s Medicine and Healthcare Products Regulatory Agency (MHRA). This helps ensure that medicines:

- are effective.
- do not cause too many side effects.
- are manufactured under good conditions.

In order to provide patients with the best or most suitable treatment, it is sometimes necessary for doctors and pharmacists to supply medicines that have not gone through this approval process. They will not do this unless they believe the medicine to be safe and effective.

It is also sometimes necessary to use medicines for uses other than those for which they have been approved.

In this leaflet treatments that have not gone through this approval process are called ‘Special treatments.’

Why Do Doctors Prescribe / Use ‘Special Treatments’?

- Research may have shown that the treatment is better than one that has been officially approved, but the manufacturer may not have asked for the treatment to be approved, or may be waiting for official approval.
- It may be that no other effective treatment is available – this is often the case with some rare diseases.
- A medicine may only be approved for use in one group of patients (e.g. adults), but doctors may have found that it also works for others (e.g. children). They may wish to use it in these other patients, if it is the most effective or appropriate treatment available.
- The medicine may not have gone through the approval process because it is one that needs to be made up specially e.g. a liquid medicine that has to be made so that a child can swallow it easily.

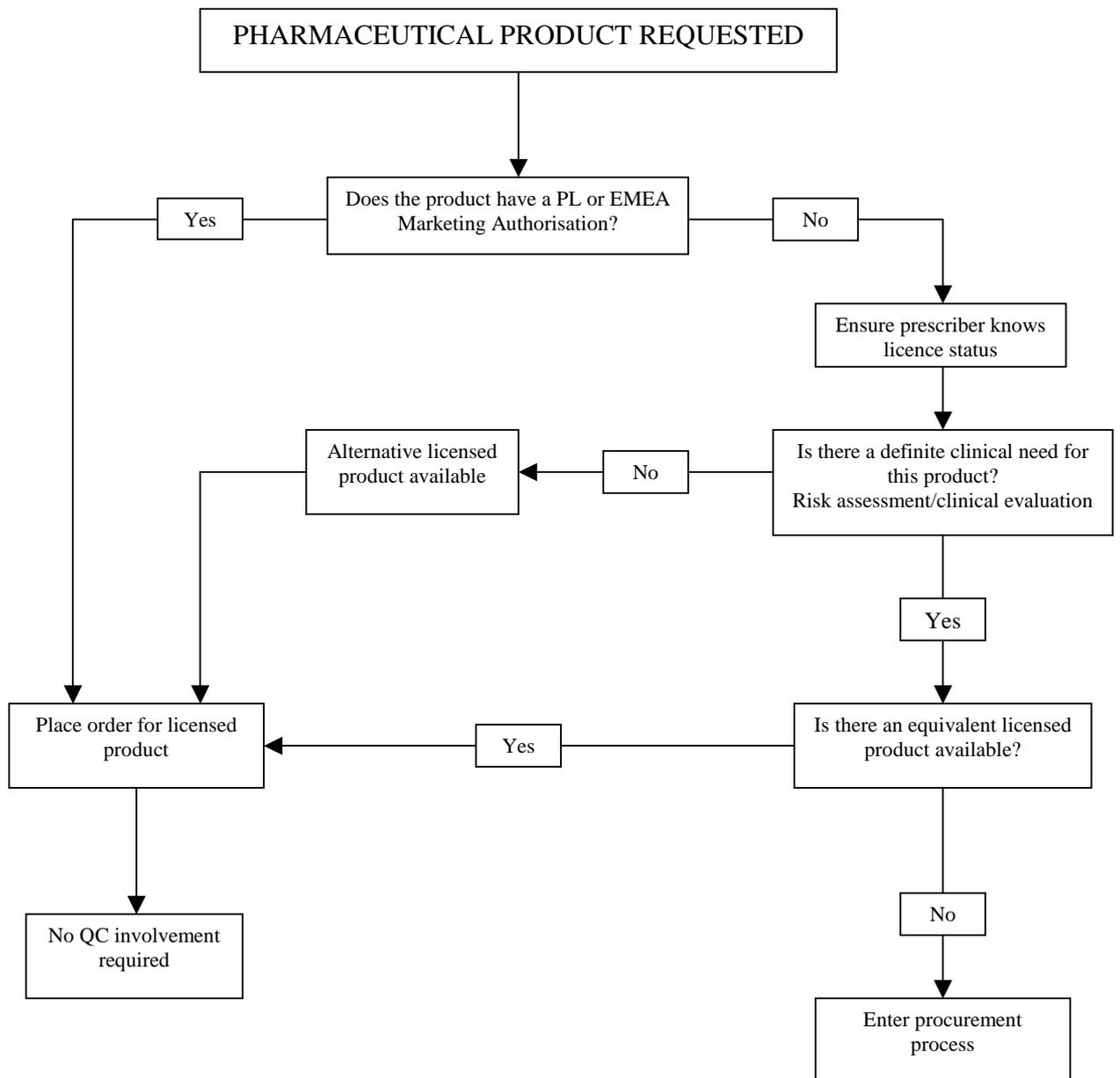
What Differences Might I Notice If I am Prescribed/ Supplied with a Special Treatment?

- Your doctor or pharmacist may tell you that the treatment has not been officially approved (or licensed), but will normally explain that it is safe and effective, and why it is the preferred treatment.
- In some cases your doctor or pharmacist may give you some separate information about the medicine. If this is written please read it carefully, and follow any instructions you are given.
- You may notice that a manufacturer’s information leaflet supplied with the medicine is not ‘quite right’. For instance, you may notice that it does not include information about the condition for which you are being treated, or about the use of the medicine in children or old people, or it may state a dose that is different from that which the doctor has prescribed.
- Many of these medicines have to be made up specially or may take longer to obtain than other medicines. Your pharmacist may therefore need to make special arrangements for the supply of the medicine. You may also be told that it will be necessary for you to ask the doctor for another prescription up to two weeks before the next supply of the medicine is needed.

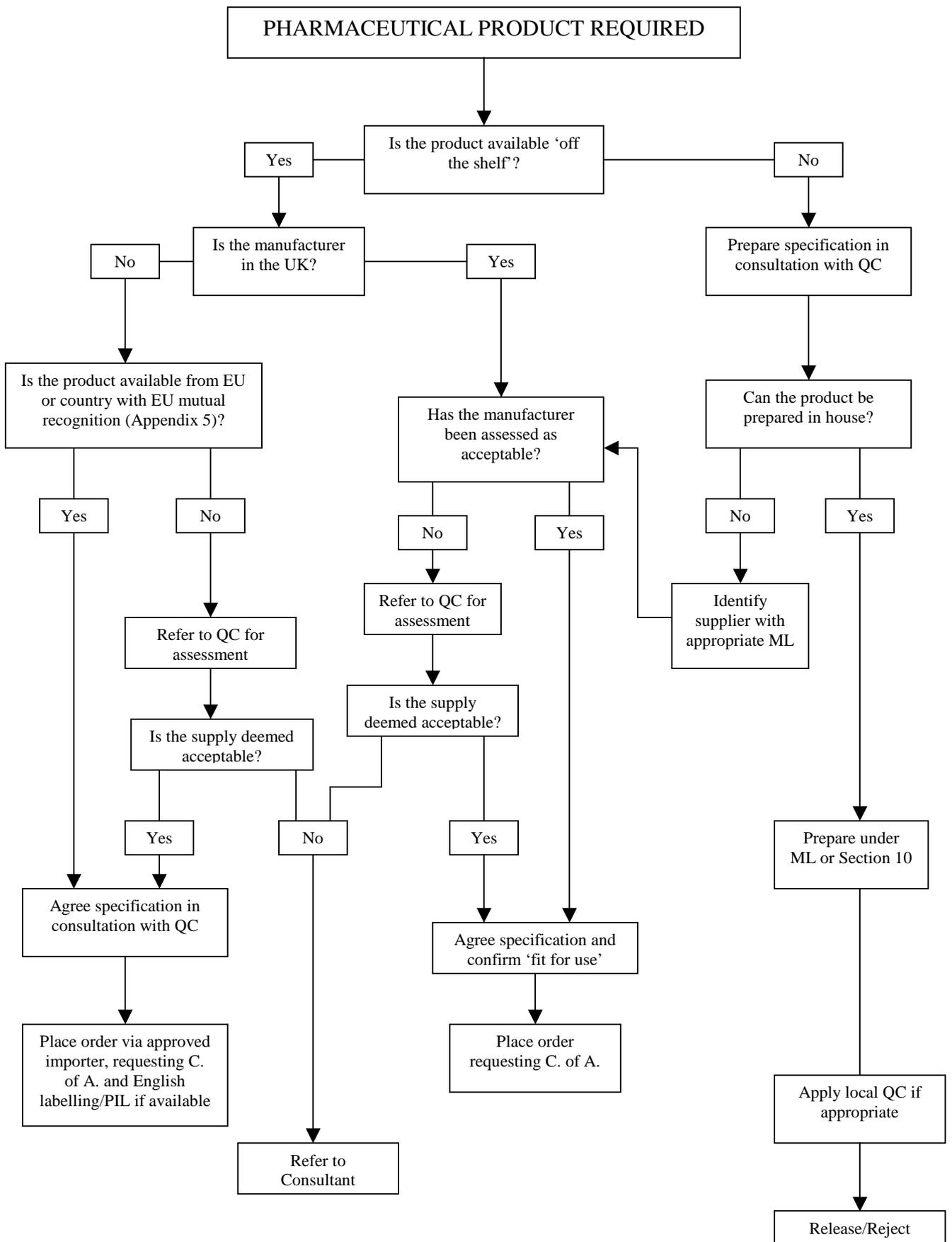
Doctors and pharmacists will only prescribe / supply one of these ‘special treatments’ when it is considered to be the most appropriate treatment.

The fact that a treatment has not gone through the government’s official approval process does not mean that is less effective, less safe or of a poorer quality than one that has.

UNLICENSED MEDICINES IN HOSPITALS
MODEL PROCUREMENT AND QC DECISION TREE – CLINICAL ASSESSMENT



UNLICENSED MEDICINES IN HOSPITALS
 MODEL PROCUREMENT AND QC DECISION TREE – PROCUREMENT



UNLICENSED MEDICINES IN HOSPITALS
 MODEL PROCUREMENT AND QC DECISION TREE – QC AND RELEASE

