

Draft guidance for registered pharmacies preparing unlicensed medicines

January 2014

The General Pharmaceutical Council is the regulator for pharmacists, pharmacy technicians and registered pharmacies in England, Scotland and Wales.

DRAFT

About this guidance

This guidance should be read alongside the standards for registered pharmacies¹.

The standards for registered pharmacies aim to create and maintain the right environment, both organisational and physical, for the safe and effective practice of pharmacy. The standards are grouped under five principles.

This document gives guidance, under each principle, which should be followed when an unlicensed medicine is prepared in a registered pharmacy. By following this guidance the pharmacy will:

- demonstrate that it meets our standards, and
- provide assurances that the health, safety and wellbeing of patients and the public are safeguarded.

Responsibility for ensuring this guidance is followed lies with the pharmacy owner. If the registered pharmacy is owned by a 'body corporate' (for example a company or NHS organisation) the superintendent pharmacist also has responsibility. Everyone responsible needs to take into account the nature of the pharmacy and the services provided and, most importantly, the needs of patients and members of the public.

As well as meeting our standards, the pharmacy owner and superintendent pharmacist must make sure they keep to all legal requirements, including medicines legislation, and health and safety, data protection and equalities legislation.

Pharmacy owners and superintendent pharmacists should make sure that all staff members, including non-pharmacists, involved in preparing unlicensed medicines are familiar with this guidance and appropriately trained in all areas that are relevant to their duties.

Pharmacists and pharmacy technicians involved in preparing unlicensed medicines must maintain the quality of their practice, keep their knowledge

¹ [Standards for registered pharmacies](#)

and skills up to date, and work within their professional competence as required by the standards of conduct, ethics and performance².

We expect this guidance to be followed, however we recognise that there are a number of ways to meet our standards and achieve the same outcomes for patients, of providing safe treatment, care and services. If you do not follow this guidance and provide and manage services in a different way to that described in this guidance, you should be able to show how your alternative ways of working safeguard patients, identify and manage any risks and meet our standards.

In this document, when we use the term 'you' this means:

- a pharmacist who owns a pharmacy as a sole trader, and
- a pharmacist who owns a pharmacy as a partner in a partnership, and
- a pharmacist who is the appointed superintendent pharmacist for a body corporate, and
- the body corporate itself.

² [Standards of conduct, ethics and performance](#)

The scope of this guidance

This guidance applies to the process of preparing an unlicensed medicine by (or under the supervision of) a pharmacist in a registered pharmacy in Great Britain.

This guidance applies to registered pharmacies preparing unlicensed medicines, whether this happens rarely, occasionally or is part of the core business of the registered pharmacy. The circumstances under which unlicensed medicines may be prepared are covered by specific laws.

If the activity is not covered by the exemptions set out in legislation, you will need a Manufacturing Specials (MS) licence from the Medicines and Healthcare products Regulatory Agency ([MHRA](#)). If the activity is part of the core business of the pharmacy you should get advice from the pharmacy's legal advisers or insurers, or the MHRA, on whether the service model you use needs an MHRA licence.

This guidance applies to all the following:

- the one-off preparation of an unlicensed medicine in accordance with a prescription for an individual patient
- the preparation of a stock³ of unlicensed medicines which will later be supplied from the pharmacy, by you, against a prescription for an individual patient
- the preparation of methadone⁴ for supply in accordance with a prescription (either for immediate supply in accordance with a prescription, or initially as stock³ to be supplied from the pharmacy, by you, in accordance with a prescription at a later time)
- the preparation of an unlicensed medicine based upon the pharmacist's judgement
- the preparation of an unlicensed medicine by a pharmacist based on the specification of the patient.

³ Preparation for stock at a pharmacy is acceptable as long as it is subsequently supplied by that pharmacy or another pharmacy which is part of the same legal entity.

⁴ The preparation of an unlicensed medicine (including unlicensed methadone) is also commonly referred to as extemporaneous preparation.

Throughout this document we use the terms 'preparing' and 'preparation' which refer to making a medicine from ingredients. These terms are not intended to include the process of simply diluting or dissolving a product in a vehicle designed for that purpose as part of its marketing authorisation – for example, adding a set amount of water to reconstitute an antibiotic powder.

DRAFT

Introduction

The law⁵ sets out the restrictions on how medicines are licensed, manufactured, advertised, administered, sold and supplied.

The vast majority of medicines supplied from registered pharmacies are licensed medicines. By 'licensed medicines' we mean those that have a valid Marketing Authorisation (MA) in the UK. Throughout this document when we talk about licensed or unlicensed medicines, we are referring to medicines which either have an MA (that is, they are licensed), or do not (that is, they are unlicensed).

Licensed medicines are manufactured by authorised licensed pharmaceutical manufacturers and are covered by a rigorous approval process which is overseen by the MHRA.

The manufacturers who make these medicines are also regulated and licensed by the MHRA. For more information about the approval and inspection of manufacturers please see the MHRA's [website](#)⁶.

Having all these arrangements in place makes sure that:

- medicines that are licensed are assured to a certain level of efficacy (when used in line with their licence), quality and safety
- products are only available if they are effective (when used in line with their licence), and
- those that manufacture licensed medicines are doing so to a high standard that is consistent throughout the industry.

This means that the public, and patients, can have a high degree of confidence that licensed medicines (when prescribed in line with their licence) are effective and safe for them to take and that they have been made in a way which meets a certain standard.

In general, when a prescriber issues a prescription they will prescribe a medicine that is licensed and indicated for the condition to be treated. And as

⁵ Medicines Act 1968 and the Human Medicines Regulations 2012

⁶ www.mhra.gov.uk

a rule, UK and European law says that only authorised (licensed) medicines should be supplied ('placed on the market'). UK and European law governs the circumstances under which prescribers can prescribe, and request, an unlicensed medicine to be supplied. You can find more information on the prescribing of an unlicensed medicine on the General Medical Council's (GMC's) [website](#)⁷.

However, there are exemptions in the legislation which allow unlicensed medicines to be prescribed and supplied to individual patients.

The law says that an unlicensed medicine may be prescribed to fulfil the special needs of a patient when there is no suitable licensed product available. For example, a lactose-intolerant patient may need a lactose-free preparation, or a child may need a preparation in liquid form.

The law also allows unlicensed medicines to be manufactured by the holders of MS ('specials') licences. These manufacturers are regulated by the MHRA and comply with strict licensing requirements.

The law also recognises that a pharmacist in a registered pharmacy should have the pharmaceutical skill and knowledge to safely prepare and supply a medicine without the need to be licensed as a manufacturer.

In general, legislation⁸ requires the medicine itself be licensed⁹. However the law allows a pharmacist to prepare medicines in a registered pharmacy without the need for the product to be licensed.

A patient has every right to expect that when an unlicensed medicine is prepared by a pharmacy professional in a registered pharmacy, it is of an equivalent quality as the licensed medicine they will receive (such as those produced by a regulated and licensed manufacturer). As certain high-profile past cases^{10,11} have shown, preparing an unlicensed medicine in a pharmacy is an activity that can pose a risk to patients and have potentially serious consequences when risks and process are not managed properly.

⁷ www.gmc-uk.org

⁸Section 10 of the Medicines Act 1968 & Regulation 4 of the Human Medicines Regulations 2012

⁹Regulations 17 and 46 of the Human Medicines Regulations 2012

¹⁰ [Peppermint water case](#) (BBC coverage)

¹¹ [Meningitis outbreak](#) (BBC coverage)

When a patient is supplied with a medicine, it is of vital importance that the medicine is safe and fit for purpose. Pharmacists making supplies must also consider their individual professional standards, and responsibilities to the patient. There is also a legal duty that medicines supplied to patients are of the nature and quality requested or prescribed.

If you choose to prepare unlicensed medicines under this legislation, you should follow the guidance set out in this document.

The owner and the superintendent pharmacist are responsible for making sure that there are systems in place to safeguard the health, safety and wellbeing of patients and the public who use their services. This guidance covers the areas we believe may present an increased risk when medicines are prepared in a registered pharmacy. It will help the owner, and superintendent pharmacist, to meet our standards for registered pharmacies.

DRAFT

Guidance for registered pharmacies preparing unlicensed medicines

The guidance takes each of the five main principles from the standards for registered pharmacies and then, under each principle, highlights areas that need further consideration in relation to preparing medicines.

Principle 1: The governance arrangements safeguard the health, safety and wellbeing of patients and the public.

The following areas relate to this principle in the standards for registered pharmacies. Each area is expanded on below, and contains the relevant guidance.

- 1.1 Risk assessment
- 1.2 Regular audit
- 1.3 Reactive review
- 1.4 Recall procedures
- 1.5 Accountability – personnel
- 1.6 Record keeping

1.1 Risk assessment

A risk assessment is a careful and thorough look at what, in your work, could cause harm to patients and what you need to do to prevent this. The preparation of medicines is a pharmacy service which could potentially cause harm, and therefore you should carry out a risk assessment to ensure safe outcomes for patients.

Risk assessments should be specific to the individual pharmacy, the staff working in it, and to each medicine to be prepared.

You should consider the risks before deciding whether your pharmacy should prepare medicines, or whether you might consider other options for supplying a particular medicine. For example you may:

- thoroughly investigate whether a licensed product exists and is available, and obtain that, or
- buy an unlicensed medicine from a reputable source such as an authorised manufacturer or importer.

You should carry out the necessary checks to satisfy yourself that any arrangements you have in place to manage the risks involved meet the requirements of principle 1. If you intend to prepare medicines you will need to be able to produce evidence for the arrangements you have in place to manage the risks identified – for example, in the form of a risk assessment.

The risk assessment should be reviewed regularly (see section 1.2, Regular audit) and should also be reviewed when circumstances change (see section 1.3, Reactive review).

You can find more information on managing risk in the GPhC Inspection Decision Making Framework¹². This gives indicators of outcomes in relation to the standards for registered pharmacies.

The risk assessment should state what the risks are, and may include finding out whether an equivalent relevant licensed product exists and is available. It should also include:

- a formula from a recognised source, for example from an official pharmacopeia
- a method validation
- a calculation verification
- the use of specialist equipment
- consideration of contamination
- hygiene measures
- product-specific risks
- assurances around ingredients and starting materials
- the suitability of premises
- relevant staff skills
- training and competence
- the circumstances that would trigger a new risk assessment.

This is not a complete list of all issues that need to be taken into account.

¹² [GPhC Inspection Decision Making Framework](#)

1.2 Regular audit

You should have robust systems in place so that you can demonstrate that:

- your pharmacy continues to be a safe place in which to prepare unlicensed medicines for patients, and
- you can produce medicines which are safe, effective and of a suitable quality.

You should carry out a regular audit, at an interval that you can demonstrate to be appropriate, on the process of preparing unlicensed medicines. The audit should form part of the evidence which provides assurance and demonstrates that the pharmacy continues to be safe and appropriate to carry out this activity.

While this is not a full list of issues that need to be taken into account, the audit should look at the:

- premises (including temperature, light and moisture controls; and where applicable – for example in aseptic preparation – air quality and other environmental requirements)
- equipment and facilities
- quality controls, the preparation process
- hygiene issues (including avoiding cross-contamination and microbial contamination)
- staff training and skills
- records (including the method of preparation, traceability of ingredients used, labelling applied and how the records themselves are kept).

Also, any incidents and complaints should be reviewed, and reported if this is appropriate.

1.3 Reactive review

A review should take place when any of the following happens:

- changes in key staff (those who have specialist training, knowledge and experience and are involved in preparing medicines)
- the introduction of new staff
- a change in the equipment

- a change in the form, or source, of ingredients
- any incidents
- the environment or facilities available are no longer fit for the task
- concerns or feedback received
- a review of near misses and error logs indicates concerns about this activity.

This reactive review should say when a new risk assessment is needed. It can form part of that new risk assessment, when one needs to be carried out.

Concerns, feedback, near misses and errors should be documented, taken into account, and should be acted on to improve safety.

1.4 Recall procedures

As well as having policies and systems for handling complaints, under the standards you must raise concerns when you suspect that medicines are not fit for purpose. You should have systems in place so that you can demonstrate that you can effectively manage an appropriate response and take action where there may be a problem with an unlicensed medicine you have prepared.

If there is a problem with an unlicensed medicine that you have prepared, you should have systems in place to be able to contact members of the public and recall unlicensed medicines that you have made for them.

These procedures should include who is responsible for taking action, and how that is to be carried out. It should also include details of the other bodies or authorities that need to be told about the product's recall.

Any problems that may have occurred during the preparation of the product may only become apparent later. Or there may be a problem with one of the ingredients or starting materials used obtained from a supplier, and this may only be discovered later.

1.5 Accountability – personnel

Under the standards you must make sure that there are clear lines of accountability for staff providing pharmacy services.

It should be clear which pharmacist is accountable for the preparation of an unlicensed medicine. Records that show which pharmacist is accountable for supervising the preparation of each medicine, or batch of medicines, should be made, and kept for an appropriate time.

It should also be clear which pharmacy technician and which other personnel are involved in preparing an unlicensed medicine. Records that show which pharmacy technicians or other members of staff were involved in the preparation of each medicine, or batch of medicines, should be made and kept for an appropriate time.

1.6 Record keeping

You should keep detailed records of the preparation of the medicine to safeguard patients. Records should contain enough detail to make sure that if there is a recall, or an incident affecting a patient's safety, the method of preparation can be clearly reconstructed. You should keep records for as long as you consider, and can demonstrate, to be appropriate. Ask the pharmacy's professional indemnity insurance provider for advice about how long records should be kept for.

The records should include information on the following:

The process	Description of the key preparation steps used
	Calculations: working shown and double checked (detailed)
	The name of the supervising pharmacist
	The name of the pharmacy technician involved (if applicable)
	The names of other personnel involved (if applicable)
	The quality assurance or testing process used
	Environmental factors (For example temperature and moisture conditions)

The formula	The complete formula
	The source of the formula: pharmacopeia formula or other validation

The ingredients <small>For each ingredient or starting material used</small>	The source: manufacturer, brand and the wholesaler or distributor
	Certificate of conformity (if applicable)
	Certificate of analysis (if applicable)
	Batch number
	Expiry date
	Quantity used and details of the person measuring, and person double-checking, quantities
	TSE guidance ¹³ should be followed (if applicable, that is, where an ingredient is of animal origin)
	Description of the container and closure used (For example whether they were glass or plastic)

The product	Date prepared
	A reference number or identification
	Expiry date (give reasons)
	Date supplied to the patient or customer

The patient or customer	The patient or customer's name
	The patient or customer's address
	The patient or customer's contact details (for example, phone number, email address)
Also, if supplied against a prescription	The patient's doctor (name, address and phone number)
	The patient's age (if it is on the prescription)
	Other prescription details (date and type)
	A sample of the label that has been put on the medicine

¹³ The [TSE guidance](#) is the MHRA guidance: 'Minimising the Risk of Transmission of Transmissible Spongiform Encephalopathies via Unlicensed Medicines for Human Use'. See the *Other sources of information* section at the end of this document for more information.

Principle 2: Staff are empowered and competent to safeguard the health, safety and wellbeing of patients and the public.

The following areas relate to this principle in the standards for registered pharmacies. Each area is expanded on below, and contains the relevant guidance:

2.1 Trained and competent staff

2.2 Training records

Preparing unlicensed medicines in a registered pharmacy, instead of buying licensed medicines from a reputable licensed supplier, carries a greater risk.

You should assess the risks and consider whether your pharmacy staff, as well as your premises, equipment and facilities, are suitable for and capable of providing this service.

2.1 Trained and competent staff

Staff should have done recognised training courses before they can be involved in this activity. Staff may also be involved in this activity if they are still doing such a training course, but their work in this area must be closely supervised until their training is complete. To prepare a medicine from ingredients, staff need expertise and skill over and above that needed to dispense a licensed medicine.

Staff working with potentially hazardous substances (such as cytotoxic products), or in areas that require more stringent precautions (such as aseptic preparation), should have done specific, recognised and relevant training.

2.2 Training records

You should document and keep evidence of the training done for as long as you consider, and can demonstrate, to be appropriate. And these records should be made available to the relevant authorities if they ask to see them.

You should ask the pharmacy's professional indemnity insurance provider for advice about how long records should be kept for.

DRAFT

Principle 3: The environment and condition of the premises from which pharmacy services are provided, and any associated premises, safeguard the health, safety and wellbeing of patients and the public.

The following areas relate to this principle in the standards for registered pharmacies. Each area is expanded on below, and contains the relevant guidance:

3.1 Measures to minimise contamination

3.2 Hygiene control records

You should assess the risks and consider whether your pharmacy premises are suited to, and capable of, providing this service. You should get specialist advice if you are considering the preparation of sterile (aseptic) or hazardous medicines (for example cytotoxics, hormones or immunosuppressants).

There are highly specialised requirements for the safe preparation of aseptic medicines, and there are potentially significant adverse consequences to patients if there is an error with, or contamination of, these medicines. If you are considering the aseptic preparation of medicines you should get specialist advice from a body such as the MHRA or regional NHS Quality Assurance staff (some of which also operate on a consultancy basis and can provide services across Great Britain and to non-NHS organisations too).

3.1 Measures to minimise contamination

There should be enough space to provide this service safely, and the environment of the premises should be suitable for the preparation of medicines.

Specific steps should be taken to make sure that the risk of cross-contamination and microbial contamination is eliminated or minimised within the pharmacy.

These factors should be considered as part of the initial risk assessment.

3.2 Hygiene control records

You should make records of the steps taken to make sure that the environment, conditions and equipment are clean enough for the preparation of medicines. You should keep the records for as long as you consider, and can demonstrate, to be appropriate. These will form part of the evidence that the pharmacy is suitable for the preparation of unlicensed medicines.

DRAFT

Principle 4: The way in which pharmacy services are delivered safeguards the health, safety and wellbeing of patients and the public. This includes the management of medicines and medical devices.

The following areas relate to this principle in the standards for registered pharmacies. Each area is expanded on below, and contains the relevant guidance:

4.1 Quality assurance

4.2 Patient information

4.1 Quality assurance

Quality assurance, in this context, is the procedures, processes and arrangements in place that make sure a finished product is of the quality needed for its intended use.

When an unlicensed medicine is prepared in a pharmacy it is essential that the patient is supplied with a medicine that is safe and fit for purpose.

You should have procedures in place which include a specific method, process, or system that is used consistently to assure yourself that the unlicensed medicine produced is of suitable quality to be supplied to the patient.

When more than a single one-off preparation is made, this quality assurance should be robust enough to safeguard all the patients who may be supplied from a single batch of medicines.

4.2 Patient information

At the outset, you should make it clear to the patient that you will be preparing the medicine, and as such, that it will be unlicensed. You should explain what this means, (including what this means in relation to the amount of information and evidence available about the medicine).

When a licensed medicine is supplied from a pharmacy it comes with a package leaflet. The information that needs to be given to the patient is set out in the law and the medicine's licence. (That information could appear on the package instead of in a leaflet if the manufacturer wants to give it to the patient in that way.) The package leaflet gives the patient important information about the medicine, directly from the manufacturer.

When a pharmacy supplies an unlicensed medicine there is no legal requirement to give a package leaflet, or similar detailed written information. Therefore the patient will rely on the information that you tell them (or give them in writing). You should make sure that you give the patient any important information that they might need so that they can use the medicine safely.

You should consider what extra information you should give the patient about the medicine, for example, when the medicine should be disposed of (the expiry date), or any special storage instructions.

DRAFT

Principle 5: The equipment and facilities used in the provision of pharmacy services safeguard the health, safety and wellbeing of patients and the public.

The following areas relate to this principle in the standards for registered pharmacies. Each area is expanded on below, and contains the relevant guidance:

5.1 Specialist equipment and facilities

5.2 Maintenance logs

5.1 Specialist equipment and facilities

You should have equipment and facilities which are specially designed for the purpose you wish to use them for. They should be of sufficiently high specification, and accuracy where applicable, to produce a high-quality, safe product.

Examples of specialist equipment include, but are not limited to, the following:

Accurate measuring devices for weight (measuring scales)

Accurate measuring devices for volume (for example, cylinders)

Production and mixing equipment

Cleaning equipment (including suitable detergent)

Contamination-minimising clothing (for example, masks, gloves, aprons, coats, hats)

Sterilising equipment (including suitable chemical agents, autoclaves and filtration equipment)

Fume cupboards, isolators and laminar flow cabinets.

5.2 Maintenance logs

You should keep maintenance logs for each type of specialist equipment for as long as you consider, and can demonstrate, to be appropriate. These logs will form part of the evidence that the pharmacy is suitable for the preparation of medicines.

You should ask the pharmacy's professional indemnity insurance provider for advice on how long records should be kept for.

DRAFT

Other sources of information

The MHRA produces a guide for holders of (medicines) manufacturing licences, called: [“Rules and Guidance for Pharmaceutical Manufacturers and Distributors 2014 ‘The Orange Guide’”](#), (or any subsequent revision), More information is available from the MHRA’s [website](#). If your pharmacy has a licence to manufacture medicines from the MHRA, and operates under that licence, please ask the MHRA for advice.

When pharmacies procure, and obtain, unlicensed medicines from licensed manufacturers or importers (called ‘specials’) they must comply with particular legal requirements (for example, about record keeping). This guidance *does not apply* to unlicensed medicines that pharmacies have not prepared themselves, but have obtained elsewhere from licensed manufacturers, importers or distributors. Please see the guidance from the MHRA on the manufacture of ‘specials’ and the legal requirements that pharmacies must comply with when they obtain and supply ‘specials’.

If an ingredient of animal origin is used in the preparation of an unlicensed medicine please see, and follow, the MHRA’s (interim) guidance on [Minimising the Risk of Transmissible Spongiform Encephalopathies via Unlicensed Medicinal Products for Human Use](#). This guidance gives advice for manufacturers, importers and exporters of unlicensed medicines to help them comply with The Unlicensed Medicinal Products for Human Use (Transmissible Spongiform Encephalopathies) (Safety) Regulations 2003 (SI 2003/1680), as amended. While these regulations do not apply to pharmacists preparing unlicensed medicines in a registered pharmacy, the MHRA’s guidance is designed to minimise this particular risk to patients, and – as an important patient safety consideration – should be followed. You can see more information at the following page on the MHRA’s website: [TSE Regulations](#).

The Pharmaceutical Inspection Convention, Pharmaceutical Inspection Co-operation Scheme produced a guide on the preparation of medicines called: [PIC/S Guide to Good Practices for the Preparation of Medicinal Products in Healthcare Establishments PE 010-3 2008](#).

The European Directorate for the Quality of Medicines and Healthcare has passed a resolution on quality and safety assurance requirements for medicinal products prepared in pharmacies for the special needs of patients: [Resolution CM/ResAP\(2011\)1](#).

If a pharmacy in a hospital *is not registered with us*, please ask for guidance from the [Care Quality Commission](#), [Health Improvement Scotland](#) or [Healthcare Inspectorate Wales](#), as appropriate.

DRAFT