

Guidance for registered pharmacies preparing unlicensed medicines

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

About this guidance

This guidance should be followed if an unlicensed medicine is prepared in a registered pharmacy. The preparation of an unlicensed medicine (for example unlicensed methadone, or menthol in aqueous cream) in a pharmacy is often called 'extemporaneous preparation'.

The guidance should be read alongside the **standards for registered pharmacies**¹. These aim to create and maintain the right environment, both organisational and physical, for the safe and effective practice of 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 making sure this guidance is followed lies with the pharmacy owner. If the registered pharmacy is owned by a 'body corporate' (for example a company or an NHS organisation) the superintendent pharmacist also has responsibility. Those responsible for the overall safe running of the pharmacy need to take into account the nature of the pharmacy and the range of services already 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.

¹Standards for registered pharmacies

Pharmacy owners and superintendent pharmacists should make sure that all staff, including non-pharmacists, involved in preparing unlicensed medicines are familiar with this guidance.

Individual pharmacy professionals are key to ensuring the safe preparation and supply of unlicensed medicines. Pharmacists and pharmacy technicians involved in preparing unlicensed medicines have a responsibility² to provide medicines safely to patients, maintain the quality of their practice, keep their knowledge and skills up to date, and work within their professional competence.

We expect this guidance to be followed. However, we also recognise that there can be a number of ways to meet our standards and achieve the same outcomes for patients – that is, to provide safe treatment, care and services. If you do not follow 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.

²Standards of conduct, ethics and performance

The scope of this guidance

This guidance applies only to the process of preparing³ an unlicensed medicine by (or under the supervision of) a pharmacist in a registered pharmacy in Great Britain, under the exemptions and circumstances described in the law⁴. It applies whether this happens rarely, occasionally or is part of the core business of the registered pharmacy.

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 stock⁵ of unlicensed medicines, (in anticipation of a prescription), which will later be supplied from the pharmacy, by or under the supervision of a pharmacist, against a prescription for an individual patient
- the preparation of methadone for supply in accordance with a prescription (either for immediate supply in accordance with the prescription, or initially as stock⁵ to be supplied from the pharmacy, by or under the supervision of a pharmacist, against a prescription at a later time)
- the preparation of an unlicensed medicine based upon the pharmacist's judgement⁶
- the preparation of an unlicensed medicine by, or under the supervision of, a pharmacist based on the specification of the patient.

³This guidance does not apply to unlicensed medicines that registered pharmacies have not prepared themselves, but have obtained from elsewhere such as (MS) licensed manufacturers, importers or distributors

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

⁵Preparation for stock at a pharmacy is acceptable as long as it is subsequently supplied by retail from that pharmacy or another pharmacy which is part of the same legal entity

⁶An unlicensed medicine that is prepared with the intention of selling it over the counter (one that is not a prescription-only medicine) is often called a 'Chemist's Nostrum'

If the activity is not covered by the exemptions set out in the law, you will need a Manufacturer's Specials (MS) licence from the Medicines and Healthcare products Regulatory Agency (MHRA).

If the medicines are being prepared for animal use, the exemptions that allow this, and the parts of the law that apply, are found in the Veterinary Medicines Regulations 2013. The body that regulates animal medicines and issues authorisations to manufacturers of special veterinary medicinal products is the Veterinary Medicines Directorate (VMD).

Throughout this document we use the terms 'preparing' and 'preparation' which refer to making a medicine from ingredients or starting materials. 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.

Introduction

The law⁷ sets out the restrictions on how human medicines are licensed, manufactured, advertised, administered, sold and supplied.

Most of the medicines supplied from registered pharmacies are licensed medicines. Licensed medicines are those that have a valid Marketing Authorisation (MA) in the UK, and which are covered by an approval process overseen by the MHRA.

The manufacturers who make these medicines are also regulated and licensed by the MHRA for compliance with EU Good Manufacturing Practice (GMP) standards and the strict conditions of their licence. You can find more information about the approval and inspection of manufacturers on the MHRA's website⁸.

These arrangements mean that licensed manufacturers are making medicines to a regulated standard that is consistent throughout the industry. It also means that when medicines are used in line with their licence, they are:

- assured to a certain level of efficacy, quality and safety, and
- only available if they are effective.

Overall this means that the public, and patients, can have a high degree of confidence that appropriately prescribed licensed medicines are effective and meet the clinical needs of patients.

As a rule, the law requires that only authorised (licensed) medicines should be made available and supplied ('placed on the market'). There are exemptions in the law which allow unlicensed medicines to be prescribed and supplied to individual patients.

⁷ Medicines Act 1968 and the Human Medicines Regulations 2012

⁸ www.mhra.gov.uk

In general, when a prescriber issues a prescription they will prescribe a medicine that is licensed and indicated for the condition to be treated. European and UK law sets out the circumstances under which prescribers can prescribe an unlicensed medicine for supply to a patient. You can find more information on the prescribing of an unlicensed medicine by reading the General Medical Council's (GMC's) *Good practice in prescribing and managing medicines and devices* on their website⁹.

Under the law, unlicensed medicines ('special products') must be manufactured by the holders of MS ('specials') licences who are regulated by the MHRA and who follow GMP standards and the conditions of their licences.

In general, the law also requires the medicine itself be licensed¹⁰. However, the law¹¹ allows a pharmacist to prepare and supply medicines in a registered pharmacy without the need for the product to be licensed. A pharmacist should have acquired the necessary knowledge and skill during their initial education and training leading to registration.

A patient has every right to expect that when an unlicensed medicine is prepared by, or under the supervision of, a pharmacist in a registered pharmacy, it is of an equivalent quality to any licensed medicine they will receive (such as those produced by a regulated and licensed manufacturer). As certain high-profile past cases¹² have shown, preparing an unlicensed medicine in a pharmacy is an activity that can pose a significant risk to patients and have potentially serious consequences when risks and processes are not managed properly.

⁹ www.gmc-uk.org

¹⁰ Regulations 17 and 46 of the Human Medicines Regulations 2012

¹¹ Section 10 of the Medicines Act 1968 and Regulation 4 of the Human Medicines Regulations 2012

¹² Peppermint water case

When a patient is supplied with an unlicensed medicine, it is important that the unlicensed medicine is safe and appropriate. Pharmacists making supplies must also consider their individual professional standards and their responsibilities to the patient. There is also a general legal duty that all medicines supplied to patients are of the nature and quality requested or prescribed.

The law also allows a pharmacist in a registered pharmacy to prepare medicines for animal use in line with a prescription, prescribed under the cascade¹³, from a veterinary practitioner.

The authorised specials manufacturers of veterinary medicines are inspected by the VMD for their compliance with the principles of GMP. If they manufacture human medicines they would also be regulated by the MHRA.

If you choose to prepare unlicensed medicines in your pharmacy under the exemptions in the law, 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.

¹³ Veterinary Medicines Regulations 2013

Guidance for registered pharmacies preparing unlicensed medicines

The standards for registered pharmacies are grouped under five principles, and this guidance is set out under each of those five principles.

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.

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

You should consider the risks before deciding whether your pharmacy should prepare unlicensed medicines in general, or whether you might consider other options for supplying particular medicines.

You should carry out a risk assessment if an unlicensed medicine is prepared in your pharmacy, and 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 your intention is that your pharmacy will prepare medicines, you will need to be able to produce evidence for the arrangements you have in place to manage the risks identified.

The risk assessment should be reviewed regularly (see section 1.2) and should also be reviewed when circumstances change (see section 1.3).

The risk assessment should state what the risks are, and may include finding out whether equivalent relevant licensed products exist and are available.

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

- a formula from a recognised source, for example from an official Pharmacopoeia
- a verification of the preparation method (eg the Pharmacopoeia method)
- 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.

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
- 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 show to be appropriate, on the process of preparing unlicensed medicines. The audit should form part of the evidence which provides assurance and shows 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, if applicable, look at:

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

You should learn from any incidents, complaints or other forms of relevant information and use the learning to make appropriate changes.

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, which should be documented, 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.

1.4 Recall procedures

It is important that if there is a problem with an unlicensed medicine that has been prepared in your pharmacy, you have the systems in place to contact members of the public and recall unlicensed medicines that have been made in your pharmacy.

These procedures should say who is responsible for taking action, and what action to take. They should also include details of the other bodies or authorities that need to be told about the medicines' recall.

Under the standards you must have arrangements in place that allow all staff to raise concerns when they suspect that medicines are not fit for purpose.

1.5 Accountability – staff

It should be clear which pharmacist is accountable and responsible for the preparation of an unlicensed medicine.

It should also be clear which pharmacy technician and other staff are involved in preparing an unlicensed medicine.

1.6 Record keeping

You should keep detailed records of the preparation of the unlicensed medicine to safeguard patients. This is so 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 show, to be appropriate, taking into account any consumer protection laws which apply. If the medicine being prepared is for animal use there are specific requirements in the law for record keeping that also apply. Ask the pharmacy's professional indemnity insurance provider for advice about how long you should keep records 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 person who prepared the worksheet
	The date that the worksheet was prepared
	The name of the supervising pharmacist (and the name of the pharmacist signing off the final product as ready to be supplied to the patient, if different)
	The name of the pharmacy technician involved (if applicable)
The formula	The complete formula
	The source of the formula: Pharmacopoeia formula or other source
	Validation of the formula
The ingredients For each ingredient or starting material used	The source: manufacturer, brand and the wholesaler or distributor
	Certificate of conformity ¹⁴ (if applicable)
	Certificate of analysis ¹⁵ (if applicable)
	Batch number
	Expiry date (if available)
	Quantity used and details of the person measuring, and person double-checking, quantities
	TSE guidance ¹⁶ should be followed (if applicable, that is, where an ingredient or product contact material is of animal origin)
	Description of the container and closure used (for example whether they were glass or plastic)

¹⁴ Certificate of conformity provides confirmation that the product supplied complies with a specified set of requirements or specifications, but does not contain any test results

¹⁵ Certificate of analysis provides a summary of testing results on samples of products or materials together with the evaluation for compliance to a stated specification

¹⁶ 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

The product	Date prepared
	A reference number or identification (batch number)
	Expiry date (give reasons or validation in support)
	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)
	A sample of the label that has been put on the medicine
	The name of the person who produced the label
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)
Incidents	Suspected adverse reactions reported
	Complaints and concerns

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.

2.1: Trained and competent staff

Staff should complete recognised training courses before they can be involved in this activity. However, 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 an unlicensed medicine from ingredients, staff need expertise and skill over and above that needed to dispense a licensed medicine. Many pharmacists and pharmacy technicians should have acquired this knowledge and skill during their initial education and training leading to registration. If they do not have the necessary knowledge, skills or competence to safely carry out the task, you should consider how you ensure that they obtain (or if they have previously been trained in this area, refresh) the necessary specialist skills.

It is important that training is regularly repeated to make sure that all staff remain up to date and competent. This is particularly important when the activity is only carried out from time to time.

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 show, to be appropriate. These records should be made available to the relevant authorities if they ask for them.

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

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.

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 when you are considering preparing 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. 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).

See the *Other sources of information* section at the end of this document for more information on this subject.

The following areas relate to this principle in the standards for registered pharmacies.

3.1 Measures to minimise contamination

There should be enough space, and segregation where required, 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.

See the *Other sources of information* section at the end of this document for links to information provided by governmental infection control agencies.

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. These will form part of the evidence that the pharmacy is suitable for the preparation of unlicensed medicines.

You should keep the records for as long as you consider, and can show, to be appropriate. You should ask the pharmacy's professional indemnity insurance provider for advice on how long you should keep records for.

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.

4.1 Ingredients

The ingredients and starting materials used in the preparation of the unlicensed medicine will affect the quality of the final product. Therefore you should make sure that any ingredients or starting materials your staff use are obtained from a reputable source: for example, a licensed manufacturer or distributor.

4.2 Quality assurance

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

To have a robust system of quality assurance that provides the necessary safeguards, you need to have a range of systems in place, such as those described in this guidance. These include:

- using worksheets and official formulas
- confirmation of quantities and identities of ingredients
- staff whose training is suitable and up to date, and
- appropriately maintained equipment.

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.

4.3 Patient information

At the outset, you should make sure that there is a system in place so that the Responsible Pharmacist (or other staff competent to be delegated this task) tells the patient that the pharmacy will be preparing an unlicensed medicine. They should explain to the patient what this means (including what this means in relation to the amount of information and evidence available about the medicine).

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 your pharmacy staff give them. You should give appropriate advice and information (in writing if possible). This applies equally when there is limited, or no, direct contact with the patient when the medicine is supplied.

You should make sure that the pharmacy staff give the patient any important information they might need so that they can use the medicine safely. The information should include advice on the use of any dosing device that needs explanation to deliver the correct dose. You should also make sure that pharmacy staff consider what extra information they should give the patient about the medicine: for example, the expiry date or any special storage instructions.

If the medicine is prepared in line with a British Pharmacopoeia (BP) formula or a general monograph in the BP for the dosage form, there are particular labelling requirements for unlicensed medicines.

There are also specific labelling requirements when the prepared medicine is for animal use, which has been prescribed by a veterinary practitioner under the cascade.

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.

5.1 Specialist equipment and facilities

You should make sure that the pharmacy has equipment and facilities which are specially designed for the intended purpose that staff will 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, including validation and calibration records, for each type of specialist equipment for as long as you consider, and can show, 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 you should keep records for.

Other sources of information

- *Rules and Guidance for Pharmaceutical Manufacturers and Distributors 2014 'The Orange Guide'* (or any subsequent revision). You can find more information on the MHRA's website.
- *Minimising the Risk of Transmissible Spongiform Encephalopathies via Unlicensed Medicinal Products for Human Use* contains information for if an ingredient, or product contact material, of animal origin is used in the preparation of an unlicensed medicine.
- *Veterinary Medicines Guidance Note No 13 Guidance on the Use of Cascade* contains information on the extemporaneous preparation of medicines.
- The following agencies are a source of information on infection control: Health Protection Scotland; Public Health England; Health Protection Agency (for Wales).

Other references that may be useful and of interest include:

- *Handbook of Extemporaneous Preparation*, Ed. Jackson and Lowey on behalf of the NHS Pharmaceutical Quality Assurance Committee, Pharmaceutical Press, 2010.
- *Quality Assurance of Aseptic Preparation Services Edition 4*, Ed. A.M. Beaney on behalf of the NHS Pharmaceutical Quality Assurance Committee, Pharmaceutical Press, 2006.
- *PIC/S Guide to Good Practices for the Preparation of Medicinal Products in Healthcare Establishments PE 010-3 2008*.
- *Resolution CM/ResAP(2011)1*. 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.

More information

If you would like copies of this document in Welsh, please go to www.pharmacyregulation.org/standards/guidance where you can download a PDF. If you are seeking this document in other formats, please contact our communications team at communications@pharmacyregulation.org.

If you have questions or comments about the content of this guidance, please contact our Standards Team:

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We have also produced guidance on other topics that you may find useful:

www.pharmacyregulation.org/standards/guidance

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