Guidance for Pharmacists on Extemporaneous Dispensing

Pharmaceutical Society of Ireland

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Contents

1. Introduction

The purpose of this guidance is to assist pharmacists in discharging their legal and professional obligations to patients in the area of extemporaneous dispensing. This guidance will help to assure the safe and appropriate preparation and supply of extemporaneously prepared medicinal products to patients, where the supply of such products is necessary.

An extemporaneously prepared medicinal product refers to the process by which a pharmacist, using traditional compounding techniques, produces a medicinal product to meet the special needs of a patient, or group of patients[1].

The level of extemporaneous dispensing in Ireland appears to be increasing. This view is supported by the significant number of queries in relation to this, and related areas, that are being received on an on-going basis by the PSI. A number of legislative changes at a European level have also emphasised the need for a review of national guidance dealing with these products. Further information on these changes is provided in Appendix 1.

The extemporaneous preparation of medicinal products is a recognised part of a pharmacist's skill set. However, it must also be recognised that where an extemporaneous product is prepared by a pharmacist it has not undergone an evaluation of its quality, safety and efficacy by a competent authority as is the case for authorised (i.e. licensed) products. Accordingly, the responsibility for assuring the quality and safety of these extemporaneously prepared products, with a view to the achievement of their therapeutic purpose, rests with the pharmacist under whose authority they are prepared. In the discharge of that responsibility, the added value which these products contribute to the care of the patient must also be taken into account. For example the individual medical needs of the patient should be carefully considered and the possible availability on the market of an appropriate authorised alternative should first be examined by the pharmacist. The pharmacist should always be satisfied that he or she has the necessary facilities and competence to undertake the extemporaneous dispensing, and is thereby in a position to supply a product of appropriate quality and safety.

Due to the lack of age-appropriate products, extemporaneous dispensing plays an important part in meeting the needs of paediatric patients. However the potential risks of extemporaneous dispensing for paediatric patients has been well documented. For example, an article published in 2003[2] states: *'Extemporaneous dispensing is not without risk. There are no published standards for the process in the UK or many European countries. In contrast to manufactured medicines there is little or no opportunity for the pharmacist to apply analytical procedures to assure the quality of the product. Frequently the only assurance of quality will be a work sheet recording amounts of ingredients with facility for operators to indicate that ingredients have been added and/or checked. Errors in preparation, some of them with potentially serious consequences, have been noted'.* Therefore, particularly careful consideration must be given to the assessment of the appropriateness of providing an extemporaneously prepared product for a child.

It is recognised that this guidance does not address specific practice settings and that there are further resources available to help pharmacists safely discharge their responsibilities in this area, which should be referred to where applicable. For example, international good practice standards for the preparation of sterile and non-sterile products in a pharmacy setting are set out in the *Guide to Good Practices for the Preparation of Medicinal Products in Healthcare Establishments*, published by the Pharmaceutical Inspection Convention/ Pharmaceutical Inspection Co-operation Scheme (PIC/S).

1 This is not to be confused with the term 'exempt' medicinal product which is the term used to describe all products which are unauthorised/unlicensed. The appropriate sourcing and supply of exempt medicinal products is explained in detail in the PSI's *Guidelines on the Sourcing of Medicinal Products for Sale or Supply by a Retail Pharmacy Business.*

2 Nunn, A.J., 2003. Making medicines that children can take. *Arch Dis Child 2003;88:369-371*

2. Legislative Basis and Implications

The legal basis for the preparation of a medicinal product in a pharmacy, otherwise than in accordance with a manufacturer's authorisation from the Health Products Regulatory Authority (HPRA), is contained in Regulation 5(1) (a) of the Medicinal Products (Control of Manufacture) Regulations 2007. The legal basis for the supply of a medicinal product, otherwise than in accordance with a marketing authorisation, is set out in Regulation 6(4) and Schedule 1 to the Medicinal Products (Control of Placing on the Market) Regulations 2007, and Article 3.2 of Directive 2001/83/EC[3].

Under this legislation, it is important to note that the supply of extemporaneously prepared medicinal products is permitted only in certain limited circumstances, as follows:

(i) in response to a *bona fide* unsolicited order of a practitioner (i.e. on foot of a prescription), where the medicinal product is for use by an individual patient or group of patients under the practitioner's direct responsibility and in order to fulfil the special needs of the patients concerned; or

(ii) in response to a request from a patient, where the extemporaneously prepared medicinal product is not subject to prescription-only control and is produced in the pharmacy in accordance with the specifications of the Pharmacopeia.

Extemporaneous preparation is not permitted in any other circumstances.

Whilst legislation does not prohibit batch manufacture to maintain a limited stock of a particular product, caution should be exercised in view of the short shelf life of such products. Pharmacists must always be satisfied that any product they prepare is safe and fit for purpose at the time of preparation, at the time of supply to the patient and throughout the expected shelf life (see also *Section 3.6 Expiry Dates*).

Please note that a pharmacy cannot legally wholesale an extemporaneously prepared medicine to another pharmacy unless they have the appropriate licence from the HPRA.

Where an extemporaneously prepared medicinal product is prepared in the pharmacy, under either of the circumstances provided in the legislation cited above, the pharmacist must always make a written record as to its preparation. This should include the precautions taken to ensure that the product is of the character required and a record of any conversations with the prescribing doctor or patient that led to the decision to extemporaneously prepare the medicinal product.

In all cases, the pharmacist must be satisfied that the medicinal product concerned is not the subject of an advertisement and that no other authorised medicinal product of appropriate composition is available for use in the particular circumstances.

In this context, it is important to note that the decanting, relabelling and/or altering of the presentation of an authorised non-prescription medicinal product or the combining of two or more non-prescription medicinal products is not permitted.

3 Directive 2001/83/EC on the Community code relating to medicinal products for human use (OJ L 311, 28.11.2001, p. 67-128) (as amended).

3. Guidance

3.1 Key Responsibilities for Pharmacists

In light of the legal requirements set out above and in consideration of the obligations of the pharmacist under the statutory Code of Conduct, the appropriateness of supplying an extemporaneously prepared medicinal product should always be carefully considered. The pharmacist must be satisfied, having taken all the particular circumstances into account, that the supply of any such preparation is necessary, that it is in the best interests of the patient, and that it will add value to the care of the patient.

It is recognised that the prescriber and the dispensing pharmacist have, within their areas of responsibility, a duty of care to the patient receiving these pharmaceutical preparations. In the exercise of their professional judgement, the pharmacist may deem it necessary to review the clinical need for an extemporaneously prepared product with the prescriber. This should involve consideration of the various possible alternatives to the supply of an extemporaneously prepared medicinal product. The prescriber should be made aware of any concerns that the pharmacist may have regarding the supply of the product prescribed and the ethical and legal implications for all concerned. The necessity and importance of this dialogue is also emphasised in the European documents discussed in Appendix 1.

3.2 Decision Process (see also Decision Tree)

In general, in the interest of patient safety and where at all possible, only medicinal products that are appropriately authorised for use in Ireland should be supplied to a patient. Where this is not possible, efforts should be made to source an 'exempt' medicinal product that is authorised in another country or in a country where the standards of manufacture and control correspond with those in EEA countries (e.g. USA, Canada or Australia). Information on Irish authorised manufacturers and wholesalers is available on the HPRA website (www.hpra.ie). The authorisation status of wholesalers and manufacturers based in other EEA countries can be checked with the competent authority in the relevant country, e.g. the Medicines and Healthcare products Regulatory Agency (MHRA) in the UK. Further information on the sourcing of 'exempt' medicinal products can be found in the PSI *Guidelines on the Sourcing of Medicinal Products for Sale or Supply by a Retail Pharmacy Business*.

When deciding whether it is necessary and in the patient's best interest to extemporaneously prepare a medicine, the pharmacist should check if the prescribed medicinal product can be sourced through any of the following channels within an appropriate time frame:

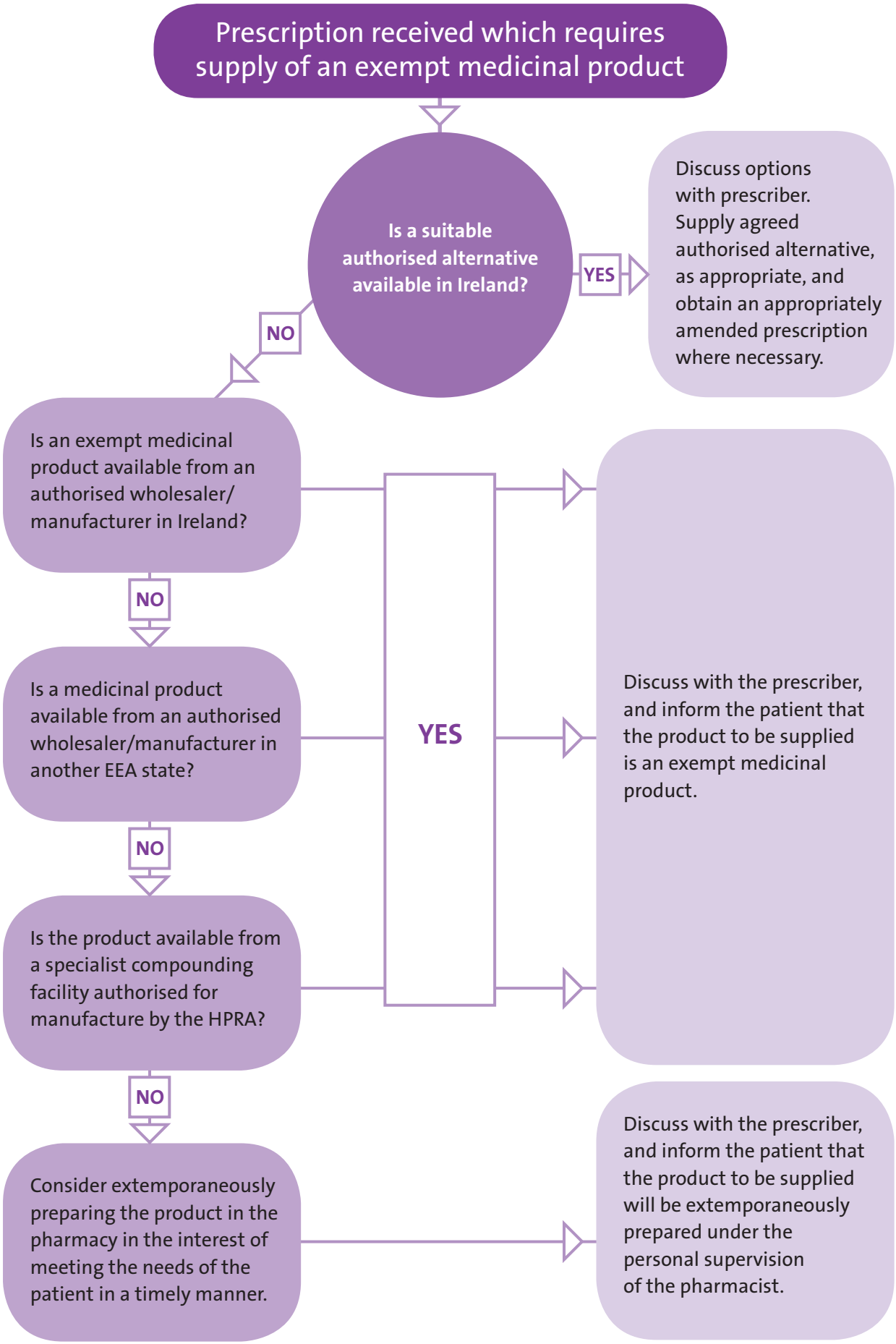
- From an authorised wholesaler or manufacturer of medicinal products in Ireland, including one of those specialising in the sourcing and supply of exempt (i.e. unauthorised/unlicensed) medicinal products;
- From an authorised wholesaler or manufacturer of medicinal products established in another EEA country, which can supply a product that has been authorised in that country, or if such a product is not available, an appropriately authorised alternative;
- From an authorised wholesaler or manufacturer of medicinal products established in another EEA country, which can supply a product that has been authorised in a country where the standards of manufacture and control, correspond with those in EEA countries. These supplies may only be procured through manufacturers or wholesalers, authorised within the EEA, who are permitted to make such importations.

Consideration might also be given to the manipulation of the dosage form of an authorised medicinal product. In this context, it should be noted that the crushing or other manipulation of such authorised products (including the mixing with food or drink) constitutes an unauthorised use unless the procedure is provided for in the relevant Summary of Product Characteristics (SmPC), such as adding a specified amount of water to reconstitute an antibiotic powder.

3.2.1 Specialist Compounding Facilities

If the prescribed product or an appropriate alternative is not available through any of the above channels, consideration may be given to sourcing the product from a specialist compounding facility, which holds an appropriate manufacturer's licence from the HPRA for that purpose. Although these manufacturers hold a manufacturing licence it should be borne in mind that the products themselves have not been granted a marketing authorisation or undergone the relevant assessment required to obtain a marketing authorisation.

3.3 Decision Tree



3.4. Preparation of an Extemporaneous Product

Pharmacists should only engage in extemporaneous preparation where all the routes of procurement described above have been exhausted, or where it has not been possible to obtain the patient's prescribed medicine via any of these routes without undue delay, or where the cost is prohibitive in the context of the patient obtaining their prescribed medicine.

In light of the above requirements and in the interest of patient care and safety, a risk assessment should be carried out by the pharmacist prior to undertaking the dispensing of an extemporaneously prepared medicinal product which takes into account the nature of the product requested, its use, the preparation techniques involved and any risks that the finished product may present to the patient. In doing this, the pharmacist should consider if the preparation and supply of the product prescribed will add value to the care of the patient.

Pharmacists should also consider the urgency of the situation and endeavour to supply the prescribed product to meet the needs of the patient within an appropriate time frame. Where a more specialised product e.g. a sterile product, requiring specialist equipment and skills has been prescribed, it may be appropriate for the pharmacist to obtain this product from a specialist compounding manufacturer or to refer the patient to a pharmacy specialising in the preparation of these products. It is acknowledged that certain pharmacies extemporaneously prepare medicines on a regular basis and therefore may be better equipped to fulfil this need. Facilitating the needs of the patient in a safe and timely manner should be the primary concern of the pharmacist.

3.5 Risk Assessment

It is important to consider the potential risks that are associated with the extemporaneous preparation of a medicinal product in the pharmacy. These will vary depending on the type of product being prepared, for example whether it is a simple dilution of a cream, or a suspension for a child. The pharmacist should consider whether they have the equipment and facilities needed to safely prepare the required product, as well as the skills and knowledge to carry out any calculations or specialised preparation steps needed. There will always be a certain degree of risk involved when extemporaneously preparing a product, for example:

- Calculation errors
- Validity of the formulation
- Microbial contamination
- Inappropriate starting materials
- Labelling errors
- Poor patient acceptability of the finished product
- Unknown stability and shelf life of the finished product
- Health and safety of staff members involved in the preparation of the product

The policies and procedures in place in the pharmacy should address any risks identified, and ways to minimise these risks.

A review of the proposed ingredients and their potency in the finished product should form an essential part of the risk assessment process, as certain ingredients may pose greater risks to patients where a formulation is not appropriately prepared.

Risks to the pharmacist or other pharmacy staff involved in preparing the product should also be considered. For example, the formulation may involve the handling of potentially hazardous materials that may be carcinogenic or cause sensitisation, e.g. coal tar, chlorpromazine and salicylic acid. Specialised clothing such as protective gloves, masks and hair nets should be available and worn where appropriate.

Such hazards and risks should be reviewed by the pharmacist and all relevant information considered before deciding to extemporaneously prepare a medicinal product. As part of the risk assessment the pharmacist should ensure that all components have been appropriately stored and handled, and that all equipment needed has been maintained in a manner that will safeguard the health and safety of the patient, the public and the pharmacy staff.

3.5.1 Calculations

Calculation errors pose the greatest risk of causing patient harm. Where at all possible, all calculations and measurements should be double checked by a second, appropriately trained, member of staff; this does not necessarily need to be another pharmacist. If this is not possible, explaining calculations and workings to another colleague can be enough to identify an error that may otherwise have been missed.

Potential causes of calculation errors can include:

- Unclear instructions from the prescriber
- Conversion between units e.g. milligrams to micrograms
- Confusion between a drug in its free base and its salt form
- Misplaced decimal points
- Errors whilst carrying out dilutions
- A lack of knowledge and familiarity with traditional terminology e.g. double strength chloroform water, single strength chloroform water and concentrated chloroform water

3.5.2 Validity of the Formulation

Often previously used formulations are the primary resource used in extemporaneous dispensing. However it must be borne in mind that such records may not be current or appropriately referenced. Pharmacists must ensure that they are satisfied with the reliability and on-going validity of the formulation used, from a quality, safety and efficacy perspective and that they are following evidence-based practice where possible.

In this context, pharmacists should endeavour to use formulations in accordance with the specifications of the Pharmacopeia and/ or make contact with the relevant specialist secondary care services for information on formulation e.g. Our Lady's Children's Hospital, Crumlin.

3.6 Expiry Dates

In the interests of the patient and of the pharmacist, an appropriate expiry date should always be included on the label of the product. The pharmacist should be satisfied that the expiry date applied to any extemporaneously prepared product is appropriately justified for the specific product concerned, paying due regard to the pharmaceutical data and evidence available. Pharmacists should be mindful that once the container is opened, it may be necessary to also apply a clinically justified in-use expiry date.

3.7 Labelling

Extemporaneously prepared medicinal products must be appropriately labelled in accordance with the requirements set out in the Medicinal Products (Prescription and Control of Supply) Regulations 2003 (as amended) and in addition must meet all requirements set out in the Council of Europe Resolution (see Appendix 1). There are additional labelling requirements for extemporaneously prepared products compared to those for authorised products dispensed against a prescription (more than one label may be needed in order to include all the required information). As well as requirements set out in legislation, the label should cross-reference the record sheet used to record the workings in the preparation of the product (see Section 3.8).

Labels should be prepared before the product is compounded so that the finished product can be labelled straight away to prevent potential mislabelling, and dispensing errors. Clear labelling of the extemporaneously prepared product is essential in the interest of patient safety. There should also be a process in place to double check the label before supply to the patient to ensure that it contains accurate information and all directions necessary for the patient to safely use the product.

The label of an extemporaneously prepared product should include (in the exceptional circumstances of batch manufacture some information may not be relevant):

- Name of the patient
- Name, address and telephone number of the pharmacy
- Date of preparation
- Date on which the product was dispensed
- Name of the product, if applicable, or a description of the product
- Generic name of the active substance(s), strength and quantity
- Name, strength and quantity of any other ingredient
- Total quantity of the final product to be supplied
- Directions for the appropriate use of the product
- Route of administration
- Relevant cautionary and advisory labels
- Warning ‘Keep out of the reach of children’
- Expiry date (including an in-use expiry date as appropriate) or information about limits for use
- Special storage or handling requirements e.g. for certain liquid preparations ‘Shake well before use’
- Batch number, if applicable

3.8 Record Keeping

A clear record in respect of each extemporaneously prepared product must be made and kept to ensure full traceability of the ingredients, formulae and method used, and the names of all pharmacists and staff members involved. The information to be recorded should be clearly documented in a written procedure. A recall procedure should be in place in case a defect or error is identified and the product has to be returned to the pharmacy.

At a minimum, the following must be recorded each time a medicine is extemporaneously prepared for supply to a patient (in the exceptional circumstances of batch manufacture some information may not be relevant):

- Patient's name
- Patient's address and contact details
- Name and address of the patient's prescriber
- Other prescription details as applicable e.g. date, type of prescription
- Date of preparation
- Formulation used, and source e.g. pharmacopoeial formula
- Calculations and workings
- Details of each preparation step
- Name, strength and quantity of each ingredient or material used
- Source of starting ingredients or materials i.e. manufacturer and wholesaler
- Batch number and expiry date of each ingredient or material used
- Storage conditions and expiry date of the finished product
- Identity of the staff member who carried out the preparation process and the identity of the pharmacist under whose supervision the process was carried out
- Results of any quality control tests carried out

A record sheet (can also be called a work sheet) should be made for each individual preparation and a duplicate dispensing label affixed thereon. This record should be maintained for at least two years on the pharmacy premises and be available for inspection. The record sheet should facilitate a checking mechanism at each stage of the procedure and provide a clear audit trail of the ingredients used and process followed.

3.9 Appropriate Facilities and Equipment

Consideration should be given to the appropriateness of the premises and the availability of equipment for extemporaneous preparation of medicines. There should be adequate bench space which is clean, orderly, clear of clutter and well lit. Only one product should be prepared at a time within the designated area to avoid mix-ups and/or cross contamination, and the finished product should be appropriately stored before being supplied to the patient. The necessary resources needed to carry out extemporaneous dispensing should also be accessible in the pharmacy.

All equipment should be appropriately stored, handled, maintained and calibrated. In particular, it is necessary that weights are calibrated on a regular basis to ensure that they are accurate as this can be a source of error. It is important that equipment is cleaned before and after each use. Consideration should also be given to the type of container used to supply the finished product, for example how it may affect the product's stability and use.

PSI *Guidelines on the Equipment Requirements of a Retail Pharmacy Business* provides further guidance on the requirements for extemporaneous dispensing; it is recommended that this document is read in conjunction with this guidance.

Staffing levels available at the time the medicine is being prepared should also be taken into consideration, in order that the required level of concentration, and time to complete the necessary records, can be dedicated to the process.

3.10 Quality Control

The European legislation, outlined in Appendix 1, applies significant requirements to products prepared in a pharmacy setting from the point of view of the testing of these products, in the process of quality control.

The European Pharmacopoeia monograph on Pharmaceutical Preparations specifies the necessity for tests to be applied to particular dosage forms, as described in their respective dosage form monographs, which are also applicable in the case of extemporaneously prepared products. The requirements on testing in the European Pharmacopeia monograph deal with the appearance of products, identity and purity tests, uniformity and reference standards.

The extent of quality control applied to a product should be proportionate with the level of risk the finished product could pose to the patient and should be judged on a case by case basis. Consideration should be given to the individual patient's age and condition, whether the product will be ingested or used topically, as well as the potency of, and risk posed by, the active substances and/or excipients. Where it is not practical to carry out this testing (e.g. due to the batch size, urgency, etc.), other suitable methods should be implemented to ensure that the appropriate quality is achieved, in accordance with the risk assessment carried out. At a minimum, the starting materials and finished product should be examined visually before supply to a patient.

4. Education and Training

The superintendent and supervising pharmacist must ensure that all staff involved in providing this service are appropriately trained. All training should be appropriately documented.

Pharmacists should self-assess their training and Continuing Professional Development (CPD) needs in the area of extemporaneous dispensing and monitor their competence from the perspective of their evolving practice requirements. Pharmacists should also be mindful that they may need to refresh their knowledge, if there is a considerable time lag between episodes of using these skills.

5. Policies and Procedures

Superintendent and supervising pharmacists should ensure that there are written policies and procedures in place to address all aspects of the provision of this service. This will help to ensure that products are consistently prepared to appropriate quality standards. All pharmacy staff should be familiar with these policies and trained on the procedures relevant to their role, and records of such training maintained. The policies and procedures should be regularly reviewed to ensure they are fit for purpose and in compliance with best practice.

Any errors or near misses which occur when extemporaneously preparing medicines should be formally documented. It is important to review and reflect on all errors or near misses, and in light of this retrain staff members and amend the pharmacy's policies and procedures, as appropriate, to decrease the possibility of a similar incident happening again.

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1	June 2015

6. Self-assessment Checklist

This self-assessment checklist is a practical tool intended to aid compliance with this guidance and to assist superintendent and supervising pharmacists in drawing up the relevant policies and SOPs. The checklist captures many important elements of the guidance; it is not exhaustive and should only be used to assess pharmacy practice in combination with this guidance and all other relevant guidance and requirements.

Ask Yourself	Yes	No	N/A	Required Action
Are authorised products supplied to patients where available?				
Are all pharmacists aware of the limited circumstances when it is legally permitted to extemporaneously prepare a medicinal product?				
Is the prescriber contacted to discuss the supply of an extemporaneously prepared medicinal product and any potential alternatives in order to ensure that the patient is receiving the best possible care?				
Is the patient and/or their carer always informed that a medicinal product has been extemporaneously prepared prior to supply?				
Is a product only extemporaneously prepared when it is not possible to procure it through another appropriate route (as outlined in the Decision Tree) and when it is in the best interest of the patient?				
Is a risk assessment carried out prior to extemporaneously preparing a medicinal product?				
Before extemporaneously preparing a medicinal product, is the pharmacist satisfied that they have the appropriate skills and equipment to prepare the product safely and to the appropriate standard?				

Ask Yourself	Yes	No	N/A	Required Action
Is the pharmacist satisfied that the formulation and preparation technique used is correct and evidence based, where possible?				
Are all calculations used in the preparation of a medicinal product double checked by an appropriately trained member of staff, where possible?				
Are all extemporaneously prepared products appropriately labelled?				
Is an appropriate expiry date included on the label of the product?				
Is a clear record for each extemporaneously prepared medicinal product made?				
Are there appropriate quality control procedures applied to each product prepared?				
Are there written policies and procedures in place for all aspects of this service?				
Is the superintendent and supervising pharmacist satisfied that all pharmacists practising in the pharmacy, and relevant staff members, are trained on, and following, the policies and procedures?				

Appendix 1

The Implications for extemporaneous dispensing should also be considered in light of the following:

(i) The Council of Europe adoption of the Resolution CM/ResAP(2011)1, on quality and safety assurance requirements for medicinal products prepared in pharmacies for the special needs of patients.

This considers the following important issues:

- the added value of pharmacy preparations and the responsibilities of healthcare professionals
- the preparation process (including a model procedure for risk assessment of the preparation based on a 'decision matrix')
- product dossiers (including quality control and stability testing)
- compliance with pharmacopoeial requirements
- labelling of extemporaneously prepared medicines
- communication and information for patients and their carers

The full document is available at - https://wcd.coe.int/ViewDoc.jsp?id=1734101&Site=CM

(ii) The European Pharmacopoeia Monograph entitled 'Pharmaceutical Preparations' (Monograph No: 2619 contained in Supplement 7.7 of the European Pharmacopoeia).

This applies to all pharmaceutical preparations including to the extent that it is practical, those medicinal products that are prepared extemporaneously.

In the case of unlicensed pharmaceutical preparations (which includes those that are prepared extemporaneously), it is recognised in the monograph that all health professionals involved, including the prescriber and the dispensing pharmacist, have, within their areas of responsibility, a duty of care to the patient receiving these pharmaceutical preparations.

Specific reference is made to the need for a suitable level of risk assessment to be undertaken whenever the supply of an unlicensed pharmaceutical preparation is contemplated. It is pointed out that the risk assessment is to identify:

- the importance of different parameters (e.g. quality of active substances, excipients and containers; design of the preparation process; extent and significance of testing; stability of the preparation); and
- the risk that the preparation may present to the particular patient or patient group.

Compliance with the pharmacopoeial standards and requirements as set out in the monograph has been mandatory since the 1st April 2013.

(iii) The dependence of certain of the exemptions included in the Medicinal Products (Control of Placing on the Market) Regulations 2007 (S.I. No. 540 of 2007) on the requirement that such "extemporaneously prepared" products be prepared in accordance with the prescriptions of a Pharmacopoeia, which in Ireland is the European Pharmacopoeia.