Labelling & Packaging of Unlicensed Medicines (Specials):
Best Practice Guidance for the NHS (December 2021)

Report from a Short Life Working Group Chaired by the Head of Patient Safety (Advice & Guidance) NHS England and NHS Improvement. (for membership, see appendix 2)

Background

Medication errors account for approximately 10% of all incidents reported to the National Reporting & Learning System.[1] These errors include when medicines have similar-looking or similar-sounding names, and/or have shared features of product packaging.[2] These 'wrong drug' errors, known as look-alike/sound-alike (LASA) errors, make up a high proportion of all medication errors and represent a significant threat to patient safety.

This type of error can occur during prescribing, dispensing, supply, or administration of medicines and can lead to administration of the wrong medication with potentially fatal consequences.

Following two 'wrong drug' errors reported in 2020, and the subsequent publication of a National Patient Safety Alert,[3] NHS England and NHS Improvement (NHSE/I) committed to working with NHS and non-NHS manufacturers of Specials to agree guidance promoting best practice on the labelling and packaging of Specials.

For the purposes of this guidance, Specials are unlicensed medicines that are manufactured in MHRA-licensed Specials Manufacturing Units, at the request of an authorised healthcare professional. They are manufactured to meet the special clinical needs of patients, which cannot be met by an available UK-licensed medicine. Manufacture of Specials is allowed under the Human Medicines Regulations 2012 (see Supplementary Chapter V).[4] Although, if an appropriately licensed product becomes available, manufacture and use of the Special should cease.

There is an expectation that:

- NHS Manufacturing Units will adopt this guidance, to ensure that the labelling and packaging of Specials meets the requirements of the NHS
- NHS pharmacy procurement teams will use the guidance to support risk assessment when purchasing Specials
- Non-NHS manufacturers will consider how they can apply these principles of this guidance to further improve the labelling and packaging of their products.

Whilst improvements can be made to the packaging and labelling of medicines, it should be remembered that one of the underpinning principles of safe medicines use is that all staff must carefully read the label before the supply, dispensing or administration of any medicine; adoption of this guidance will however further support staff, and will help to reduce errors and improve patient safety.

In addition, healthcare organisations and individual healthcare staff involved in the administration of medicines, need to be mindful of the recommendations set out in the Royal

Pharmaceutical Society / Royal College of Nursing 'Professional Guidance on the Administration of Medicines in Healthcare Settings'[5] – including:

11. The organisation has a procedure to minimise the risks associated with the handling or administration of medicines.

13. Sufficient information about the medicine is available to enable identification and correct use of the medicine.

14. Before administration, the person administering the medicine must have an overall understanding of the medicine being administered and seeks advice, if necessary, from a prescriber or a pharmacy professional.

15. The organisation's administration procedure is followed. This may include, but is not limited to, checking the following:

15.6 The identity of the medicine (or medical gas) and its expiry date (where available)

16. A risk assessment informs organisational policies/procedures for second signatories, witness requirements, and delegating.

Organisations should consider how these recommendations specifically apply to Specials.

Purchasing for Safety

The Department of Health report, "Building a Safer NHS for Patients"[6] recommended that consideration of patient safety was built into NHS purchasing policy and processes and that input from the world of design was sought to identify new opportunities for facilitating the safer use of medicines. In this process, medicinal products are reviewed by purchasing and pharmacy groups and products that are designed in such a way as to promote safer practice are selected in preference to others wherever possible.

This guidance should be used by Pharmacy procurement teams to support an overall 'purchasing for safety' policy; especially when purchasing Specials from NHS and non-NHS manufacturers. The Royal Pharmaceutical Society's 'Professional Guidance for the Procurement and Supply of Specials'[7] clearly states that 'a product specification defines the quality requirements of the purchaser (acting on behalf of the prescriber) and should be agreed with the supplier. The product specification is the document against which the purchaser should be able to hold the manufacturer accountable for the quality of the medicine. The RPS guidance states that the product specification should include 'how the product should be labelled, packaged and stored'.

This guidance will support purchasers to stipulate how they expect Specials to be labelled and packaged. To ensure consistency, this is best undertaken collaboratively, at a regional or national level, to avoid manufacturers being overwhelmed by individual requests. See Appendix 1 for more information on purchasing for safety.

An effective purchasing for safety strategy and process requires close collaboration between all members of the pharmacy team at local and national levels (including Procurement,

Quality Assurance, Technical Services, Medicines Information & Clinical Services) and joint working with medicines manufactures and regulators.

Labelling & Packaging of Unlicensed 'Specials' Medicines – Short Life Working Group

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Recommended Standards	
GENERAL	
British Pharmacopoeia Guidance	The following requirements are set out in the British Pharmacopoeia and are applicable to unlicensed medicines manufactured or prepared in accordance with medicines legislation. Critical items of information, which should be located together on the pack and appear in the same field of view, are: name, strength, route of administration, dosage and warnings (highlighted in bold) 1. **The international non-proprietary name (INN) as approved by WHO (where relevant) or common name of the product**. 2. **A statement of the active ingredients expressed qualitatively and quantitatively per dosage unit or for a given volume or weight**. 3. **Intended route of administration**. 4. **Instructions for use, including any special warnings**. 5. The pharmaceutical form. 6. The contents of the container by weight, volume or by number of doses. 7. Excipients of known effect. For injectable, topical (including inhalation products) and ophthalmic medicines, all excipients. 8. **'Keep out of reach and sight of children'.** [Note 1] 9. The expiry date expressed in unambiguous terms (dd/mm/yy). 10. Any special storage precautions. 11. The manufacturer's MS number, where appropriate. 12. The manufacturer's name and address. 13. The batch number. **14. Statutory warnings required by The Human Medicines Regulations 2012 for particular actives, e.g. paracetamol (Schedule 25, Part 4 of the 2012 Regulations).** Note 1: This is a statutory requirement for relevant medicinal products.

	For small containers certain details may be omitted, but the label should contain, as a minimum, the following information: **1. The common name of the product** **2. A statement of the active ingredients expressed qualitatively and quantitatively per dosage unit or for a given volume or weight.** 3. **Intended route of administration.** 6. The contents of the container by weight, volume or by number of doses. 9. The expiry date expressed in unambiguous terms (dd/mm/yy). 13. The batch number. In such cases, the label for the outer packaging should contain all the relevant label information. See also MHRA 'Best practice guidance on the labelling and packaging of medicines'.[8]
User Testing	Specials manufacturers should develop their own methods for testing their packaging/labelling on users.

PACKAGING	
Selection	Manufacturers should consider the type of packaging used to ensure, where possible: • use of different containers for medicines administered via different routes of administration to avoid confusion eg medicines for internal and external use should not be in identical or look-alike containers • packaging is 'robot friendly' (see below). • labelling requirements, set out below, can be accommodated on the packaging chosen. **Robot Friendly**: Where possible, products must be packaged in containers that are suitable for use within an automated dispensing system; if primary packaging is not suitable then consideration should be given to using secondary packaging to allow products to be safely loaded into, stored in, and dispensed by an automated dispensing system without risk of breakage or spillage. Outer packaging must be sealed; to avoid problems when placed in an automated dispensing system. If the product needs to be opened on receipt, then organisations should reseal the product so that it can be stored in an automated dispensing system. If asked, manufacturers should be able to explicitly state if their product is either considered suitable for storage in an automated dispensing system or it is not; so that mitigating actions can be taken by the purchaser.

LABELLING	
General	In addition to the specific labeling requirements set out in the British Pharmacopoeia, manufacturers should: • Choose a clear, easy-to-read font, such as a sans-serif typeface e.g. Arial, Helvetica or Univers. • Consider the value of selective use of colour (see below). • Ensure the choice of font size indicates the importance of the information. ▪ Use as large a font size as possible, that does not result in overcrowding of information. ▪ The most important information on the label should be in the largest font size eg generic name. ▪ Consider the hierarchy of information and make sure that the most important information stands out more clearly than the rest. • Ensure products supplied have a sufficient space to apply a dispensing label if required. • Use HSE-approved Hazard pictograms (symbols) where appropriate. • Avoid use of abbreviations where possible eg 'micrograms' should be spelt out in full. • The agreed EAN linear (or 2-D) barcode should be present on secondary packaging (and on primary packaging wherever possible).
Specific Considerations	**Drug Concentrations**: • Express the strength as quantity per unit volume (eg mg/ml), with additional reference to total quantity in total volume. This is particularly important for injectable products and other medicines available in solution or suspension, even if other units of concentration such as percentage and ratios are also present. This should be emphasised for single-dose containers. • Where the strength of the medicine is expressed in mmol, it should be represented as mmol/container volume as well as mmol/mL or mmol/unit volume. • Care to be taken with the spacing between mg and mL. Adjust the spacing to leave sufficient space around the '/' to achieve maximum legibility. • When using numbers of 1,000 and above use commas to help prevent misreading. • Where possible, always use whole numbers.

	• Do not use trailing zeros: 2mg NOT 2.0mg • Do not use values of <1 unit of measure: 100mg NOT 0.1g. • Different strengths of the same medicine should be expressed in the same way, such as 250mg, 500mg, 750mg, 1,000mg – NOT 1g. **Routes of Admin**: • Make positive statements: use 'do's', rather than 'do not's' (e.g. "For Intravenous Administration" rather than "Not for Intrathecal Administration"). • Non-standard routes of administration should be stated in full. • Use specific directions and avoid using technical terms that are not well understood, e.g. "For Injection or Infusion'' NOT "For Parenteral Use". • Use the phrase 'For external use only' within a rectangle if the product is an embrocation, liniment, lotion, liquid antiseptic or other liquid preparation or gel and is for external use only. • Highlight the route of administration, particularly if it is different to the norm. **Further Dilution**: Concentrated products that require further dilution before administration represent a higher risk. • Use clear warnings that are visibly differentiated to indicate that the product is a concentrate and requires further dilution) • Highlight the fact that the medicine requires dilution. • State a minimum dilution volume where appropriate. • Where appropriate, healthcare organisations should consider providing additional locally generated information, either electronically or paper-based, on how to use products; especially those that staff may be unfamiliar with or are complex to prepare/administer. The information should be available at the point of preparation/administration.

	Expiry Dates: • Print data in an unambiguous format and clearly identifiable location, at the end of bulk text; preferably near to batch number. • Where possible, display a specific expiry date. Where this is not possible, the explanatory text should say 'use before' for clarity eg 'Use before April 2022' – meaning the product would expire on 31 March 2022.
Positioning of Labels	To avoid potential confusion between products; critical information should be visible on as many sides of a product's packaging as possible: • Manufacturers should make every effort to ensure critical information is in the same field of vision on at least three, non-opposing faces of the secondary packaging. This means putting the information on the top or bottom face, one of the side faces, and on one of the end faces. • Critical information is defined as, at least, that stipulated by the British Pharmacopoeia (see above) . • The text on every face, excluding the ends, should be orientated in the same direction and in the same order.
Considerations for Differentiation	According to cognitive theory of visual searching, similarity between the desired selection (target) and other items (non-targets) increases the difficulty of the search.[2] It is therefore beneficial to enhance certain properties of a medication to distinguish it from other products with similar names and/or packaging, so-called feature-based processing. Examples of how certain features can be enhanced includes; • Font size / style – including bolding, initialising and use of uppercase lettering. • Colour. • Tall Man lettering. Or a combination of the above. **Font**: • The use of typeface, type weight, and shape to make medicine strengths stand out; this is particularly important if all secondary packaging from a manufacturer looks similar. • Use of bold or semi-bold type, and avoid lightweight type. • Inverting the key information text to draw the eye to it eg white text on a black background.

	Colour: Colour coding is not recommended however **judicious use of colour to aid differentiation** is the recommended method to help to minimise selection errors. It uses colour to make features on a medicine pack stand out or to help distinguish one item from another. The chosen colour is not associated with a particular feature. It is important that there is no pattern in the colour scheme. The only exception to this is when the medicine aligns to the critical care syringe labelling guidelines[9]; in such circumstances consider whether the colour used should match with the recommendations in the guidelines. Innovative pack design that may incorporate the judicious use of colour is to be encouraged to ensure accurate identification of the medicine. Consider: • Use of colour to highlight key differences in information: the drug name, the quantity or concentration. • Use of opposing colour to distinguish between, for example, different strengths of the same medicine and between similarly named medicines. • Applying the colour scheme consistently throughout the primary and secondary packaging. • Need to develop an awareness of users with limited colour perception. • Ensuring adequate contrast between text and background. • Using a strong contrast between the type and background colours. Dark coloured type (e.g. black, dark blue) should be on a light-coloured background (e.g. white, pale pink, pale yellow). **Tall Man Lettering**: The use of Tall Man lettering has been adopted by many countries[10,11,12] and in specific instances in the UK eg cephalosporins.[8] The efficacy of Tall Man lettering has recently been evaluated and found to be a marginally effective intervention to reduce LASA error.[13] • Consider use of Tall Man (capital) letters to highlight specific sections of similar medicine names. The choice of which letters to capitalised should be carefully considered to highlight the differences.

Container Specific Information	
Ampoules	• Print the medicine name longitudinally, along the length of the ampoule. • Do not use transparent labels. • Use as large a label as possible, ensuring an area is left label-free to allow for inspection of contents.
Vials	• If the width of the vial is less than the height of the label, then orientate the text longitudinally • Match the design of the vial label to that of the carton. • Where the flip cap and label are coloured, the cap should use the predominant differentiating colour used on the label and carton.
Prefilled Syringes	• Label outer packaging of multipacks as well as syringes themselves • Ensure that an area of clear space is left to allow for inspection of contents. • Volume markings should always be visible and not covered by labels. • Consider the use of different coloured components, for example, plungers or caps, to emphasise differences. • Orientate text along the length of the syringe.
Infusion Bags	• Key information should always be clearly readable, including when the bag is hanging for use. • Consider appropriate areas for the placement of key information. Options may be towards the bottom or down the side of the bag. • Give emphasis to the volume of the infusion, and position it next to the infusion name • When listing ingredients on infusion bags, the strength should be represented as quantity per container. • Epidural and intrathecal injections are normally associated with the colour yellow. Consider incorporating this colour into the packaging. • If printing directly onto the infusion bag, readability on the filled final container, after sterilisation (if appropriate), must be considered. • Consider use of additional labels on overwraps as a means of further emphasising key information. • Be aware of the importance of label design for outer packaging. Poor labelling of cartons is a recognised source of selection errors in clinical areas.

Note: NHS England has published the first set of product specifications to support the production and supply of ready-made chemotherapy medicines.[14]

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Appendix 1 Purchasing for Safety

As part of an overall 'purchasing for safety' policy, NHS organisations should consider;

- **Risk assessment**
  - Risk assessment is at the core of any purchasing for safety policy and should be undertaken by staff with a full understanding of the purpose and end use of the product being procured. Risks should be identified and minimised, reporting systems should be available and acted upon. If a product is assessed locally as a high risk of causing a patient safety incident this should be reported to regional Quality Assurance (QA) and procurement specialists. These lists can then form the basis of discussion with the manufacturers about possible changes in presentation.
  - Whilst products supplied by manufacturers will generally meet the requirements for their intended use, there may be occasions that specific clinical areas or specific patients may require specific packaging or labelling. After completion of the risk assessment, if specific changes in packaging or labelling are deemed necessary (e.g. braille, large print labels etc.), then engagement with the manufacturer as soon as possible to seek potential alterations is advised.

- **Packaging**
  - Does the product packaging meet your requirements for use in pharmacy automated dispensing systems and/or ward-based automated medicines cabinets? If not, engage with the manufacturer and seek improvements or purchase from an alternative manufacturer where possible. Use of automated systems significantly reduces the risk of incorrect selection of products.
  - Is the packaging of the product distinct from other products currently purchased? If there is a risk of confusion between products from the same or different manufacturers, then either engage with the manufacturer to make necessary changes or seek to purchase from an alternative manufacturer where possible.
  - Ensure products purchased meet the specific principles for packaging set out in this guidance.

- **Labelling**
  - Is the labelling of the product distinct from other products currently purchased? If there is a risk of confusion between products from the same or different manufacturers, then either engage with the manufacturer to make necessary changes or seek to purchase from an alternative manufacturer where possible.
  - Ensure products purchased meet the specific principles for labelling set out in this guidance.

Appendix 2 Membership of Short Life Working Group

Graeme Kirkpatrick (Chair)	National Patient Safety Team: NHSE/I
Tim Root (Deputy Chair)	Specialist Pharmacy Service
Christine Alexander	NHSS Pharmaceutical 'Specials' Service
Jonathan Back	Healthcare Safety Investigation Branch
Ravinder Bratch	Chartered Institute of Ergonomics & Human Factors
Adrian Evans	MHRA: IE&S
Mark Jackson	NHS Pharmaceutical Quality Assurance Committee
Yogini Jani	UCL Centre for Medicines Optimisation Research & Education Chair – Safer Use of Medicines Group, RPS Science & Research Committee
John Landers	NHS Pharmaceutical Aseptic Services Group
Pauline Lockey	National Patient Safety Team: NHSE/I
Jan MacDonald	MHRA: VRMM
Baxter Millar	NHSS Pharmaceutical 'Specials' Service
Andrew Myers	Huddersfield Pharmacy Specials
Jeff Rothwell	Association of Pharmaceutical Specials Manufacturers
Cindy Taplin	National Patient Safety Team: NHSE/I
Nicola Wake	Specialist Pharmacy Service